Tab Name: 1 Site Visit Logs

conformal™ The Shape of Stroke Prevention	Title:	Document No.
	Site Visit Log	**F-045**
	Page 1 of 1	**Revision C**

Study	Site Number	Site Name	Principal Investigator

Visit Date (DD-MON-YYYY)	Visit Purpose (SIV, IMV, COV, Other)	Sponsor Representative	Signature of Sponsor Representative	Signature of Site Representative

Log Page ____ of ____

conformal™ The Shape of Stroke Prevention	Title:	Document No.
	Site Visit Log	**F-045**
	Page 1 of 1	**Revision C**

Study	Site Number	Site Name	Principal Investigator

Visit Date (DD-MON-YYYY)	Visit Purpose (SIV, IMV, COV, Other)	Sponsor Representative	Signature of Sponsor Representative	Signature of Site Representative

Log Page ____ of ____

conformal™ The Shape of Stroke Prevention	Title:	Document No.
	Site Visit Log	**F-045**
	Page 1 of 1	**Revision C**

Study	Site Number	Site Name	Principal Investigator

Visit Date (DD-MON-YYYY)	Visit Purpose (SIV, IMV, COV, Other)	Sponsor Representative	Signature of Sponsor Representative	Signature of Site Representative

Log Page ____ of ____

conformal™ The Shape of Stroke Prevention	Title:	Document No.
	Site Visit Log	**F-045**
	Page 1 of 1	**Revision C**

Study	Site Number	Site Name	Principal Investigator

Visit Date (DD-MON-YYYY)	Visit Purpose (SIV, IMV, COV, Other)	Sponsor Representative	Signature of Sponsor Representative	Signature of Site Representative

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Tab Name: 2 Delegation of Authority Logs

conformal™ The Shape of Stroke Prevention	Title:	Document No.
	Delegation of Authority Log	**F-041**
	Page 1 of 1	Revision G

Study	Site Number	Site Name	Principal Investigator

Electronic Records Statement: My electronic signature as it applies to entering electronic data or signing records, including on Sponsor-owned or Sponsor-outsourced electronic systems, is the legally binding equivalent of my handwritten signature. I will not share password(s) assigned to me for this study with any other person.

By signing this form, you are acknowledging and in agreement with the above Electronic Records Statement.

Staff Member Name	Role	Delegated Tasks (See table below)	Staff Member Signature	Initials	Study Dates	PI Initials	PI Approval Date DD/MMM/YYYY
	☐ Principal Investigator ☐ Sub/Co-Investigator ☐ Study Coordinator ☐ Lead Echocardiographer ☐ Other (please specify): ___________________				Start Date:		
					End Date:		
	☐ Principal Investigator ☐ Sub/Co-Investigator ☐ Study Coordinator ☐ Lead Echocardiographer ☐ Other (please specify): ___________________				Start Date:		
					End Date:		
	☐ Principal Investigator ☐ Sub/Co-Investigator ☐ Study Coordinator ☐ Lead Echocardiographer ☐ Other (please specify): ___________________				Start Date:		
					End Date:		
	☐ Principal Investigator ☐ Sub/Co-Investigator ☐ Study Coordinator ☐ Lead Echocardiographer ☐ Other (please specify): ___________________				Start Date:		
					End Date:		

Task Codes

1. Eligibility assessment	6. EDC access (eCRF completion, correction, queries)	11. Perform NIHSS or mRS assessments
2. Informed consent administration	7. eCRF sign off (EDC)	12. Other:____________________
3. Perform CLAAS procedure	8. Maintain regulatory binder	13. Other:____________________
4. Perform study assessments	9. Device accountability/return	14. Other:____________________
5. Documentation of source data	10. Perform imaging protocol	15. Other:____________________

Study	Site Number	Site Name	Principal Investigator

Electronic Records Statement: My electronic signature as it applies to entering electronic data or signing records, including on Sponsor-owned or Sponsor-outsourced electronic systems, is the legally binding equivalent of my handwritten signature. I will not share password(s) assigned to me for this study with any other person.

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Study	Site Number	Site Name	Principal Investigator

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Study	Site Number	Site Name	Principal Investigator

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					End Date:		
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					End Date:		
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					End Date:		
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					End Date:		

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3. Perform CLAAS procedure	8. Maintain regulatory binder	13. Other:____________________
4. Perform study assessments	9. Device accountability/return	14. Other:____________________
5. Documentation of source data	10. Perform imaging protocol	15. Other:____________________

Tab Name: 3 Site Training Records

Conformal Medical, Inc.
15 Trafalgar Square, Ste. 101
Nashua, NH 03063

CONFORM Protocol Clarification Memo #7

Date: March 12, 2024
Study: CONFORM Pivotal Trial

TOPIC: Echocardiographer DOA Requirements and Training Requirements

This memo clarifies the DOA requirements for the Echocardiographer effective as of March 04, 2024.

Investigational Sites may delegate one echocardiographer on the Delegation of Authority Log to assume the responsibility of Imaging in the CONFORM Pivotal Trial. The Echocardiographer assuming the responsibility on the DOA, must be a qualified physician to perform imaging and cannot be the Principal Investigator.

Training shall be conducted for all imaging personnel: Protocol Synopsis, Imaging Protocol(s), GCP certificate or any other documentation deemed necessary for study conduct. Training logs for all imaging personnel shall be collected and maintained in the Investigational Site File/Regulatory Binder.

Aly Dechert
Clinical Trial Manager
Phone: 708-218-1292
Email: adechert@conformalmedical.com

CC: Karis Oasan, Director, Clinical Operations
Master study files

conformal™ The Shape of Stroke Prevention	Title:	Document No.
	Clinical Training Log	**F-046**
	Page 1 of 1	**Revision C**

Date of Training (DD-MMM-YYYY)	**Study Name**	**Site Number**	**Site Name**	☐ N/A – Not Site Specific

Trainer Name:		**Trainer Signature:**	☐ N/A – Self Train
Print Trainee Name (First, Last)	**Trainee Study Role**	**Trainee Signature**	**Date** DD-MMM-YYYY

Document Name *List all documents/items used to train*	**Version, Version Date** *If applicable*

Parent Doc: SOP-042

conformal™ The Shape of Stroke Prevention	Title:	Document No.
	Clinical Training Log	**F-046**
	Page 1 of 1	**Revision C**

Date of Training (DD-MMM-YYYY)	**Study Name**	**Site Number**	**Site Name**	☐ N/A – Not Site Specific

Trainer Name:		**Trainer Signature:**	☐ N/A – Self Train
Print Trainee Name (First, Last)	**Trainee Study Role**	**Trainee Signature**	**Date** DD-MMM-YYYY

Document Name *List all documents/items used to train*	**Version, Version Date** *If applicable*

Parent Doc: SOP-042

conformal™ The Shape of Stroke Prevention	Title:	Document No.
	Clinical Training Log	**F-046**
	Page 1 of 1	**Revision C**

Date of Training (DD-MMM-YYYY)	**Study Name**	**Site Number**	**Site Name**	☐ N/A – Not Site Specific

Trainer Name:		**Trainer Signature:**	☐ N/A – Self Train
Print Trainee Name (First, Last)	**Trainee Study Role**	**Trainee Signature**	**Date** DD-MMM-YYYY

Document Name *List all documents/items used to train*	**Version, Version Date** *If applicable*

Parent Doc: SOP-042

Tab Name: 4 Study Personnel Documents

No documents behind this tab

Tab Name: 5 Protocol

2.3 Investigator Signature Page

Study title: The CONFORM Pivotal Trial

An evaluation of the safety and effectiveness of the CLAAS System for Left Atrial Appendage Occlusion

Protocol version: K

2.4 Investigator's Responsibility

As the site Principal Investigator, I understand that I must obtain written approval from my Institutional Review Board prior to participation in the trial. This approval must include my name and a copy must be provided to Conformal Medical (or designee), along with the approved Patient Informed Consent Form prior to the first enrollment at my study site.

As the site Principal Investigator, I must also:

1. Conduct the study in accordance with the study protocol, the signed Clinical Trial Agreement, applicable laws, 21 CFR Part 812 and other applicable United States Food and Drug Administration (FDA) regulations, any conditions of approval imposed by the FDA (and/or other regulatory bodies) or IRB/REB/EC, International Conference on Harmonization (ICH) Good Clinical Practice guidelines, and the Declaration of Helsinki, and ensure that all study personnel are appropriately trained prior to any study activities.
2. Ensure that the study is not commenced until all approvals have been obtained.
3. Supervise all use of the Conformal CLAAS System at my institution.
4. Ensure that written informed consent is obtained from each subject prior to any data collection and any study-specific procedures or assessments, using the most recent IRB/REB/EC approved Informed Consent Form.
5. Provide all required data and reports and agree to source document verification of study data with patient's medical records by Conformal Medical (or designee) and any regulatory authorities.
6. Allow Conformal Medical personnel or its designees, as well as regulatory representatives, to inspect and copy any documents pertaining to this clinical investigation according to national data protection laws.

2.5 Investigator Signature

Protocol Version: K

I have read and understand the contents of this Clinical Investigation Plan and agree to abide by the requirements set forth in this document.

Investigator Name (print)	Investigative Site (print)
Investigator Signature	Date

The CONFORM Pivotal Trial

An Evaluation of the Safety and Effectiveness of the Conformal CLAAS System for Left Atrial Appendage Occlusion

Clinical Investigation Plan

Protocol #21-101

Revision K

Version Date: December 17, 2024

NCT: 05147792 (Pivotal Phase)

NCT: 06049615 (Conscious Sedation Sub-Study)

Sponsor: Conformal Medical, Inc.
15 Trafalgar Square, Ste. 101
Nashua, NH 03063

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Table of Contents

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1 Acronyms

Acronym	Definition
ACT	activated clotting time
ADE	adverse device effect
AE	adverse event
AF	atrial fibrillation
ASA	acetylsalicylic acid (aspirin)
ASADE	anticipated serious adverse device effect
ASD	atrial septal defect
BARC	Bleeding Academic Research Consortium
CEC	clinical events committee
CI	confidence interval
CIP	clinical investigation plan
CRF	case report form
CT	computed tomography
DAPT	dual antiplatelet therapy
DFU	Directions for Use
DICOM	Digital Imaging and Communications in Medicine
DOAC	Direct Oral Anticoagulants
DRT	Device Related Thrombus
DSMB	data safety monitoring board
EC	ethics committee
ECG	electrocardiogram
eCRF	electronic case report form
EDC	electronic data capture (system)
EFS	early feasibility study
eGFR	estimated glomerular filtration rate
ePTFE	Expanded polytetrafluoroethylene
EU/EEA	European Union/European Economic Area
F/U	Follow-up
Fr	French (catheter scale system)
FDA	U.S. Food and Drug Administration
GCP	good clinical practice
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICF	Informed Consent Form
ICH	International Conference on Harmonization

Acronym	Definition
IFU	instructions for use
INR	international normalized ratio
IP	implanted patient population
IRB	institutional review board
ISO	International Organization for Standardization
ITT	intention to treat
LAA	left atrial appendage
LAAC	left atrial appendage closure
LAAO	left atrial appendage occlusion
LVEF	left ventricular ejection fraction
MedDRA	Medical dictionary for regulatory activities
MI	myocardial infarction
MRI	magnetic resonance imaging
NeuroARC	Neurologic Academic Research Consortium
NYHA	New York Heart Association
OAC	Oral Anticoagulant (Coumadin/Warfarin or DOAC)
PFO	patent foramen ovale
PI	principal investigator
QD	quaque die (daily)
QVSFS	questionnaire for verifying stroke-free status
REB	Research Ethics Board
RIC	Roll-In Cohort
SADE	serious adverse device effect
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SOC	Standard of Care
SOP	standard operating procedures
TBD	to be determined
TEE	transesophageal echocardiography
TIA	transient ischemic attack
TSP	Transseptal Puncture Access
TTE	trans-thoracic echocardiography
UADE	unanticipated adverse device effect
US	United States
VARC	Valve Academic Research Consortium

2 Document Control

2.1 Revision History

Version (Date)	Protocol Section Modified	Summary of Changes	Justification for Modification
A 22-Dec-2021	N/A	Initial Release	Initial Release
B 22-Jun-2022	Multiple	Refer to document no. C-15, *CONFORM Protocol - Summary of Changes*	Address FDA study design considerations and CMS recommendations
C 12-Apr-2023	Multiple	Refer to document no. C-15, *CONFORM Protocol - Summary of Changes*	Address FDA study design considerations Edits for clarification
D 15-Aug-2023	Multiple	Refer to document no. C-15, *CONFORM Protocol - Summary of Changes*	Addition of EU and Central Asia sites Edits for clarification
E 01-Nov-2023	7.5	Refer to document no. C-13, *CONFORM Protocol - Summary of Changes*	Addition of CONTROL Device
F 29-Nov-2023	Multiple	Refer to document no. C-13, *CONFORM Protocol - Summary of Changes*	Address EU MDR clinical investigational protocol requirements Edits for clarification
G 05-Mar-2024	Multiple	Refer to document no. C-13, *CONFORM Protocol – Summary of Changes*	Update study design and safety considerations Edits for clarification
H 11-Mar-2024	Multiple	Refer to document no. C-13, *CONFORM Protocol – Summary of Changes*	Added language regarding VizaraMed Multiflex Steerable Sheath Edits for clarification
J 11-Sept-2024	Multiple	Refer to document no. C-13, *CONFORM Protocol – Summary of Changes*	Update to procedures and assessments Edits for clarification
J.1 1-Nov-2024	Multiple	Refer to document no. C-13, *CONFORM Protocol – Summary of Changes*	Edits for clarification
K 17-Dec-2024	Multiple	Refer to document no. C-13, *CONFORM Protocol – Summary of Changes*	Edits for clarification

2.2 Protocol Approval Page

Study title:	The CONFORM Pivotal Trial An evaluation of the safety and effectiveness of the CLAAS System for Left Atrial Appendage Occlusion
Protocol version:	K

Coordinating Principal Investigator — Date

William A. Gray, MD

Principal Investigator

Lankenau Medical Center

Coordinating Principal Investigator — Date

Shephal Doshi, MD

Principal Investigator

Pacific Heart Institute

Date

Ken Malomo

Director, Clinical Operations

Conformal Medical, Inc.

2.3 Investigator Signature Page

Study title: The CONFORM Pivotal Trial

An evaluation of the safety and effectiveness of the CLAAS System for Left Atrial Appendage Occlusion

Protocol version: K

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2.5 Investigator Signature

Protocol Version: K

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Investigator Name (print)	Investigative Site (print)
Investigator Signature	Date

3 Study Contacts

Sponsor:	**Conformal Medical, Inc.** 15 Trafalgar Square, Ste. 101 Nashua, NH 03063 USA **Conformal Contact:** Ken Malomo Director, Clinical Operations Tel: 978.491.8774 email: kmalomo@conformalmedical.com
Authorized Representative for Conformal Medical in European Union:	**FGK Representative Service Ireland, Ltd**
Coordinating Principal Investigators:	**William A. Gray, MD** System Chief, Division of Cardiovascular Disease, Main Line Health and President, Lankenau Heart Institute Lankenau Medical Center 100 East Lancaster Avenue Suite 356 MOB East Wynnewood, PA 19096 USA grayw@mlhs.org Tel: (484) 476-1000 **Shephal K. Doshi, MD** Director, Cardiac Electrophysiology Services Providence St. John's Health Center / Pacific Heart Institute 2001 Santa Monica Blvd., #280W Santa Monica, CA 90404 skdoshi@pacificheart.com Tel: (310) 829-7678
Clinical Events Committee:	**NAMSA** 400 Highway 169 South, Suite 500 Minneapolis, MN 55426
Data Safety Monitoring Board:	**Yale University School of Medicine** 135 College Street, Suite 101 New Haven, CT 06510 USA
TEE and Echo Imaging Core Laboratories:	**Contact:** Alexandra Lansky, MD Director Tel: 203.737.2142 Fax: 203.737.7457

	email: alexandra.lansky@yale.edu
Cardiac CT Imaging Core Lab	Philipp Blanke MD St Paul's Hospital 081 Burrard Street Vancouver, BC, V6Z 1Y6 email: blanke@sphcorelab.com
Clinical Site Monitoring:	**Conformal Medical, Inc. or Designee**
Biostatistics	**NAMSA** 400 Highway 169 South, Suite 500 Minneapolis, MN 55426

4 Protocol Synopsis

Study Title	**The CONFORM Pivotal Trial**
Study Device	The Conformal CLAAS® Device is a permanent implant designed to occlude the left atrial appendage (LAA) to eliminate blood flow into and clot passage from the LAA. **Sizes**: Regular and Large to accommodate LAA Ostium Diameter size range of 10-40 mm **Delivery System**: CLAAS Delivery Catheter and Access Sheath available in either Single or Double Curves
Clinical Trial Intended Use	The CLAAS System is intended to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who: • Are at increased risk for stroke and systemic embolism based on CHADS2 or CHA2DS2-VASc scores and are recommended for oral anticoagulation (OAC) (Coumadin or DOAC) therapy; AND • Are deemed by their physician to be suitable for OAC; AND • Have an appropriate rationale to seek a non-pharmacological alternative to OAC, taking into account the safety and effectiveness of the device compared to OAC
Objective	**Objective 1:** To evaluate the safety and effectiveness of the CLAAS System by demonstrating non-inferiority to currently marketed Left Atrial Appendage Occlusion (LAAO) systems in subjects with non-valvular atrial fibrillation. **Objective 2**: To demonstrate the safety of a post procedure pharmacologic antiplatelet regimen that consists of DAPT alone without concomitant oral anticoagulation therapy (OAC). **Objective 3:** To demonstrate the ability to safely deliver the CLAAS Device using a conscious sedation protocol without general anesthesia. To investigate this objective, a separate Sub-Study will be conducted after recruitment of the Randomized Clinical Trial (RCT) is complete at select, qualified sites based on the experience demonstrated in the RCT. **Objective 4:** Support regulatory approval(s) in territories outside US.
Study Design	This is a pivotal clinical trial that includes three components: (1) Roll-In Phase using the CLAAS system alone (2) Randomized Clinical Trial (RCT) comparing CLAAS to commercially available LAAO systems. The RCT will be performed in a staged manner

	with no more than 250 subjects treated in the initial phase to support a safety summary on the first 50 CLAAS implants. Once approved by FDA, the RCT will advance to the second stage completing recruitment of the RCT cohort. (3) Conscious Sedation Single Arm Sub-study: A, single arm sub-study investigating the use of a conscious sedation protocol; conducted after enrollment in the RCT is complete and is listed under a separate NCT number within the clinicaltrials.gov website (NCT06049615). Appendix E provides a summary of the Sub-Study with statistical rationale.
Medicare Considerations	The study eligibility criteria include subjects that are largely identified in the Medicare population. As such, the randomized trial design is considered adequate to characterize the safety and effectiveness of the CLAAS System and will appropriately support the CMS criterion for coverage.
Sample Size	The sample size requirements for each of the study cohorts is listed below. **Roll-in Phase:** a maximum of 300 subjects can be enrolled as roll-in cases. **RCT Phase**: Up to one thousand six hundred (1600) subjects will be enrolled in the randomized control trial.
Randomization	Randomization will be 1:1 to CLAAS Device (Investigational) versus currently marketed LAAO device (Control) using block randomization that is stratified by site.
Investigational Sites	Up to one hundred (100) investigational sites in North America, five (5) sites in Japan, and up to ten (10) sites in EU/EEA and Central Asia will be included in this study. The United States will account for ≥ 50% of the total subjects enrolled in the RCT cohort. Further, no more than 15% of the maximum sample size for the randomized trial will be enrolled by a single site. An ongoing list of all investigational sites shall be maintained in Sponsor files
Study Duration/ Follow-up Period	The trial is expected to take approximately 3 years to enroll, and each subject will be followed for a total of 5 years.
Primary Safety Endpoint	A composite of:

	• Major Procedure-Related Complications including (identified within 12 months of procedure and adjudicated as procedure related): a) cardiac perforation b) pericardial effusion requiring drainage c) ischemic stroke d) device embolization e) major vascular complications • Major bleeding through 12 months post procedure or • All-cause death 12 months post procedure All definitions are provided for all components in Appendix A. All events will be adjudicated by the independent Clinical Events Committee (CEC).
Primary Effectiveness Endpoint	A composite of ischemic stroke and systemic embolism through 18 months.
Secondary Endpoints	**Secondary Safety Endpoints** 1. All-Cause Mortality (including cardiovascular) through 18 months 2. Myocardial infarction evaluated through 7 days post-procedure (See Appendix A for definition) 3. Neurologic Events including Stroke (ischemic and hemorrhagic) and TIA (See Appendix A for definition) 4. Bleeding complications (See Appendix A for definition) 5. Vascular complications classified as major/minor and access site/non-access site related (See Appendix A for definition) 6. Device and procedure-related serious adverse events: Summary of all CEC adjudicated adverse events attributed to the device and/or the procedure **Secondary Performance and Efficacy Endpoints Including (all definitions provided in Appendix A):** 1. Device Success 2. Technical success 3. Procedure success 4. Embolic Events 5. Closure Success at 12 months based upon each of the following criteria: a. demonstration of peri-device flow ≤5 mm b. demonstration of peri-device flow ≤3 mm **Secondary Effectiveness Endpoints with Statistical Hypothesis Testing** The following endpoints will have formal statistical hypothesis tests with a gatekeeping approach to control the Type 1 error rate. Each endpoint will

	be based on a comparison of the treatment and control arms and is described in detail in the Statistical Analysis Plan and Section 12 of the protocol. 1. **Non-inferior closure success (≤5mm) at 45 days**, defined as peri-device residual leak ≤5mm by TEE as evaluated by an independent core lab. A 3% margin will be used. 2. **Non-inferior closure success (≤3mm) at 45-days**, defined as peri-device residual leak ≤3mm on TEE as evaluated by an independent core lab. A 5% margin will be used. 3. **Non-inferior complete closure success at 45 days,** defined as lack of any detectable (>1mm) peri-device residual leak on TEE as evaluated by an independent core lab. A 5% margin will be used. 4. **Superior closure success at 45 days,** defined as peri-device residual leak ≤3mm based on TEE as evaluated by an independent core lab. 5. **Superior closure success at 45 days, device subgroup test:** CLAAS vs. specific control device: defined as lack of any detectable (>3mm) peri-device residual leak on TEE as evaluated by an independent core lab. Tests associated with this endpoint will be performed in descending order of specific control devices (device testing will be performed only for control devices that are used >20% of cases). 6. **Superior complete closure success at 45 days,** defined as lack of any detectable (>3mm) peri-device residual leak on TEE as evaluated by an independent core lab. 7. **Superior closure success at 45 days, device subgroup test:** CLAAS vs. specific control device: defined as lack of any detectable (>1mm) peri-device residual leak on TEE as evaluated by an independent core lab. Tests associated with this endpoint will be performed in descending order of specific control devices (device testing will be performed only for control devices that are used >20% of cases).
Antiplatelet and Anticoagulant Therapy	**Antiplatelet and oral anticoagulant therapy requirements (CLAAS):** **Pre-Procedure** Pre-procedure oral anticoagulation (Warfarin or DOAC) should be managed as per site protocol. Warfarin should be discontinued in accordance with site standard of care practices including the monitoring of INR levels on the day of the procedure. The following loading doses should be administered prior to the index procedure: • **Aspirin**

	○ ASA 81-100 mg (administered 1 day prior to procedure), or ○ ASA 325 mg (chewed 1 hour prior to procedure) • **Antibiotic Prophylaxis** ○ Pre-procedure antibiotic for endocarditis prophylaxis should be delivered prior to the procedure as per local standard of care. **Intra-Procedure** Intraprocedural anticoagulation with heparin should be administered per standard of care, maintaining an activated clotting time (ACT) of 250-350s throughout the procedure. **Post-Procedure (For Patient Assigned to Receive the CLAAS Implant)** • If the final procedural – post tether release TEE demonstrates adequate seal (residual leak ≤5mm) and there is no evidence of thrombus, subjects *shall* receive DAPT (ASA 81-100 mg QD and clopidogrel* 75 mg QD) until 45 days post-procedure imaging. • **If the 45-day TEE demonstrates adequate closure:** DAPT *should* be continued to 6 months, unless deemed unsafe by the subject's physician. • At 6 months, if adequate closure has been documented, DAPT should be replaced by monotherapy (ASA 81-100 mg or, P2Y12 inhibitors) until 12-month clinical assessment and is recommended for the duration of the Trial (Clopidogrel* may be substituted for ASA as the discretion of the subject's physician). • 12 months, if adequate closure has been documented, post-procedure, anti-platelet therapy should be administered as per standard of care. • Appropriate endocarditis prophylaxis is recommended for 6 months following device implantation. The decision to continue beyond 6 months is at the discretion of the site principal investigator. *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.* **ADDITIONAL CONSIDERATIONS:** • **<u>Inadequate seal:</u>** Subjects with inadequate seal (residual leak >5mm) at the post-deployment (or any subsequent TEE) should be evaluated for treatment with DOAC and ASA for 4-6 weeks followed by TEE. If inadequate seal persists, antithrombotic therapy should be considered until seal is confirmed on follow up imaging. Antithrombotic therapy should be individualized to the

	patient based on anatomic (size of leak) and clinical (risk of anticoagulation) considerations. • **Device Related Thrombus:** Thrombus detected on the LA surface of the device, at the post-procedure TEE (or any subsequent TEE), should be evaluated for treatment with OAC and ASA for 4-6 weeks followed by repeat imaging. Antithrombotic therapy should be continued until thrombus has been confirmed to be resolved on the follow up imaging. Antithrombotic therapy should be individualized to the patient based on clinical (risk of anticoagulation) considerations. **Antiplatelet and oral anticoagulant therapy requirements, Control Group** Control subjects should be treated according to the marketed LAAO device manufacturer's Instructions for Use. *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.* Subjects found to have Leak or Device Related Thrombus identified on Cardiac CT must have confirmation by TEE.
Subject Population	The subject population from which subjects for this trial will be recruited consists of adult subjects with non-valvular atrial fibrillation who are at increased risk for stroke and systemic embolism based on CHADS2 or CHA2DS2-VASc scores, and who are recommended for oral anticoagulation therapy but have an appropriate rationale to seek a non-pharmacologic alternative to long-term oral anticoagulation, and who have been deemed appropriate for LAA closure by the site investigator and a clinician not a part of the procedural team using a shared decision process in accordance with standard of care.
Inclusion Criteria	Potential subjects must meet **ALL** of the following criteria to be eligible for inclusion in the study: ***General Inclusion Criteria*** 1. Male or non-pregnant female aged ≥18 years. 2. Documented non-valvular AF (paroxysmal, persistent, or permanent). 3. High risk of stroke or systemic embolism, defined as CHA2DS2-VASc score of ≥3. 4. Has an appropriate rationale to seek a non-pharmacologic alternative to long-term oral anticoagulation. 5. Deemed by the site investigator to be suitable for short term oral anticoagulation therapy but deemed less favorable for long-term oral anticoagulation therapy.

	6. Deemed appropriate for LAA closure by the site investigator and a clinician not a part of the procedural team using a shared decision-making process in accordance with standard of care. 7. Able to comply with the protocol-specified medication regimen and follow-up evaluations. 8. The patient (or legally authorized representative, where allowed) has been informed of the nature of the study, agrees to its provisions, and has provided written informed consent approved by the appropriate Institutional Review Board (IRB)/Regional Ethics Board (REB)/Ethics Committee (EC).
Exclusion Criteria	Potential subjects will be excluded if **ANY** of the following conditions apply: ***General Exclusion Criteria*** 1. Pregnant or nursing patients and those who plan pregnancy in the period up to one year following the index procedure. Female patients of childbearing potential must have a negative pregnancy test (per site standard test) **within 7 days** prior to index procedure. 2. Anatomic conditions that would prevent performance of an LAA occlusion (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). 3. Atrial fibrillation that is defined by a single occurrence or that is transient or reversible (e.g., secondary thyroid disorders, acute alcohol intoxication, trauma, recent major surgical procedures). 4. A medical condition (other than atrial fibrillation) that mandates long-term oral anticoagulation (e.g., history of unprovoked deep vein thrombosis or pulmonary embolism, or prosthetic mechanical heart valve). 5. History of bleeding diathesis or coagulopathy, or patients in whom antiplatelet and/or anticoagulant therapy is contraindicated. 6. Documented active systemic infection. 7. Symptomatic carotid artery disease (defined as >50% stenosis with symptoms of ipsilateral transient or visual TIA evidenced by amaurosis fugax, ipsilateral hemispheric TIAs or ipsilateral stroke); if subject has a history of carotid stent or endarterectomy the subject is eligible if there is <50% stenosis noted at the site of prior treatment. 8. Recent (**within 30 days** of index procedure) or planned (**within 60 days** post-procedure) cardiac or major non-cardiac interventional or surgical procedure. 9. Recent (**within 30 days** of index procedure) stroke or transient ischemic attack. 10. Recent **(within 30 days** of index procedure) myocardial infarction.

	11. Vascular access precluding delivery of implant with catheter-based system. 12. Severe heart failure (New York Heart Association Class IV). 13. Prior cardiac transplant, history of mitral valve replacement or transcatheter mitral valve intervention, or any prosthetic mechanical valve implant. 14. Renal insufficiency, defined as estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m2 (by the Modification of Diet in Renal Disease equation). 15. Platelet count <75,000 cells/mm3 or >700,000 cells/mm3, or white blood cell count <3,000 cells/mm3. 16. Known allergy, hypersensitivity or contraindication to aspirin, heparin, or device materials (e.g., nickel, titanium) that would preclude any P2Y12 inhibitor therapy, or the patient has contrast sensitivity that cannot be adequately pre-medicated. 17. Actively enrolled or plans to enroll in a concurrent clinical study in which the active treatment arm may confound the results of this trial. 18. Unable to undergo general anesthesia. 19. Known other medical illness or known history of substance abuse that may cause non-compliance with the protocol or protocol-specified medication regimen, confound the data interpretation, or is associated with a life expectancy of less than 5 years. 20. A condition which precludes adequate transesophageal echocardiographic (TEE) assessment. ***Echocardiographic Exclusion Criteria*** 1. Left atrial appendage anatomy which cannot accommodate a commercially available control device or the CLAAS Implant per manufacturer IFU (e.g., the anatomy and sizing must be appropriate for both the investigational (CLAAS) and a commercially available device to be enrolled in the trial). 2. Intracardiac thrombus or dense spontaneous echo contrast consistent with thrombus, as visualized by TEE prior to implant. 3. Left ventricular ejection fraction (LVEF) <30%. 4. Moderate or large circumferential pericardial effusion >10 mm or symptomatic pericardial effusion, signs or symptoms of acute or chronic pericarditis, or evidence of tamponade physiology 5. Atrial septal defect that warrants closure. 6. High risk patent foramen ovale (PFO), defined as an atrial septal aneurysm (excursion >15 mm or length >15 mm) or large shunt (early [within 3 beats] and/or substantial passage of bubbles, e.g., ≥20). 7. Moderate or severe mitral valve stenosis (mitral valve area <1.5cm^2). 8. Complex atheroma with mobile plaque of the descending aorta and/or aortic arch. 9. Evidence of cardiac tumor.

Follow-up Requirements	Follow-up visits will occur prior to hospital discharge and at 7 days via telehealth assessment and at 45 days (imaging and telehealth), 6 months (telehealth visit), 12 months (imaging and telehealth) and 18 months (clinic visit), and 2, 3, 4 and 5 years (telehealth) post procedure. *NOTE: If the subject has not yet been discharged from the index procedure hospitalization at day 7 post-procedure, the 7-day follow-up may be conducted in-hospital.*
Statistical Summary	All endpoints will be reported using appropriate descriptive statistics. Statistics for continuous variables will include sample size, mean, standard deviation, median, interquartile range, minimum, and maximum. Binary variables will be summarized using sample size, frequencies, and percentages. Kaplan-Meier analysis will be used for time-to-event analyses. The primary effectiveness endpoint will be analyzed for non-inferiority based on a margin of 0.032. The primary safety endpoint will be analyzed for non-inferiority based on a margin of 0.058. The primary effectiveness and safety endpoints will also be reported using descriptive statistics and nominal confidence bounds.
Safety Oversight	The will include subject safety protection measures that include safety committees that will assure patient safety. The study will include an independent Clinical Events Committee comprised of a multi-disciplinary team of physicians that will adjudicate all SAFETY ENDPOINT events and confirm causality and seriousness. An independent, multi-disciplinary Data Safety Monitoring Board will also be established and is tasked with reviewing all safety data at regular intervals to monitor for the incidence of serious adverse events that would warrant modification or termination of the trial.
Public Release of Study and Results	The CONFORM TRIAL (Roll-In and Pivotal Trial Phase) is listed on clinicaltrials.gov under NCT05147782. The CONFORM TRIAL (Conscious Sedation Sub-Study) is listed on clinicaltrials.gov under separate NCT06049615. In accordance with the requirements of ClinicalTrials.gov (as outlined Section 801 of the FDA Amendments Act) results will be posted when the complete data analysis is performed.

5 Study Schedule of Assessments

	Screening	Procedure[0]	Pre-Discharge	7-Day	45-Day	6 Month (180 days)	12 Month (365 days)	18 Month (545 days)	2, 3, 4, 5 Year (730, 1095, 1460, 1825 days)	Stroke/SE Assessment[1]
		Day 0	+4 hours	+2 Days	±7 Days	±30 Days	±30 Days	±30 Days	±60 Days	+14 Days
	Clinic Visit			Telehealth[2]	Clinic Visit/ Telehealth[2]	Telehealth[2]	Clinic Visit/ Telehealth[2]	Clinic Visit	Telehealth[2]	
Informed Consent	X									
Medical and Surgical History	X									X
Physical Exam/Assessment	X									X
Vital Signs	X									
CHA_2DS_2-VASc	X									
HAS-BLED	X									
Serum Creatinine or GFR/eGFR	X[3]									
CBC, Platelet count and Hgb/Hct	X[3]	X[4]								
ECG 12 Lead	X[5]									
Pregnancy Test	X[6]									
Neuro Assessment	X[7]		X					X		X
QVSFS	X[8]			X	X	X	X	X	X	X
Cardiac CT	X[9]				X[11]		X[11]			
TTE	X[9]		X[10]		X[12]					
TEE	X[9]	X			X[12]		X[12]			X
Brain Imaging	X[13]									X[14]
AE Assessment	X	X	X	X	X	X	X	X	X	X
Medication Review[15]	X	X	X	X	X	X	X	X	X	X
INR	X	X								
Randomization	X[16]									
LAA Measurements		X								

TABLE FOOTNOTES
For more in-depth information regarding the Schedule of Assessments, see **Section 9 Study Procedures and Assessments**

[0] Procedure must occur within 14 days from the date of randomization.

[1] In the event of a suspected stroke or systemic embolism, a clinical assessment is required within 14 days after the site becomes aware of the event. If the patient is unable to travel due to hospitalization or disability, chart review can be performed in lieu of clinic visit.

[2] Tele-Health Visit: Clinical evaluation can be performed via phone call, video link or clinic visit.

[3] May be performed as part of standard of care up to 60 days prior to consent.

[4] Performed within 48 hours of index procedure.

[5] Performed within 30 days prior to the index procedure may be used as the baseline ECG, provided there have been no signs or symptoms of myocardial ischemia between the time of the ECG and the screening assessment (in which case the ECG should be performed within 24 hours prior to the index procedure).

[6] Required for females of childbearing potential within 7 days of index procedure (by site standard, either serum or urine).

[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.

[8] QVSFS: Questionnaire for Verifying Stroke-Free Status within 30 days of index procedure.

[9] **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 assess other Echocardiographic Eligibility Criteria.

[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) .

[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 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.

[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.

[13] Brain Imaging: For subjects with documented history of TIA/Stroke in the 24-month period prior to enrollment, the most recent brain imaging (CT/MRI) report is required at baseline. If there is no available imaging report or there has been a suspected neuro event, brain imaging may be requested by the Sponsor as a baseline reference.

[14] Brain Imaging is ONLY required for patients with Systemic Embolism (SE) if there are new findings suggestive of TIA/Stroke.

[15] Medication assessment data collection includes the use of antiplatelet, anticoagulation and prophylactic antibiotic medication only.

[16] **Randomization only after all clinical assessments and eligibility criteria are confirmed** and shall be performed within 90 days of informed consent.

6 Introduction

This document is a clinical investigational plan for the CONFORM Pivotal Study, a prospective randomized, open-label controlled trial intended to evaluate the safety and effectiveness of the CLAAS System in patients with non-valvular atrial fibrillation who are at increased risk for stroke and systemic embolism. The trial will be conducted in North America, Japan, Europe and Central Asia. The study will be performed under an Investigational Device Exemption (IDE) and is intended to support market approval of the CLAAS System in the United States and other countries. The trial is sponsored by Conformal Medical, Inc. (Conformal). Conformal is a privately held medical device company which is providing funding for this clinical investigation.

6.1 Clinical Background – Atrial Fibrillation

Atrial fibrillation (AF) is the most common, clinically significant, cardiac tachyarrhythmia, affecting more than 33 million patients worldwide, with a projected incidence of 5 million patients per year.(1) In the United States alone, approximately 6 million individuals suffer from AF and over one million new cases are diagnosed annually; due to the aging population, the number is expected to double by the year 2030.(2, 3)

AF is associated with a substantially increased risk of stroke and thromboembolic events, primarily due to the Left Atrial Appendage (LAA) serving as a site for thrombus formation(4). Untreated patients with AF have a 2-5% annual incidence of stroke, with a history of stroke or thromboembolic events conferring an even higher risk.(5, 6) Strokes that occur with AF are large and can be quite debilitating, leading to death or costly and painful rehabilitation as well as adding significant financial burden to the medical system.

6.2 Current Standard of Care to Treat Atrial Fibrillation

The standard treatment for stroke prevention in subjects with AF is oral anticoagulant (OAC) therapy to reduce the likelihood of clot formation, which is recommended regardless of the management strategy of the underlying rhythm disorder.(7) Options include warfarin and the direct oral anticoagulants (DOACs) (dabigatran, rivaroxaban, apixaban, and edoxaban).(8-11) While pharmacotherapy can reduce stroke incidence in AF by approximately 60%,(12) OAC therapy is associated with an increased risk of bleeding complications,(13) an issue of significant concern due to the high bleeding risk of many AF patients. In addition, management of OAC therapy is burdensome and long-term compliance is poor, leaving patients at risk for embolic events.

Echocardiographic evidence that the LAA is the source of thrombi in more than 90% of patients with AF has prompted the development of novel transcatheter therapies to occlude the LAA, (14-18) The WATCHMAN® Left Atrial Appendage Closure Device (Boston Scientific Corporation, Marlborough MA) was the first Left Atrial Appendage Occlusion (LAAO) device to be extensively studied in patients. The WATCHMAN device is a self-expanding nitinol structure with a polyethylene face. The device is constrained within the delivery system until deployment within the LAA. Randomized clinical trials demonstrated the WATCHMAN to have acceptable benefit to risk ratios for LAA closure in patients with non-valvular AF and a high risk for stroke or systemic embolism and an appropriate rationale to seek a non-pharmacologic alternative to oral anticoagulation.(7, 19) The WATCHMAN device received FDA approval in March 2015 on the basis of data from the PROTECT-AF(20) and PREVAIL (19) randomized clinical trials and associated continued access registries that demonstrated that the device was non-inferior to warfarin for the primary composite endpoint of stroke, systemic embolism, or cardiovascular death. In addition, when compared to the warfarin control arm, patients receiving the WATCHMAN device

had approximately 80% reduction in hemorrhagic strokes and a >50% reduction in cardiovascular death. (7, 19)

A second-generation WATCHMAN Device, the WATCHMAN FLX™, was developed to simplify LAAO and was studied in the Pinnacle Study, a single arm study which showed comparable performance. (21) Based on the Pinnacle study results, the WATCHMAN FLX received FDA approval in July 2020.(22) Recently, Abbott Laboratories (Abbott Park, IL) received FDA Approval for the Amplatzer Amulet Left Atrial Appendage Occluder.(23) The Amulet consists of a lobe and disk connected by a flexible waist and is constructed from a nitinol mesh and a polyester patch. The Amulet is deployed using a similar procedure as the WATCHMAN and comes in 8 sizes.(24)

While LAA closure with the WATCHMAN and Amplatzer devices represents an important advance in stroke prevention for patients with AF, important limitations remain. These include the need for precise measurement of LAA diameter and depth, precision coaxial delivery, frequent residual leaks and anatomic features which make LAAO difficult to achieve.

The stroke risk for patients with AF has been extensively studied. The Swede Afib study examined the stroke risk in 180,000 untreated AF patients from 2005-2008 and further validated the CHA_2DS_2-VASc as seen in the figure below.(25)

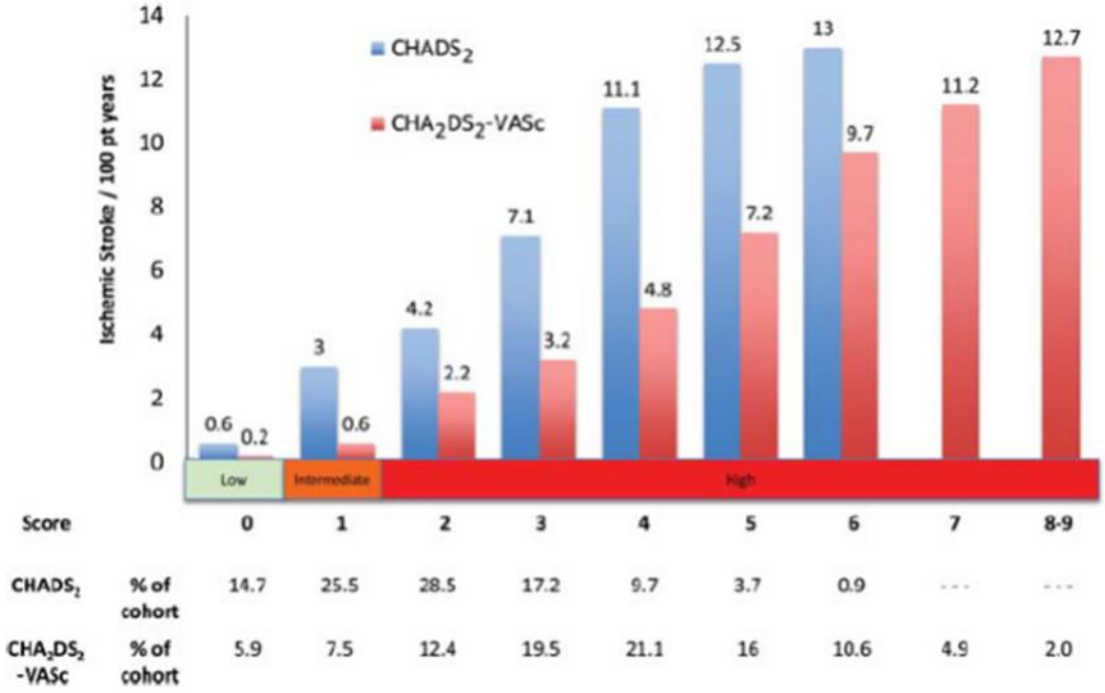


Figure 1: Extracted from European Heart Journal (2012) 33, 1500–1510(25)

These data have allowed prediction of the rate of strokes for subjects enrolled in the CONFORM Trial if untreated medically or without LAAO. Assuming a CHA_2DS_2-VASc score of 4.5 (the observed score reported for subjects recruited to the AMULET(26) and Pinnacle Trials(21)) the stroke risk is ~6% per year based upon the Swede Study. We expect the stroke risk to be similar in subjects who are enrolled in the CONFORM Trial. The poor acceptance of OAC was

also highlighted by the Swedish study which showed that >45% of subjects with indication for OAC (CHA2DS2-VASc ≥2) were untreated. These data underscore the need for alternatives to traditional pharmacologic treatment such as LAAO. Presently, there are only two LAAO implantable devices available which have the limitations listed above. Therefore, additional options for patients and caregivers are needed.

Conformal Medical, Inc (Nashua, NH), the CONFORM study sponsor, has developed the CLAAS System to address these limitations of the first generation LAAO devices. Early experiences with the CLAAS System have been published (27, 28) and an updated brief summary of the studies are provided below.

6.3 Conformal Prague Study

The Prague Feasibility Study was designed to evaluate the safety and performance of the CLAAS System. The study was performed at a single center in Prague, Czech Republic (Homolka Hospital). Subjects were treated using a conscious sedation protocol which featured Intracardiac Echo (ICE) guided transseptal puncture and device deployment with TEE confirmation prior to final release. Subjects were followed through hospital discharge and through serial follow-up assessments post index procedure at discharge, 7 days, 45 days including TEE imaging, 6 months, and 12 months including TEE imaging. The primary safety endpoint of the study is freedom from major adverse events while the primary performance endpoint is LAA closure success. A total of 15 subjects were recruited from October 2019 through January 2020, when the study was paused due to the COVID-19 Pandemic. Results of these initial 15 subjects were summarized by Turagam et al. (27)

A total of 15 subjects (age 71.3±10.8 years, 33% men, CHA2DS2-VASc of 4.1 ±1.7, HAS-BLED 3.4 ±1.4) underwent LAAC, 100% successfully. There were no procedure/device-related complications requiring intervention. Asymptomatic pericardial effusion occurred in 2 subjects. The 45-day, 6-month, and 12-month follow-up imaging in 11, 9, and 13 subjects, respectively, revealed adequate LAA seal (leak <5 mm) in all subjects; device-related thrombus was detected in 1 subject at 6 months. Over 1-year follow-up, there were no ischemic strokes and 1 minor bleed. Non procedure-/device-related death occurred in 2 subjects.

Following removal of COVID-19 restrictions, an additional 4 subjects were treated. Preliminary results indicate successful closure without procedural complications in all subjects. Additional details on this study will be available in the study Investigator Brochure.

6.4 US Early Feasibility IDE Clinical Study

The CLAAS System was also evaluated in the United States as part of an Early Feasibility IDE Clinical study (EFS) which has been performed in two phases. The first phase is being performed at five (5) clinical sites. A total of 22 subjects were enrolled in the initial phase with 18 subjects successfully implanted with the CLAAS Implant.

The first phase EFS cohort was summarized by Sommer et al.(28) Twenty-two subjects (63.7% with CHA2DS2-VASc scores ≥3, 76.2% with HAS-BLED scores ≥3) were enrolled. The device was successfully implanted in 18 subjects and unsuccessfully in 4 subjects. There were no serious procedural complications. On transesophageal echocardiography performed at 45 days, 1 significant leak (≥5 mm) was seen, which was due to a large posterior lobe not appreciated at the time of implantation, and one device-related thrombus was noted, which resolved on oral anticoagulation. There were no periprocedural strokes, major pericardial effusions, or systemic or device embolization. Of note, this phase was performed with the Large CLAAS Implant available for only the last subject. The four subjects with unsuccessful closure were treated prior to the availability of the Large Device and were found to have an LAA that was too large for the Regular Device.

The second phase of the EFS included an additional 42 subjects with 41 successful implants. There has been one reported periprocedural complication of a pericardial effusion requiring treatment. As of August 2024, there have been no reported leaks > 5 mm at 45 days post procedure. The 45-day follow-up imaging in 34 subjects revealed adequate LAA seal (leak < 5mm) in all subjects; device-related thrombus was noted in two subjects at 45 days post procedure. There has been no device embolization, ischemic strokes, or deaths reported.

The combined clinical experience supports the feasibility of LAA Occlusion with the CLAAS System; demonstrating the full functionality of the system including device delivery, retrieval and release; and supports the further evaluation of the product in a pivotal trial.

7 Investigational Device

7.1 Name of the Investigational Device

The CLAAS® System

7.2 Manufacturer

Conformal Medical, Inc.

15 Trafalgar Square, Ste. 101

Nashua, NH 03063

USA

7.3 Clinical Trial Indication for Use

The CLAAS system is intended to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who:

- Are at increased risk for stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc scores and are recommended for oral anticoagulation (OAC) therapy; AND
- Are deemed by their physician to be suitable for OAC; AND
- Have an appropriate rationale to seek a non-pharmacological alternative to OAC, taking into account the safety and effectiveness of the device compared to OAC.

7.4 Device Description

The following is a summary description of the Investigational Device. For additional information, please refer to the Instructions for Use.

7.4.1 Overview

The CLAAS System delivers a plug to the ostia of the Left Atrial Appendage (LAA) and is designed to occlude the appendage to eliminate blood flow (Figure 1). The Implant is pre-attached to the CLAAS Delivery Catheter and loaded by the user into the CLAAS Delivery Catheter (Figure 4) at the time of the procedure. The Delivery System consists of:

1) CLAAS Delivery Catheter with Implant and Loading Cone (Figure 4),

2) Access Sheath with Dilator (Figure 3)

The system is designed to track through the vascular anatomy from the femoral vein to the LAA. The system includes an Access Sheath with Dilator to accommodate vascular access using a standard femoral vein approach to the right atrium, across the atrial septum, and into the LAA. Echocardiography and fluoroscopy are used during the procedure to verify sizing and to aid in deployment of the Implant to the target location.

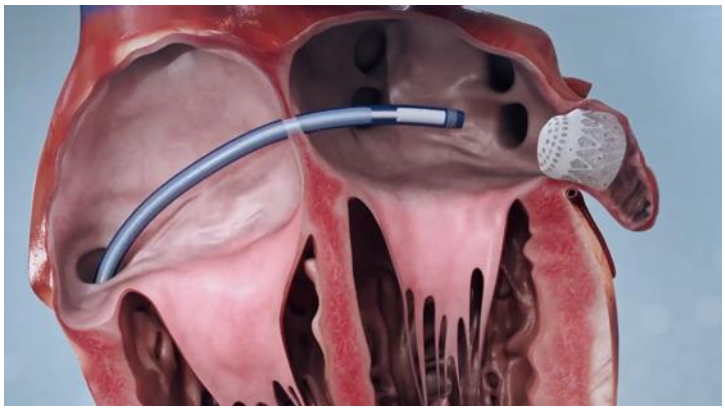


Figure 2: CLAAS Delivery System and Implant in LAA anatomy

7.4.1.1 Initial CLAAS and Next Generation CLAAS Systems

The Initial CLAAS System (including the access sheath, delivery catheter, and implant) was used from the beginning of the study enrollment in June 2022 through the end of April 2024. In April 2024, Conformal initiated several changes to the CLAAS System, referred to in this Clinical Investigational Plan as Next Generation CLAAS. These included reducing the height of the anchors on the implant, modifying the orientation of the ePTFE layers of the implant, improving the kink resistance and torque transmission of the Access Sheath and Delivery Catheter, reducing the stiffness of the dilator, and redesigning the delivery catheter handle to improve ergonomics, reliability, and performance.

7.4.1.2 CLAAS Implant

The CLAAS Implant is designed to conform to the geometry of the LAA and is delivered via a percutaneous Delivery System. The implant is designed to permanently seal off the LAA from the LA with an endothelial layer that forms across the LA face of the implant. The implant is available in two different sizes; Regular (27 mm) and Large (35 mm) to accommodate patient anatomy. Angiography and/or echocardiography at the time of the procedure may be used to determine the LAA ostium diameter to properly select the Implant size (Table 1).The implant has an inner, cylindrical, Nitinol endoskeleton (frame) that provides the mechanical base structure (#4 in Figure 3). The Nitinol endoskeleton contains 10 face struts and 20 anchors (Regular size) and 12 struts and 24 anchors (Large size) facing proximally to engage the tissue to resist movement. The endoskeleton also provides the conformable structure to enable the foam cylinder (#2 in Figure 3) to compress against the LAA tissue to facilitate sealing.

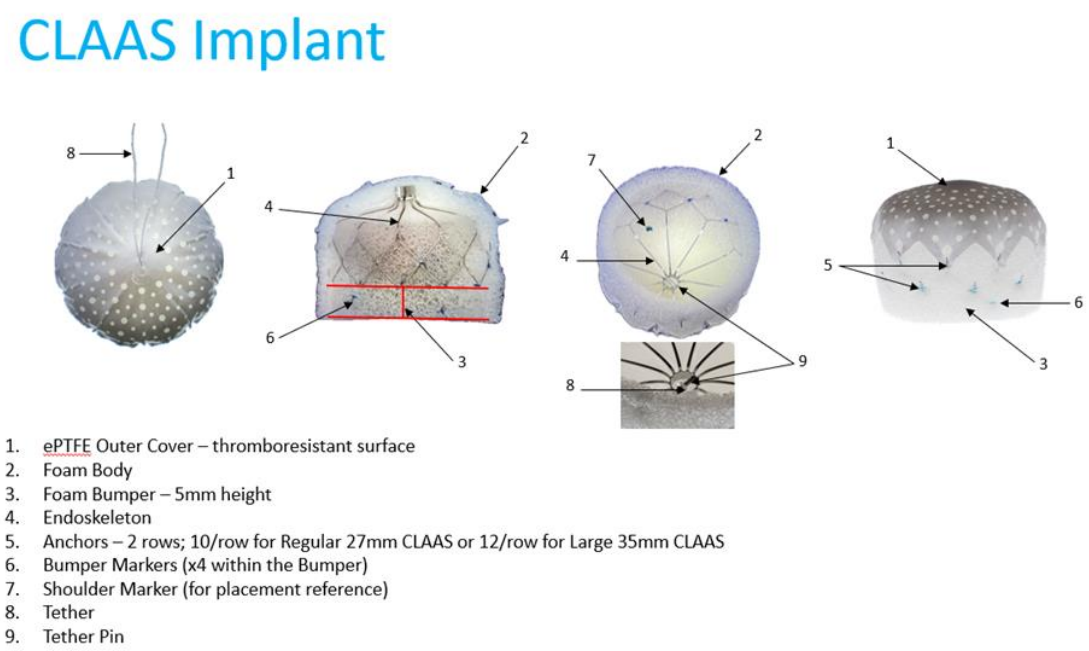


Figure 3: CLAAS Implant Components

Table 1: CLAAS Implant sizing

Implant Size	Mean LAA Ostium Diameter (D_{max} + D_{min}) / 2	LAA Ostium Diameter Range	Minimum Landing Zone Depth
Regular	≤ 25 mm	10 – 33 mm	10 mm
Large	≤ 32 mm	20 – 40 mm	10 mm

7.4.1.3 Delivery System

The CLAAS system is delivered to the target location at the LAA ostium using standard interventional techniques and imaging to ensure appropriate placement and sizing. Under echocardiographic guidance, a transseptal puncture is used to place an Access Sheath. A pigtail catheter may be advanced over a guidewire via the Access Sheath into the LAA to perform an angiogram of the LAA. In addition, Echocardiography is also used at the time of the procedure to guide the sizing and delivery of the implant.

Delivery of the Implant is achieved with a customized coaxial delivery system (nominal dimensions provided in Table 2). Vascular access is achieved with the Conformal Access Sheath with Dilator (nominal dimensions provided in Table 3). The Implant is loaded into the distal end of the CLAAS Delivery Catheter as outlined in the Instructions for Use. The system is designed with sufficient length to access the LAA from a femoral vein puncture. The CLAAS Delivery Catheter

working length is designed such that when it is locked to the Access Sheath, its distal tip is about 3cm short of the Access Sheath tip. This allows the user to advance the Implant from the CLAAS Delivery Catheter into the Access Sheath prior to deploying it into the subject. The Delivery System includes the Access Sheath with Dilator and the CLAAS Delivery Catheter. The Delivery System components are shown in Figure 4.

The Access Sheath and Dilator systems are provided in two different sizes to accommodate the different implant sizes and are also offered as either single or double curves to accommodate varying vascular anatomy. The Single Curve Access Sheath has a single, 90-degree bend at its distal end with a radius of 3.5 inches. The Double Curve Access Sheath has a double curve, which is an anterior curve distal to the primary curve. The Access Sheath components are shown in Figure 5. 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.

Table 2: CLAAS Delivery Catheter Nominal Dimensions

Component	Regular	Large
CLAAS Delivery Catheter		
Outer diameter	15.2F	17.1F
Inner diameter	13.3F	15.3F
Working length	73cm	73cm

Table 3: CLAAS Access Sheath Nominal Dimensions

Component	Regular	Large
Access Sheath		
Outer diameter	17.8F	19.8F
Inner diameter	15.7F	17.6F
Working length	77.5cm	77.5cm

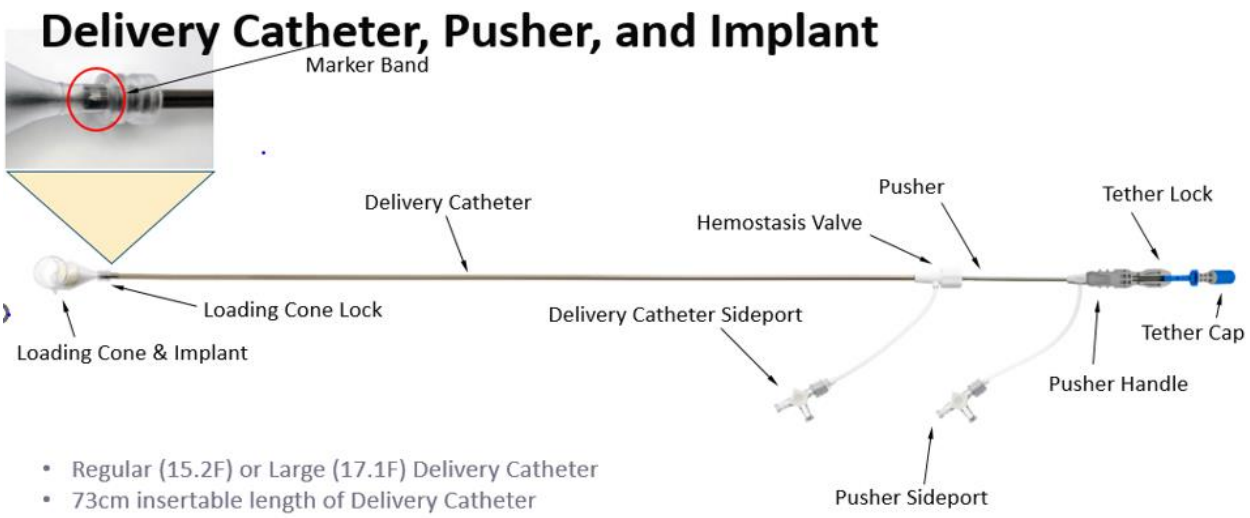
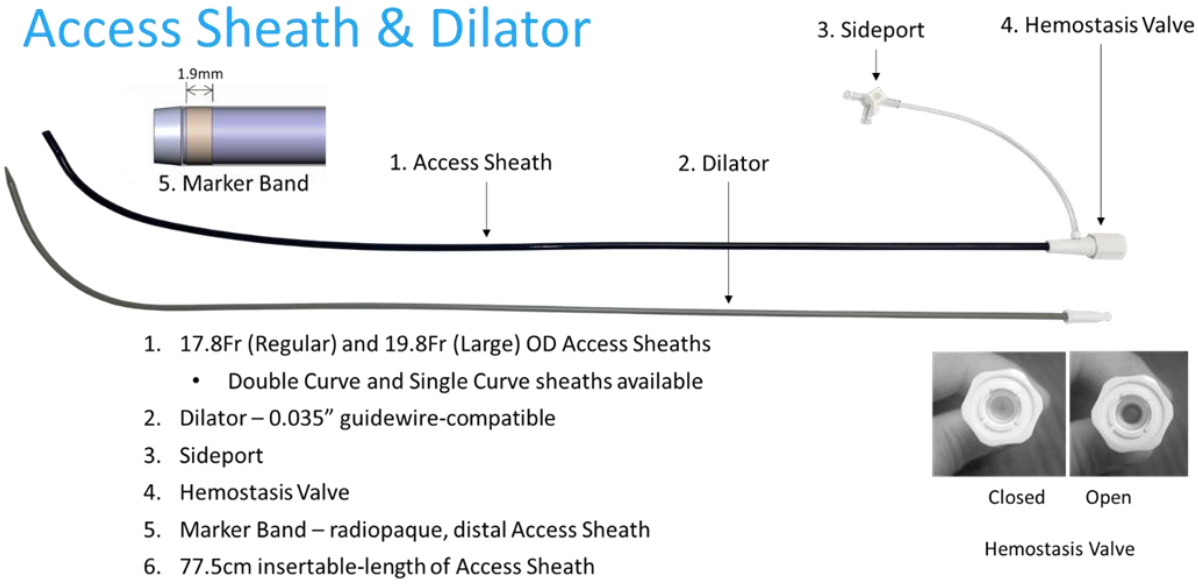


Figure 4: CLAAS Delivery Catheter with Implant and Loading Cone



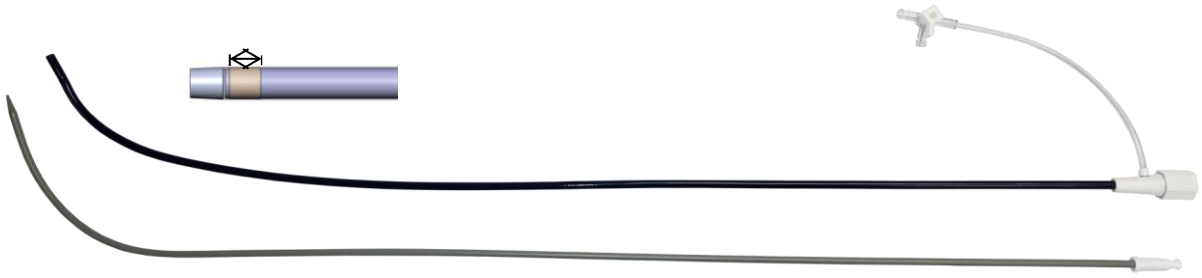


Figure 5: Single curve CLAAS Access Sheath with Dilator components

7.4.1.4 Device Traceability

Refer to the CLAAS System IFU and packaging labels for additional device identification and information.

It is estimated that each study subject undergoing the CLAAS System implant procedure will require one device to be implanted. The final number of devices used during the index procedure may be dependent upon factors, such as individual patient anatomy and procedural considerations.

A description regarding how traceability shall be achieved during and after the clinical investigation is outlined in **Section 17**.

7.4.1.5 Control Devices

The control devices for the study will be commercially available transcatheter LAAO devices. Currently, there are four FDA approved LAAO devices (WATCHMAN, WATCHMAN FLX and WATCHMAN FLX Pro from Boston Scientific; and Amulet from Abbott Laboratories) all of which can be used in subjects assigned to the Control Group. It is anticipated that additional transcatheter devices may gain FDA approval during the enrollment period of the study. When a new transcatheter LAAO product becomes commercially available, its suitability for subjects assigned to the Control Group will be assessed by the Executive Committee; and with approval by FDA, the newly available control device will be added and included in an updated protocol which will be submitted for IRB/REB/EC approval.

The control devices will be placed in accordance with the approved Instructions for Use and all subjects will be managed through the same follow-up timeframe as the treatment device in accordance with the FDA approved labeling for post procedure anticoagulation/antiplatelet medication.

8 Study Design

8.1 Study Objectives

The pivotal trial has four objectives:

Objective 1: To evaluate the safety and effectiveness of the CLAAS System by demonstrating non-inferiority to currently marketed LAAO systems in subjects with non-valvular atrial fibrillation.

Objective 2: To demonstrate the safety of a post procedure pharmacologic antiplatelet regimen that consists of DAPT alone without concomitant anticoagulation therapy.

Objective 3: To demonstrate the ability to safely deliver the CLAAS Device using a conscious sedation protocol without general anesthesia. To investigate this objective, a separate Sub-Study will be conducted after recruitment of the RCT is complete at select, qualified sites based on the experience demonstrated in the RCT.

Objective 4: Support regulatory approval(s) in territories outside US.

8.2 Study Design and Rationale

The CLAAS system is designed to provide the benefits of left atrial appendage closure with a conventional device, while potentially simplifying the implantation procedure, improving procedural safety, and reducing the peri-device leakage. The study will evaluate the safety and effectiveness of LAA closure with the CLAAS system in subjects with non-valvular atrial fibrillation who are at increased risk for stroke and systemic embolism.

This is a pivotal clinical trial that includes three components: (1) a Roll-In Phase using the CLAAS system alone, (2) a Randomized Clinical Trial (RCT) comparing CLAAS to commercially available LAAO systems, and (3) a subsequent, single arm Sub-Study investigating the use of conscious sedation; conducted after enrollment in the RCT is complete and listed under a separate NCT number within the clinicaltrials.gov website (NCT06049615).

8.2.1 Roll-In Phase: To ensure adequate implant experience, 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).\. Data from roll-in subjects will be included in a comprehensive summary of safety but will not be included as part of the primary analysis dataset (ITT). All Roll-in subjects will have the same data collection and follow-up requirements as randomized subjects. The results of the Roll-in cohort will be compared with the CLAAS subjects from the RCT group to characterize the product learning curve.

8.2.2 Randomized Controlled Trial: A prospective, unblinded, randomized, multicenter, active control trial to evaluate the safety and effectiveness of the CLAAS System by demonstrating non-inferiority against standard of care, commercially available LAA occlusion devices. The RCT will be performed in a staged manner with no more than 250 subjects treated in the initial phase to support a safety summary on the first 50 CLAAS implants. Once approved by FDA, the RCT will advance to the second stage of enrollment completing recruitment of the RCT cohort.

8.2.3 Conscious Sedation Single Arm Sub-Study: A prospective single arm trial evaluating a conscious sedation protocol. The sub-study will evaluate the safety and performance of the CLAAS device using conscious sedation in comparison with the device delivery safety and performance observed in the CLAAS arm of the RCT. The sub-study will be performed in accordance with all protocol requirements and all subjects will be evaluated for a primary endpoint

based on the product performance at the 45 Days post procedure. Enrollment in the sub-study will not commence until enrollment in the randomized cohort is complete, initial safety of the CLAAS system is confirmed by the DSMB and FDA and FDA approval of the Sub-Study has been granted through an IDE Supplement.

Appendix E provides a summary of Sub-Study with statistical rationale.

The following table outlines the general study timelines and milestones, subject to change throughout the duration of the study. A more detailed timeline may be in subsequent documents and plans, i.e., Project Plan.

Table 4: CONFORM Milestones and Timeline

Study Milestones	Forecast
FDA Regulatory Submission	Oct 2021
Regulatory Body approvals	Nov 2021
Central IRB approval	Dec 2021
ClinicalTrials.gov Registration	Dec 2021
First subject enrollment - US	June 2022
First subject enrolled - OUS	Sept 2023
Last subject enrollment	Dec 2026
Last subject last f/u for Primary Safety Endpoint (12 months)	Dec 2027
Last subject last f/u for Primary Efficacy Endpoint (18 months)	June 2028
Last Subject/Last Complete F/U (5 years post)	Dec 2031
Final Data Cleaning and Database Lock	April 2031
Final CSR	July 2031
Study Closure	Dec 2031

8.3 Number of Required Subjects

The sample size requirements for each of the study cohorts:

8.3.1 Roll-in Phase: 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 CLAAS 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). The number of cases is determined through the training and proctoring process and is based upon demonstrated proficiency.

8.3.2 RCT Phase: Up to one thousand six hundred (1600) subjects will be enrolled in the randomized control trial. The sample size is based on the power requirements for the primary effectiveness endpoint and was determined via simulation. With a non-inferiority margin of 3.2%, and one-sided alpha level of 0.025, the sample size of 1600 subjects should provide approximately 85% power for the hypothesis test of non-inferiority accounting for a 10% attrition rate. This sample size is also expected to provide greater than 80% power for the hypothesis test for the primary safety endpoint with a margin of 5.8% and a one-sided 0.025 alpha level. It should be noted that >50% of the subjects enrolled in the RCT phase will be from the US and no more than 15% of the data will be from one site.

8.3.3 Conscious Sedation Single Arm Sub-study: The sub-study is designed to demonstrate non-inferiority in CLAAS Implant success compared to the CLAAS arm of the RCT based on the 45 Day Endpoint. It is estimated that a total sample size of 130 subjects (including 6% attrition) is required to demonstrate non-inferiority. This estimated sample size will be verified and adjusted, if necessary, based on the observed rate of CLAAS Implant success rate in the RCT, prior to initiation of the sub-study. Appendix E provides a summary of the Sub-Study with statistical rationale. This Sub-Study will be identified with a separate NCT number from the randomized controlled trial (NCT06049615).

8.4 Estimated Enrollment Time

The trial is anticipated to take approximately 8 years, depending on the rate of enrollment. Enrollment is expected to take approximately 3 years, and each subject will be followed for a total of 5 years. Follow-up visits may occur as part of an expanded access and/or post-approval study, should the CLAAS System gain approval for commercial distribution prior to the subject's 5-year visit.

8.5 Study Endpoints

Study success will be defined as success on both the primary safety and primary effectiveness endpoints.

8.5.1 Primary Safety Endpoint

A composite of:

- Major Procedure-Related Complications including (identified within 12 months of procedure and adjudicated as procedure related):
    a. cardiac perforation
    b. pericardial effusion requiring drainage
    c. ischemic stroke
    d. device embolization
    e. major vascular complications
- Major bleeding through 12 months post procedure or
- All-cause death 12 months post procedure

All definitions are provided for all components in Appendix A. All events will be adjudicated by the independent Clinical Events Committee (CEC).

8.5.2 Primary Effectiveness Endpoint

The primary effectiveness endpoint is a composite of ischemic stroke (NeuroARC (29) defined) and systemic embolism through 18 months.

8.5.3 Secondary Endpoints

8.5.3.1 Secondary Safety Endpoints

1. All-Cause Mortality (including cardiovascular) through 18 months

2. Myocardial infarction evaluated through 7 days post-procedure (See Appendix A for definition)
3. Neurologic Events including Stroke (ischemic and hemorrhagic) and TIA including all stroke (See Appendix A for definition)
4. Bleeding complications (See Appendix A for definition)
5. Vascular complications classified as major/minor and access site/non-access site related (See Appendix A for definition)
6. Device and procedure-related serious adverse events: Summary of all CEC adjudicated adverse events attributed to the device and/or the procedure

8.5.3.2 Secondary Performance and Efficacy Endpoints (all definitions provided in Appendix A):

1. Device Success
2. Technical success
3. Procedure success
4. Embolic Events
5. Closure Success at 12 months based upon each of the following criteria:
    a. demonstration of peri-device flow ≤5 mm
    b. demonstration of peri-device flow ≤3 mm

8.5.3.3 Secondary Effectiveness Endpoints with Statistical Hypothesis Testing

The following endpoints will have formal statistical hypothesis tests with a gatekeeping approach to control the Type 1 error rate. Each endpoint will be based on a comparison of the treatment and control arms and is described in detail in the Statistical Analysis Plan and Section 12 of the protocol.

1. **Non-inferior closure success** (≤5 mm) **at 45 days**, defined as peri-device residual leak ≤5mm by TEE as evaluated by an independent core lab. A 3% margin will be used.
2. **Non-inferior closure success** (≤3mm) **at 45-days**, defined as peri-device residual leak ≤3mm on TEE as evaluated by an independent core lab. A 5% margin will be used.
3. **Non-inferior complete closure success at 45 days,** defined as lack of any detectable (>1mm) peri-device residual leak on TEE as evaluated by an independent core lab. A 5% margin will be used.
4. **Superior closure success at 45 days,** defined as peri-device residual leak ≤3mm based on TEE as evaluated by an independent core lab.
5. **Superior closure success at 45 days, device subgroup test:** CLAAS vs. specific control device: defined as lack of any detectable (>3mm) peri-device residual leak on TEE as evaluated by an independent core lab. Tests associated with this endpoint will be performed in descending order of specific control devices (device testing will be performed only for control devices that are used >20% of cases).

6. **Superior complete closure success at 45 days,** defined as lack of any detectable (>3mm) peri-device residual leak on TEE as evaluated by an independent core lab.
7. **Superior closure success at 45 days, device subgroup test:** CLAAS vs. specific control device: defined as lack of any detectable (>1mm) peri-device residual leak on TEE as evaluated by an independent core lab. Tests associated with this endpoint will be performed in descending order of specific control devices (device testing will be performed only for control devices that are used >20% of cases).

8.6 Subject Selection

8.6.1 Subject Population

The subject population from which subjects for this trial will be recruited consists of adult subjects presenting with non-valvular atrial fibrillation who are at increased risk for stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc scores, and who are recommended for oral anticoagulation therapy but have an appropriate rationale to seek a non-pharmacologic alternative to long-term oral anticoagulation, and who have been deemed appropriate for LAA closure by the site investigator and a clinician not a part of the procedural team, using a shared decision process in accordance with standard of care.

8.6.1.1 Enrollment of Medicare Beneficiaries

This study eligibility criteria includes subjects that are largely identified in the Medicare population. As such, the randomized trial design is considered adequate to characterize the safety and effectiveness of the CLAAS system and will appropriately support the CMS criterion for coverage.

8.6.1.2 Enrollment/Representation of Underrepresented Demographic Subgroups

Historically, specific demographic subgroups such as women and racial or ethnic minorities have been under-represented or excluded from many clinical trials, leading to a lack of information on these subgroups for many medical treatments. Certain medical products elicit different responses in specific demographic subgroups. Therefore, it is important to ensure there is an adequate representation of such demographic subgroups and to assess whether there is a different response between different demographic subgroups.

Conformal will work to ensure adequate representation and retention of women and racial or ethnic minorities in this trial. The population in this trial is expected to be older; therefore, some of the traditional reasons for low participation of women are unlikely to affect the CONFORM Pivotal Trial (e.g., fear of fetal injury, family responsibilities). The Statistical Analysis Plan includes analyses to assess heterogeneity of safety and effectiveness endpoints across demographic subgroups.

8.6.2 Eligibility Criteria

8.6.2.1 Inclusion Criteria

Potential subjects must meet **ALL** of the following criteria to be eligible for enrollment into the study:

8.6.2.1.1 General Inclusion Criteria

1. Male or non-pregnant female aged ≥18 years.

2. Documented non-valvular AF (paroxysmal, persistent, or permanent).
3. High risk of stroke or systemic embolism, defined as CHA2DS2-VASc score of ≥3.
4. Has an appropriate rationale to seek a non-pharmacologic alternative to long-term oral anticoagulation.
5. Deemed by investigator to be suitable for short term oral anticoagulation therapy but deemed less favorable for long-term oral anticoagulation therapy.
6. Deemed appropriate for LAA closure by the site investigator and a clinician not a part of the procedural team using a shared decision-making process in accordance with standard of care.
7. Able to comply with the protocol-specified medication regimen and follow-up evaluations.
8. The subject (or legally authorized representative, where allowed) has been informed of the nature of the study, agrees to its provisions, and has provided written informed consent approved by the appropriate institutional review board (IRB)/Regional Ethics Board (REB)/Ethics Committee (EC).

8.6.2.2 Exclusion Criteria

Potential subjects will be excluded if **ANY** of the following criteria apply:

8.6.2.2.1 General Exclusion Criteria

1. Pregnant or nursing subjects and those who plan pregnancy in the period up to one year following the index procedure. Female subjects of childbearing potential must have a negative pregnancy test (per site standard test) **within 7 days** prior to index procedure.
2. Anatomic conditions that would prevent performance of an LAA occlusion procedure (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).
3. Atrial fibrillation that is defined by a single occurrence or that is transient or reversible (e.g., secondary thyroid disorders, acute alcohol intoxication, trauma, recent major surgical procedures).
4. A medical condition (other than atrial fibrillation) that mandates long-term oral anticoagulation (e.g., history of unprovoked deep vein thrombosis or pulmonary embolism, or prosthetic mechanical heart valve).
5. History of bleeding diathesis or coagulopathy, or subjects in whom antiplatelet and/or anticoagulant therapy is contraindicated.
6. Documented active systemic infection.
7. Symptomatic carotid artery disease (defined as >50% stenosis with symptoms of ipsilateral transient or visual TIA evidenced by amaurosis fugax, ipsilateral hemispheric TIAs or ipsilateral stroke); if subject has a history of carotid stent or endarterectomy the subject is eligible if there is <50% stenosis noted at the site of prior treatment.

8. Recent (**within 30 days** of index procedure) or planned (**within 60 days** post-procedure) cardiac or major non-cardiac interventional or surgical procedure.
9. Recent (**within 30 days** of index procedure) stroke or transient ischemic attack.
10. Recent **(within 30 days** of index procedure) myocardial infarction.
11. Vascular access precluding delivery of implant with catheter-based system.
12. Severe heart failure (New York Heart Association Class IV).
13. Prior cardiac transplant, history of mitral valve replacement or transcatheter mitral valve intervention, or any prosthetic mechanical valve implant.
14. Renal insufficiency, defined as estimated glomerular filtration rate (eGFR) <30mL/min/1.73 m2 (by the Modification of Diet in Renal Disease equation).
15. Platelet count <75,000 cells/mm3 or >700,000 cells/mm3, or white blood cell count <3,000 cells/mm3.
16. Known allergy, hypersensitivity or contraindication to aspirin, heparin, or device materials (e.g., nickel, titanium) that would preclude any P2Y12 inhibitor therapy, or the subject has contrast sensitivity that cannot be adequately pre-medicated.
17. Actively enrolled or plans to enroll in a concurrent clinical study in which the active treatment arm may confound the results of this trial.
18. Unable to undergo general anesthesia.
19. Known other medical illness or known history of substance abuse that may cause non-compliance with the protocol or protocol-specified medication regimen, confound the data interpretation, or is associated with a life expectancy of less than 5 years.
20. A condition which precludes adequate transesophageal echocardiographic (TEE) assessment.

8.6.2.2.2 Echocardiographic Exclusion Criteria

1. Left atrial appendage anatomy which cannot accommodate a commercially available control device or the CLAAS Implant per manufacturer IFU (e.g., the anatomy and sizing must be appropriate for both the investigational (CLAAS) and a commercially available device in order to be enrolled in the trial).
2. Intracardiac thrombus or dense spontaneous echo contrast consistent with thrombus, as visualized by TEE prior to implant.
3. Left ventricular ejection fraction (LVEF) <30%.
4. Moderate or large circumferential pericardial effusion >10mm or symptomatic pericardial effusion, signs or symptoms of acute or chronic pericarditis, or evidence of tamponade physiology.
5. Atrial septal defect that warrants closure.

6. High risk patent foramen ovale (PFO), defined as an atrial septal aneurysm (excursion >15mm or length >15mm) or large shunt (early [within 3 beats] and/or substantial passage of bubbles, e.g., ≥20).
7. Moderate or severe mitral valve stenosis (mitral valve area <1.5cm^2).
8. Complex atheroma with mobile plaque of the descending aorta and/or aortic arch.
9. Evidence of cardiac tumor.

8.7 Informed Consent

Subject participation in this clinical study is voluntary. Informed Consent is required from each subject or his/her legally authorized representative. The Investigator is responsible for ensuring that Informed Consent is obtained prior to the use of any investigational devices, study-required procedures and/or testing, or data collection.

The obtaining and documentation of Informed Consent must be in accordance with the principles of the Declaration of Helsinki, ISO 14155:2020, any applicable national regulations, and local IRB/REB/EC and/or Regulatory authority, as applicable. The ICF must be accepted by Conformal or its delegate (e.g., CRO), and approved by the site's IRB/REB/EC, or central IRB, if applicable.

Conformal will provide a study-specific template of the ICF to investigators participating in this study. The ICF template may be modified to meet the requirements of the investigative site's IRB/REB/EC. Any modification requires acceptance from Conformal prior to use of the form. The ICF must be in a language understandable to the subject and if needed, Conformal will assist the site in obtaining a written consent translation. Translated consent forms must also have IRB/REB/EC approval prior to their use. Privacy language shall be included in the body of the form or as a separate form as applicable.

Failure to obtain subject consent will be reported by Conformal to the applicable regulatory authority according to their requirements (e.g., FDA requirement is within 5 working days of learning of such an event). Any violations of the informed consent process must be reported as deviations to the sponsor and local regulatory authorities, as appropriate. If new information becomes available that can significantly affect a subject's future health and medical care, that information shall be provided to the affected subject(s) in written form via a revised ICF or, in some situations, enrolled subjects may be requested to sign and date an addendum to the ICF. In addition to new significant information during a study, other situations may necessitate revision of the ICF, such as if there are amendments to the applicable laws, protocol, a change in Principal Investigator, administrative changes, or following annual review by the IRB/REB/EC. The new version of the ICF must be approved by the IRB/REB/EC. Acceptance by Conformal is required if changes to the revised ICF are requested by the site's IRB/REB/EC. The IRB/REB/EC will determine the subject population to be re-consented.

8.8 Study Enrollment Process and Subject Classification

Potentially eligible subjects who meet all general inclusion criteria, and no general exclusion criteria and who have consented to participate in the trial will undergo the protocol-specified screening assessments to confirm eligibility. Sites will maintain a subject screening log to document the reasons for meeting study criteria but failing to be enrolled.

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

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 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 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.

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 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.

8.8.6 Screen Failure Population

A Screen Fail subject is an individual who signs an informed consent form (ICF) and fails to meet selection criteria. These subjects will be termed “Screen Failures” and documented as such in the EDC database. Once a subject has transitioned to an ITT population, he/she can no longer be categorized as a Screen Failure.

8.9 Withdrawal, Loss to Follow-up, and Study Completion

8.9.1 Withdrawal

Subjects can withdraw from the study at any time. The reason(s) for withdrawal (if given) will be documented. All data available at the time of withdrawal (if any) will be used for analysis unless the subject has explicitly forbidden the use of such data and has documented this preference in accordance with local regulatory requirements. There will be no further follow-up (per this study protocol) on a subject who has withdrawn.

The withdrawal of a subject can also be initiated by the Investigator if he/she/they determine(s) it is in the best interest of the subject.

Subjects who withdraw/are withdrawn from the study should undergo follow-up-treatment and care according to the institutional standards of care provided by the physicians for subjects undergoing left atrial appendage closure.

Subjects who withdraw from the study will not be replaced.

8.10 Loss to Follow-up

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 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.

8.11 Study Completion

A study completion form must be completed for all subjects:

- In whom mortality has been documented.
- Who withdraw from the study or are withdrawn by the investigator to protect subject rights, welfare, or well-being.
- Who are lost to follow-up and administratively withdrawn from the study.
- Who have completed the final protocol-specified follow-up assessment as outlined per study cohort defined endpoints.

  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.

9 Study Procedures and Assessments

The Study Schedule of Assessments provided in Section 5, provides a listing of all procedures and assessments. The following sections outline the detailed requirements for each visit.

9.1 Screening/Baseline

The following tests and examinations must be performed prior to the index procedure for Roll-in subjects and prior to randomization for RCT cohort to verify eligibility and to collect baseline study data. Assessments performed as part of standard medical care prior to study enrollment are valid sources of data for verifying study eligibility and collecting baseline study data, provided that the previously performed assessments comply with applicable protocol requirements.

- Medical and Surgical History, including NYHA and if applicable, anginal status (may be done per standard of care **up to 30 days prior to consent**).
- Physical Exam/Assessment (may be done per standard of care **up to 30 days prior to consent**) and may be performed as a Review of Systems.
- Atrial fibrillation stroke risk assessment with the CHA_2DS_2-VASc score

- Major bleeding risk assessment with the HAS-BLED score
- Vital signs (includes Height, Weight, Pulse, Blood Pressure) (may be done per standard of care **up to 60 days prior to consent**).
- Neurological assessments (**within 30 days prior to index procedure as baseline characterization but not required for randomization**) to include:
    - Questionnaire for Verifying Stroke-Free Status (QVSFS).
    - NIH Stroke Scale (NIHSS); the NIHSS must be performed by a neurologist or NIHSS-certified research staff.
    - Modified Rankin Scale (mRS) to establish the disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability at baseline; the mRS must be performed by a neurologist or research staff who have completed mRS training.
    - Neurological assessments may be performed by a non-delegated neurology professional (e.g., board-certified or board-eligible neurologist, neurology fellow, neurology physician assistant, or neurology nurse practitioner, or NIHSS- and/or mRS-certified staff where applicable), as long as assessments are completed as part of standard of care and documentation of current certification is maintained in site Regulatory files.
    - Subjects in whom an incidental neurologic event is suspected on the basis of the QVSFS, NIHSS, or other signs or symptoms, will require a neurologic examination and evaluation performed by a neurologist or clinical designee (e.g., neurology fellow).
- Female subjects of childbearing potential must have a pregnancy test (by site standard, either serum or urine) **performed within 7 days of index procedure**.
- Laboratory testing per site standard practice as part of a catheterization procedure. Recording of the following Standard of Care labs shall be included as part of the study: Serum Creatinine or GFR/eGFR; platelet count, HCT/Hgb (may be done per standard of care **up to 60 days prior to consent**).
- A 12-lead electrocardiogram (ECG). An ECG performed **within 30 days prior to the index procedure** may be used as the baseline ECG, provided there have been no signs or symptoms of myocardial ischemia between the time of the ECG and the screening assessment (in which case the ECG should be performed **within 24 hours prior to the index procedure**).
- Brain Imaging (CT/MRI):
    - For subjects with documented history of TIA/Stroke in the 24-month period prior to enrollment, the most recent brain imaging (CT/MRI) report is required at baseline. If there is no available imaging report or there has been a suspected neuro event, brain imaging may be requested by the Sponsor as a baseline reference if there is a suspected neuro event.

- Brain Imaging is ONLY required for subjects with Systemic Embolism (SE) if there are new findings suggestive of TIA/Stroke.

- Medication assessment at baseline includes the use of antiplatelet, anticoagulation, and prophylactic antibiotic medication
- Relevant levels of INR.

9.2 Screening/Baseline Imaging

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 assess other Echocardiographic Eligibility Criteria.

Historical imaging **performed within 6 months prior to consent** (TEE or Cardiac CT) may be used to assess the Echocardiographic Eligibility Criteria.

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, then imaging should be repeated prior to randomization.

9.3 Pre-Procedural Review

The Sponsor may require a pre-procedure case review with the implanting physician as part of the training process. It is anticipated that the review will be performed on the initial five cases at sites without appropriate prior CLAAS experience. The pre-procedure review will include assessment of eligibility criteria (clinical and imaging) and procedural planning. Pre-procedural review of TEE or CT images (Including historical images performed **within 6 months of consent**), will be performed by the implanting physician and the Sponsor or Sponsor-delegated individuals, in collaboration with members of the Executive Committee and Core Lab.

The Sponsor may require review of additional subjects, as needed. Further details regarding pre-procedural review by the Sponsor is described in the Study Manual of Procedures.

9.4 Randomization (RCT Cohort Only)

When it is determined the subject has met all inclusion criteria and no exclusion criteria (including echocardiographic exclusion criteria), the subject may undergo the procedure and if the subject is targeted for the RCT phase, will be randomized in a 1:1 fashion to either the CLAAS or Control device according to a computer-generated randomization scheme. Randomization will be stratified by investigational site.

Randomization **shall be within 90 days of informed consent**. The LAA occlusion procedure shall take place **within and including 14 days from the date of randomization**.

9.5 Index Procedure

Trained Conformal representatives may be present during the CLAAS Implant procedure. Representatives from the manufacturer of the Control Device may be present during the Control implant procedure. 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.

Platelet count, HCT/Hgb lab testing must be collected within 48 hours prior to the index procedure.

9.5.1 Randomized Cohort: The LAA occlusion procedure shall take place within 14 Days from the date of Randomization.

9.5.2 Roll-In Cohort: The LAA occlusion procedure shall take place within 90 days of obtaining informed consent.

9.5.3 Pre-Procedure Medical Therapy

Pre-procedure oral anticoagulation should be managed as per site protocol. Warfarin should be discontinued in accordance with site standard of care practices including INR levels on the day of the procedure.

The following loading doses should be administered prior to the index procedure:

- **Aspirin**
    - ASA 81-100 mg (administered 1 day prior to procedure), or
    - ASA 325 mg (chewed 1 hour prior to procedure)
- **Antibiotic Prophylaxis**
    - Pre-procedure antibiotic for endocarditis prophylaxis should be administered prior to the procedure as per local standard of care.

9.5.4 Intraprocedural Medical Therapy

Intraprocedural anticoagulation with heparin should be administered per physician standard practice in accordance with published guidelines and local standards of care, with a goal of maintaining an activated clotting time (ACT) of 250-350 sec throughout the procedure. The highest and lowest intraprocedural ACT measurements shall be recorded in the CRF for all subjects.

Total heparin dose and prophylactic antibiotics shall be recorded in the subject's medical record and recorded on the eCRF.

9.5.6 Transseptal Puncture

Percutaneous femoral vein access and transseptal puncture should be performed per physician standard practice using a standard commercially available transseptal access system.\

9.5.7 Procedural Imaging

Procedural ultrasound imaging will be performed by a qualified physician (e.g. Physician echocardiologist) who is *not* the implanting physician.

A procedural ultrasound evaluation (e.g., TEE imaging), prior to introducing the device/delivery system into the body, will include evaluation for pericardial effusion, presence of LAA thrombus, and LAA sizing, and is required to confirm eligibility and evaluate baseline status. If subject is randomized, but the subject eligibility is not achieved after ultrasound evaluation, the subject shall

be considered a Screen Failure and will be followed for 45 days to evaluate safety. If subject is not randomized and subject eligibility is not achieved during ultrasound evaluation, the subject may be exited from the study with no additional follow-up required.

This protocol includes specific requirements for procedural TEE imaging acquisition in accordance with the Imaging Core Lab requirements. The details of this TEE Imaging Acquisition Protocol are provided in the Study Manual of Procedures. Imaging for core lab assessment shall document the following:

- Baseline assessment (prior to device introduction),
- Intra-Procedural (pre and post tether release) assessments, and
- Final procedural assessment (post implant delivery system removal).

All procedural angiographic and echocardiographic images must be uploaded using the image submission guidelines outlined in the Study Manual of Procedures.

At any time during the study, echocardiographic imaging obtained during a repeat procedure or for diagnostic purposes should also be uploaded for analysis.

9.5.8 Implant Deployment

Implantation of either the CLAAS or Control Implant should be performed as per the manufacturer's IFU.

Procedural details will be captured as appropriate on the procedural worksheets and subsequently recorded on the eCRF. Any Adverse Events or Device Deficiencies observed shall also be recorded in the EDC.

The procedure is considered complete once the last venous access sheath is removed or the subject has been discharged from the catheterization lab, whichever is first.

9.6 Anticoagulation/Antiplatelet Therapy Requirements – CLAAS

9.6.1 Post-Procedure

- If the final **post procedural**, post tether release TEE demonstrates adequate seal (residual leak ≤5mm) and there is no evidence of thrombus, subjects *shall* receive DAPT (ASA 81-100 mg QD and clopidogrel* 75 mg QD) until 45 days post-procedure imaging.
- At **45 days**, if adequate closure has been documented on imaging**,** DAPT *should* be continued to 6 months, unless deemed unsafe by the subject's physician.
- At **6 months**, if adequate closure has been documented on the 45-day TEE, DAPT should be replaced by monotherapy (ASA 81-100 mg preferred, P2Y12 inhibitor permitted) until 12-month clinical assessment; and is recommended for the duration of the trial (clopidogrel* may be substituted for ASA at the discretion of the subject's physician).
- At **12 months**, if adequate closure has been documented on imaging, medical therapy should be administered based upon institutional standard of care.

NOTE: A substitute P2Y12 inhibitor (i.e., prasugrel, ticagrelor) may be used as per managing physician's judgement. For subjects who are known clopidogrel non-responder an alternative P2Y12 inhibitor should be used.

9.6.2 Additional Considerations:

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 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.

9.6.3 Antiplatelet and Oral Anticoagulant Therapy Requirements (CONTROL):

Control subjects should be treated according to the marketed LAAO device manufacturer's Instructions for Use.

9.6.4 Endocarditis Prophylaxis

Appropriate endocarditis prophylaxis is recommended for 6 months following device implantation. The decision to continue beyond 6 months is at the discretion of the principal investigator or operator.

9.7 Pre-discharge Follow-up

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).
- A neurological assessment (NIHSS and mRS) to evaluate neuro status of subject. If the assessment is indicative of a potential neurological deficit, further evaluation by a board-certified neurologist or designee (e.g., neurology fellow) must be performed.
- Adverse event assessment

Prior to hospital discharge, research staff should review the follow-up requirements with the subject to ensure compliance with the subsequent follow-up assessment.

9.8 7-day Follow-up + 2 Days (Telehealth Visit)

All subjects must undergo a follow-up assessment on days 7 to 9 post-procedure to enable timely documentation of safety endpoint events.

If the subject has not yet been discharged from the index procedure hospitalization at day 7 post-procedure, the 7-day follow-up may be conducted in-hospital, and no separate telehealth visit is necessary. In-hospital/clinic visit will satisfy the telehealth visit, if appropriate.

The 7-day follow-up assessment must include:

- Questionnaire for Verifying Stroke Free Status (QVSFS). If any question is answered "Yes," a formal neurologic examination and evaluation must be performed by a board-certified neurologist or clinical designee (e.g., neurology fellow).
- Current concomitant medications documentation. If DAPT has been interrupted or terminated, the stop date (and resumption date, if applicable) and the reason for interruption/termination should be recorded.
- Adverse event assessment

9.9 45-day Follow-up ± 7 Days (Telehealth Visit and Imaging)

All subjects will complete an assessment at 45 days (± 7 days) post-procedure with imaging (TEE or CT) and clinical evaluation through a minimum of a telehealth visit. The 45-day follow up visit will include the following assessments:

- Questionnaire for Verifying Stroke Free Status (**QVSFS**) If any question is answered "Yes," a formal neurologic examination and evaluation must be performed by a board-certified neurologist or clinical designee (e.g., neurology fellow).
- **Imaging evaluation**, preferably TEE, must be performed in all subjects who left the index procedure with an implanted device.
    - 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 subject'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 (recommended assessment within 2 weeks; at latest, 4-6 weeks from date of original study or at the subject'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.
- Current concomitant medications documentation. If DAPT has been interrupted or terminated, the stop date (and resumption date, if applicable) and the reason for interruption/termination should be recorded.
- Adverse event assessment

Prior to concluding the visit, research staff should also review the follow-up requirements with the subject to help ensure study compliance.

NOTE: Subjects who were withdrawn due to no longer meeting eligibility criteria at the time of the index procedure TEE, but never had a procedure attempt, must be followed through 45-days post

procedure for telehealth/phone call visits including 7-days and 45-days (imaging not required and protocol mandated medication therapy not required). After the 45-Day follow-up, these subjects will have completed all required study assessments.

9.10 6-month Follow-up (± 30 days) (Telehealth Visit)

All subjects will have a clinical assessment performed via a telehealth visit (at a minimum) at 6 months (± 30 days), to include the following assessments:

- Questionnaire for Verifying Stroke Free Status (QVSFS) If any question is answered "Yes," a formal neurologic examination and evaluation must be performed by a board-certified neurologist or clinical designee (e.g., neurology fellow).
- Current concomitant medications documentation. If DAPT has been interrupted or terminated, the stop date (and resumption date, if applicable) and the reason for interruption/termination should be recorded.
- Assessment for change to monotherapy.
- Adverse event assessment.

Prior to concluding the visit, research staff should also review the follow-up requirements with the subject to help ensure continued study compliance.

9.11 12-Month Follow-up ± 30 Days (Telehealth Visit and Imaging)

All subjects will complete an assessment at 12 months (± 30 days) post-procedure with imaging (TEE) and clinical evaluation through a minimum of a telehealth visit. The 12-month follow up visit will include the following assessments:

- Questionnaire for Verifying Stroke Free Status (**QVSFS**) If any question is answered "Yes," a formal neurologic examination and evaluation must be performed by a board-certified neurologist or clinical designee (e.g., neurology fellow).
- **Imaging evaluation**, preferably TEE, must be performed in all subjects who left the index procedure with an implanted device.
    - 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 subject'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 (recommended assessment within 2 weeks; at latest, 4-6 weeks from date of original study or at the subject'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.

- Current concomitant medications documentation. Anticoagulant/antiplatelet therapy per SOC/ investigator decision.
- Adverse event assessment

Prior to concluding the visit, research staff should also review the follow-up requirements with the subject to help ensure study compliance.

9.12 Eighteen-month Follow-up ± 30 Days (Clinic Visit)

All subjects will complete a clinical assessment at 18 months (± 30 days) post-procedure with an in person clinical visit to complete the Primary Endpoint Assessment. The 18 month follow up visit will include the following assessments:

- Neurological assessment may be performed by a non-delegated neurology professional (e.g., board-certified or board-eligible neurologist, neurology fellow, neurology physician assistant, or neurology nurse practitioner, or NIHSS- and/or mRS-certified staff where applicable), as long as assessments are completed as part of standard of care and documentation of current certification is maintained in site Regulatory files.:
  - Questionnaire for Verifying Stroke-Free Status (QVSFS) If any question is answered "Yes," a formal neurologic examination and evaluation must be performed by a board-certified neurologist or clinical designee (e.g., neurology fellow).
  - NIH Stroke Scale (NIHSS).
  - Modified Rankin Scale (mRS) to establish the disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability at baseline.
- Current concomitant medications documentation.
- Adverse event assessment.

Prior to concluding the visit, research staff should also review the follow-up requirements with the subject to help ensure continued study compliance.

NOTE: 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.

9.13 Annual Follow-up 2 – 5 Years ± 60 Days Post Index Procedure (Telehealth)

All subjects will complete annual telehealth visits (at a minimum) at 2, 3, 4 and 5-years (± 60 days) post-index procedure to include the following assessments:

- Questionnaire for Verifying Stroke Free Status (QVSFS) If any question is answered "Yes," a formal neurologic examination and evaluation must be performed by a board-certified neurologist or clinical designee (e.g., neurology fellow).
- Current concomitant medications documentation.

- Adverse event assessment.

Prior to concluding the visit, research staff should also review the follow-up requirements with the subject to help ensure continued study compliance.

9.14 Suspected Stroke or Systemic Embolism Neurologic Events (Unscheduled Visit)

Subjects with confirmed stroke/TIA shall be followed in accordance with clinical standard of care until the neurologic event is completely resolved or resolved with stable deficit.

Subjects with a suspected TIA/stroke shall be documented as an Unscheduled Visit in the Electronic Database System, if identified at a timepoint that does not coincide with a scheduled follow-up visit. The requirements for a suspected TIA/stroke include the following assessments:

- Medical and Surgical History (documenting new findings on history since baseline assessment) and neurologic physical exam/assessment performed by a neurologist or clinical designee (e.g., neurology fellow).
- Physical Exam/Assessment
- A targeted neurologic assessment performed by a neurology professional (board-certified or board-eligible neurologist, neurology fellow, neurology physician assistant, or neurology nurse practitioner, or NIHSS- and/or mRS-certified staff where applicable), as long as assessments are completed as part of standard of care and documentation of current certification is maintained in site Regulatory files. Neurological assessment includes:
    - Questionnaire for Verifying Stroke-Free Status (QVSFS)
    - NIH Stroke Scale (NIHSS)

    NOTE: the NIHSS should be evaluated in light of the subject's condition and should consider factors such as post-procedure anesthesia confusion and inability to raise leg due to constraints for other reasons such as hemostasis maintenance or underlying orthopedic limitations.

    - Modified Rankin Scale (mRS) to establish the disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability at baseline.
    - Brain Imaging as indicated based on clinical presentation; should include brain MRI/CT, in accordance with NeuroARC (29). CT imaging should only be used in cases where MRI (DW Imaging) is contraindicated. Brain Imaging is NOT required for subjects with Systemic Embolism (SE) without new findings suggestive of TIA/Stroke.
    - TEE to evaluate LAAO implant (TEE required for subjects with confirmed TIA/Stroke or Systemic embolism).
- Current concomitant medications documentation.
- Adverse event assessment.

For subjects with suspected Systemic Embolism, examination should be as per the managing physicians and does not necessarily require the neurologic work-up outlined above.

10 Study Completion

Subject participation in the study ends after the 5-year follow-up assessment, and the study completion form should be submitted at this time.

11 Protocol Deviations

All deviations from the requirements of this Clinical Investigation Plan will be considered protocol deviations. For any protocol deviation, a Protocol Deviation form should be completed in the eCRF indicating the type and reason for the deviation in accordance with FDA requirements outlined CFR 812.140 (a) (4), ISO 14155:2020, and other applicable regulations.

Protocol deviations include but are not limited to:

- Failure to obtain informed consent, or failure to obtain informed consent prior to the performance of study-specific procedures or assessments.
- Enrollment of a subject who did not meet all study inclusion criteria, or who met one or more study exclusion criteria.
- Failure to complete protocol-specified assessments, or completion of protocol-specified assessments outside of the protocol-defined time frame.

The Investigator shall not deviate from the protocol, however if a deviation from the protocol is deemed necessary by the Investigator to protect the safety or physical well-being of a subject, the Investigator is requested to notify the Sponsor as soon as possible (if possible, before the deviation has occurred) and IRB/REB/EC, if required.

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).

Protocol deviations shall be reviewed and reported in the study reports, i.e., Annual Progress Report, as applicable.

12 Safety Reporting

Investigators are responsible for reporting and assessing all adverse events as applicable per protocol and all device deficiencies that could have led to a serious adverse device effect. These events will be documented in the case report forms for the study. In addition, the investigator is responsible for reporting any new and/or updated information related to already reported events.

In this study, subjects should also be encouraged to report adverse events (AEs) spontaneously or in response to general, non-directed questioning. During the study, the subject may volunteer information that resembles an adverse event (AE). If it is determined that an AE has occurred, the investigator should obtain all the information required to complete the AE CRFs.

12.1 Reportable Events by Investigational Sites

Investigators are responsible for reporting and assessing the following events:

- All serious adverse events
- All device and procedure-related adverse events
- UADE (Unanticipated Adverse Device Effects)/ USADE (Unanticipated Serious Adverse Device Effects)
- Pre-procedure events (e.g., events related to pre-procedure medication changes)
- All adverse events of special interest. The following events regardless of seriousness or relatedness will be collected:
    - Bleeding events
    - Embolic events (e.g., stroke, TIA, systemic embolism)
    - Neurologic events
    - Device embolizations
    - Device Related Thrombus

The following clinical events will not be considered reportable adverse events, unless the investigator considers the event to be related to the investigational device or procedure, or an AE of special interest:

- Pre-existing medical conditions or a repeat of symptoms are not required to be reported as adverse events *unless* there is a worsening in severity or frequency during a study.
- Planned procedures (scheduled prior to the index procedure) that occur after the index procedure are not considered reportable AEs. Complications from such procedures, however, must be reported.
- Abnormal non-cardiac laboratory findings are not considered a reportable AE unless:
    - The investigator determined that the finding is clinically significant, OR
    - The abnormal laboratory finding required intervention, OR
    - The abnormal laboratory finding required termination of the subject's participation in the study.

Investigators shall report relevant adverse events as follows:

- All sections of the Adverse Event CRF shall be completed for each applicable AE

- Each unique event/diagnosis must be documented separately
- Assess the relationship of the event to the investigational device and procedure
- The AE Term should be reported as a medical diagnosis if available, rather than clinical symptoms
- Death events should not be recorded as an adverse event, but as an outcome to a single serious adverse event
- The AE CRF must be reviewed and signed by the investigator
- If an AE is deemed not to related to the device, procudere implant or medications and is not cardiovascular or neurological in nature AND; does not meet serious adverse criteria it does not need to be reported.

12.2 Safety Event Definitions

The definitions provided have references within the following regulations: 21 CFR Part 812, EU MDR 2017/745 and MDCG 2020-10/1.

Term	Definition
Adverse Event (AE)	An adverse event is any untoward medical occurrence, unintended disease or injury or untoward clinical signs (including an abnormal laboratory finding) in a subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated. **Note 1**: This definition includes events related to the investigational medical device or the *comparator* **Note 2**: This definition includes events related to the procedures involved. **Note 3**: This includes '*comparator*' if the comparator is a medical device.
Adverse Device Effect (ADE)	Adverse Event related to the use of an investigational medical device **Note 1:** This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any *malfunction* of the investigational medical device and/or delivery system. **Note 2:** This definition includes any event resulting from *use error* or from intentional misuse of the investigational medical device. **Note 3:** This includes '*comparator*' if the comparator is a medical device.
Serious Adverse Event (SAE)	Adverse Event that led to any of the following a) death, b) serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:

	1) a life-threatening illness or injury, or 2) a permanent impairment of a body structure or a body function including chronic diseases, or 3) in-patient or prolonged hospitalization, or 4) medical or surgical intervention to prevent life- threatening illness or injury, or permanent impairment to a body structure or a body function c) fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment **Note 1:** Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered a serious adverse event.
Serious Adverse Device Effect (SADE)	Adverse Device Effect that has resulted in any of the consequences characteristic of a serious adverse event.
Unanticipated Adverse Device Effect (UADE)	Any serious adverse effect on the health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety or welfare of subjects. **NOTE:** An anticipated serious adverse device effect (ASADE) is a serious adverse device effect which by its nature, incidence, severity, or outcome has been identified in the investigational plan.
Unanticipated Serious Adverse Device Effect (USADE)	Serious Adverse Device Effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment **Note 1:** Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.
Serious Health Threat	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons **Note 1:** This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.
Device Deficiency	Any inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance.

	Note 1: Device deficiencies include *malfunctions*, *use errors*, and inadequacy in the information supplied by the manufacturer including labelling. **Note 2:** This definition includes device deficiencies related to the *investigational medical device* or the *comparator*.

12.3 Device Deficiencies

Investigators are instructed to report all possible device deficiencies, malfunctions, misuse or use error observed during the trial. These incidents will be documented in the case report form provided as follows:

- **Device deficiency**: Inadequacy in the identity, quality, durability, safety, or performance of an investigational medical device, including malfunction, use errors or inadequacy in information supplied to the manufacturer. NOTE: Device deficiencies include malfunction, use error, and inadequate labeling. They may or may not affect device performance or lead to an adverse event.
    - **Device malfunction**: Failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the Instructions for Use or protocol. NOTE: A device malfunction occurs when the device is used in compliance with the Instructions for Use but does not perform as described in the Instructions for Use.
    - **Use error:** Act or omission of an act that results in a different medical device response than intended by the manufacturer or expected by the user. NOTE 1: Use error includes slips, lapses and mistakes. NOTE 2: An unexpected physiological response of the subject does not itself constitute a use error.
    - **Device misuse:** Any use of the investigational device by an investigator that is contradictory to the application described in the Instructions for Use will be categorized as device misuse. This is a form of Use Error.

Investigators shall report Device Deficiencies as follows:

- All sections of the Device Deficiency eCRF shall be completed for each DD
- Assess and report if the device deficiency could have led to a serious adverse device effect:
    - If either suitable action had not been taken,
    - If intervention had not been made, or
    - If circumstances had been less fortunate
- If an adverse event results from a device deficiency it should be reported on an Adverse Event eCRF
- If possible, the investigational device should be returned to Conformal Medical for analysis. See the Manual of Procedures for device returns.

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
- Unanticipated adverse device effects
- All adverse events of special interest, regardless of seriousness, as defined above

12.4 Unanticipated (Serious) Adverse Device Effect (UADE/USADE)

Investigators (or designee) must report any potential unanticipated (serious) adverse device effects to the Sponsor (or Sponsor's representative) and their IRB/REB/EC as soon as possible but no later than within 1 business days after the investigator first learns of the event. Potential UADEs should be reported immediately on the eCRF and to the Sponsor (telephone, email, other). Guidelines of how to report potential UADEs are listed in the Study Manual of Procedures.

If an event is determined by Conformal Medical to be a UADE, the Sponsor will report the event to the FDA and other applicable regulatory authorities. The seri the event and will be responsible for notifying FDA, other applicable regulatory authorities, and all participating IRB/ REB/ECs (or other, as required) and all investigators.

12.5 Serious Health Threat (SHT)

Per ISO 14155:2020, a serious health threat is a signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons.

NOTE 1: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.

12.6 Safety Event Reporting Timelines for Investigational Sites

Event	Timeline to Report to Conformal Medical	How to Report
Adverse Event (AE) / Adverse Device Effect (ADE)	Within 10 business days, or as soon as is feasibly possible upon awareness of the event	eCRF
Serious Adverse Event (SAE) / Serious Adverse Device Effect (SADE)	Within 2 business days of awareness of the event	eCRF
Unanticipated Adverse Device Effect (UADE) / Unanticipated Adverse Device Effect (USADE)	Within 2 business day of awareness of the event	email to sponsor

Device Deficiency	Within 2 business days of awareness of the event	eCRF

NOTE: If the eCRF is not available, the site should notify the Sponsor via email within the associated timeline(s) above based on date of awareness of event.

Email Notification: Safety@conformalmedical.com

The email should include the Subject ID, date of awareness of the event, date of onset of symptoms, the AE term, the seriousness, the relatedness to the investigational device and/or procedure, any actions taken, and the outcome, if known.

12.7 Expected Adverse Events – Risk/Benefit Analysis

The device and procedure are both associated with risks. Below is a summary of the expected risks that may occur. They are divided between those events associated with the procedure versus those associated with the CLAAS system. There may be additional risks that are unknown at this time. Risks associated with concomitant medications related to LAAO index procedure may be outlined in the informed consent form, if required by local IRB/REB/EC or equivalent.

12.7.1 Procedural Risks: The risks of delivery of the CLAAS device are like those of other procedures that require a transseptal puncture, TEE and transcatheter delivery of an implant through the venous system, across the interatrial septum, and into the left atrium using a large bore catheter (e.g., EP procedures and/or other LAA devices such as WATCHMAN and Amulet). These risks are well recognized and experienced clinicians that are well versed in the use of large bore catheters have mitigated these risks to the extent possible in their standard of care. The recognized procedural risks observed in prior studies with CLAAS and other LAAO products include (in alphabetical order):

- Acute Kidney Injury potentially requiring need for dialysis
- Air embolus
- Allergic reaction to contrast media necessary for imaging during procedure
- Anesthesia risks (e.g., nausea/vomiting, aspiration pneumonia)
- Arrhythmia
- Bleeding/anemia requiring transfusion
- Cardiac Perforation, Puncture, Tamponade, and/or Effusion requiring drainage and/or “open heart” surgery
- Chest pain/angina
- Damage to cardiac structure (e.g., valve, chordae)
- Death

- Deep Vein Thrombosis or Pulmonary Embolism
- Dyspnea
- Electrolyte imbalance
- Fever
- Heart Failure
- Hematuria
- Hemodynamic Instability (hypotension/hypertension)
- Hemothorax
- Iatrogenic ASD requiring treatment
- MI including ST segment elevation
- Pericardial Effusion/tamponade
- Pleural Effusion
- Pulmonary Edema
- Respiratory failure
- Stroke/TIA or Systemic embolization
- Systemic Infection including pneumonia
- TEE/intubation risks including throat pain, trauma to airway or esophagus with or without bleeding
- Thrombocytopenia
- Thromboembolic event
- Venous access site complications including pain, AV fistula, pseudoaneurysm, infection, hematoma, bleeding requiring transfusion and/or the need for surgical repair

12.7.2 Device Risks: In addition to the risks of undergoing an interventional procedure, there should be consideration to the risks which are specific to the CLAAS Implant and CLAAS Delivery System. Conformal Medical has identified a set of risks that the rates of which may be different due to the design of the CLAAS system as outlined below. A number of the risks have been determined to be present with other interventional (e.g., WATCHMAN or Amulet) as well as surgical implants designed to occlude the LAA. These risks include but are not limited to:

- Arrhythmias
- Cardiac perforation, puncture, tamponade, and/or effusion caused by device
- Chest pain
- Deep Vein Thrombosis or Pulmonary Embolism

- Death
- Device embolization or thrombosis
- Device malfunction/breakage resulting in the inability to reposition, recapture or retrieve requiring further intervention
- Device manipulation resulting in the inability to reposition, recapture or retrieve requiring further intervention
- Device migration requiring intervention
- Infection
- Heart Failure
- Major bleed requiring transfusion
- Myocardial Erosion
- Prolonged procedure time risk
- Re-intervention due to incomplete seal
- Re-intervention to remove device
- Residual leak in LAA
- Stroke/TIA or Systemic embolization
- Thrombus formation

12.8 Methods to Minimize Risks

Extensive risk management activities have been conducted during the development of the CLAAS System to identify and analyze known and foreseeable hazards and reasonably foreseeable sequences or combinations of events that could result from using this product and the risks associated with each hazard. Mitigations have been implemented in the design, processes, and/or labeling and Instructions for Use of the product to reduce the residual risk of each hazard to levels that are as low as reasonably practicable.

The clinical investigational plan is specifically designed to manage and minimize risks through the selection of qualified and experienced investigators, thorough training of investigators and the investigational team, careful subject selection, adherence to pre-determined time points to assess subject clinical status, and regular clinical monitoring visits by Sponsor-appointed monitoring personnel. In addition, an independent Data Safety Monitoring Board will review accumulating safety data at regular intervals to monitor for the incidence of serious adverse events that would warrant modification or termination of the trial. Also, an independent Clinical Events Committee will meet regularly to adjudicate the relationship of site-reported adverse events to the investigational device and procedure.

12.9 Potential Benefits

The targeted subject population consists of patients presenting with non-valvular atrial fibrillation, and who are at increased risk for stroke and systemic embolism and are recommended for OAC

therapy but have an appropriate rationale to seek a non-pharmacological alternative to OAC, and who have been deemed appropriate for LAA closure by the Site PI and a physician not on the interventional team or an advanced provider using a shared decision-making process. Compared with LAA closure with a commercially available device, LAA closure with the CLAAS System may offer a simpler, safer implantation procedure and an increased likelihood of achieving successful closure.

Subjects in the CONFORM Pivotal Trial may not derive any direct benefit from their participation in the trial; however, subjects may gain satisfaction from having made an altruistic contribution to medical science, and the results of the trial may contribute to improved treatments that could benefit future patients who require LAA occlusion for the prevention of stroke and systemic embolism.

12.10 Benefit-Risk Assessment

A risk analysis of the CLAAS System has been performed and concluded that the identified risks have been reduced to a level as low as reasonably practicable. When combined with the risk management measures incorporated into the design of the clinical trial, the potential benefits of the clinical use of the CLAAS System in the CONFORM Pivotal Trial are judged to justify the potential risks to study participants. The potential benefits and risks of study participation will be evaluated on an individual basis and discussed with each subject prior to enrollment in the study.

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.

13 Study Committees and Safety Oversight

13.1 Executive Committee

The Executive Committee will be comprised, at a minimum, of the Principal Investigators, one or more representatives from the Imaging Core Labs, and one or more Sponsor Representatives. The Executive Committee will be responsible for scientific and operational management of the trial and will meet regularly prior to and during the trial to monitor trial progress and make recommendations related to potential modifications/enhancements to the investigational plan.

13.2 Clinical Events Committee (CEC)

An independent Clinical Events Committee (CEC) will adjudicate all site-reported potential endpoint events and any other events the Sponsor deems necessary, in an ongoing fashion during the trial. Relationship of these events to the assigned device and/or procedure will also be adjudicated, and sub-classified as implant-related, delivery system-related or study medication related (anti-coagulation or antithrombotic) or related to a comorbid condition. The committee will include at least three voting members consisting of qualified physicians (cardiologists, interventional cardiologists, electrophysiologists and/or neurologist) experienced in clinical trials who are otherwise independent of the Sponsor and the conduct of the study. Members will also be selected with consideration of their experience in the conduct of clinical trials and prior participation on a Clinical Events Committee.

Members will not have scientific, financial, or other conflicts of interest related to Conformal Medical, Inc. or the Investigator(s). The CEC will operate and conduct all meetings and event

reviews independent of the Sponsor unless specific expert knowledge regarding the characteristics or function of the study device is requested by the CEC from the Sponsor.

The adjudication process, event definitions and required source document materials for each type of event will be pre-specified prior to the onset of the trial. The CEC members will review data collected from all relevant medical records, as well as all imaging study reports associated with an event to perform adjudication. All adjudication decisions will be made by the CEC in an independent and blinded fashion (to the extent possible) based upon review of all available medical evidence. Treatment assignment to investigational device/control device will be de-identified in any source documentation reviewed by the CEC to maintain blinding and reduce any potential bias.

13.3 Data Safety Monitoring Board (DSMB)

An independent Data Safety Monitoring Board (DSMB) will be responsible for the oversight and safety monitoring of the study. The DSMB will advise the Sponsor regarding the continuing safety of the trial subjects and those yet to be recruited to the trial, as well as the continuing validity and scientific merit of the trial. The DSMB will include qualified cardiovascular trained physicians and a biostatistician with expertise in the study procedure and in clinical trials who are otherwise independent of the Sponsor and the conduct of the study, and do not have scientific, financial or other conflicts of interest related to Conformal Medical, Inc. or the Investigator(s).

During the enrollment phase of the trial, the DSMB will review accumulating safety data at regular intervals to monitor for the incidence of serious adverse events that would warrant modification or termination of the trial.

Any DSMB recommendations for study modification or termination prompted by concerns regarding subject safety or issues relating to data monitoring or quality control will be submitted in writing to the Sponsor for consideration and final decision. However, if the DSMB, at any time, determines that a potential serious risk exists to subjects in this trial, the DSMB will immediately notify the Sponsor.

DSMB responsibilities, personnel, procedures, and data review content and frequency will be outlined in the DSMB Charter.

13.4 Core Laboratories

Independent Imaging Core Laboratories will be utilized to analyze echocardiogram and CT imaging during the trial. Echocardiograms performed during and after the implant procedure and CT performed at 12-M follow-up; or at the request of Conformal, will be de-identified and reviewed by the Core Labs. Members of the Core Lab will have no affiliation with the CONFORM Pivotal Trial. The Manual of Procedures provides all Core Lab instructions for image acquisition as well as image uploading.

14 Statistical Considerations and Analysis Plan

Key statistical information is provided below. Additional details, including plans for handling missing data, poolability, subgroup analyses, and sensitivity analyses are outlined in a separate standalone Statistical Analysis Plan.

14.1 Sample Size Rationale

14.1.1 Effectiveness Endpoint

The sample size is driven by the power requirements for the primary effectiveness endpoint and was determined via simulation.

The 18-month study endpoint is defined as the composite of ischemic stroke or systemic embolism through 18 months. The estimated event rate used for power calculations is 4.14%. The estimated rate has been derived from the reported rate for WATCHMAN FLX through 12 months and Amulet through 18 months as described below.

The 12-month CEC-adjudicated major clinical event rates of 2.6% and 0.3% were reported for ischemic stroke and systemic embolism respectively (21) for WATCHMAN-FLX, which is the most prevalent product in use). The values of 2.6% and 0.3% were summed to produce a 12-month estimated rate of 2.9%. A linearized rate over the time from between 12 and 18 months was calculated to arrive at the final estimated anticipated rate of 4.4%. This reflects a 50% increase in the event rate from 12 to 18 months. For Amulet, the reported rate of ischemic stroke and systemic embolism was reported as 2.8% at 18 months. (26)

It is anticipated that the enrollment of control cases in CONFORM, will comprise approximately 80% WATCMAN-FLX cases and approximately 20% of Amulet cases. Using a weighted average of event rates based on this composition yields an overall estimated rate of 4.1%.

With a non-inferiority margin of 3.2%, and one-sided alpha level of 0.025 the sample size of up to 1600 subjects should provide greater than 85% power for the hypothesis test of non-inferiority accounting for a 10% attrition rate.

A non-inferiority margin of 3.2% is reasonable given precedent of similarly sized margins in previous studies, the expected underlying event rates, and power requirements for the study. For an expected event rate of 4.1%, a 3.2% margin corresponds to a relative increase of 78%.

14.1.2 Safety Endpoint

The planned sample size is expected to provide sufficient power for the hypothesis test for the primary safety endpoint. Specifically, assuming an underlying safety event rate in both groups of 15% (similar to those reported for the Amulet study (26) with a 5.8% non-inferiority margin, a total of approximately 1200 subjects would provide greater than 80% power based on an un-pooled z-test at the one-sided 0.025 alpha level. Given the larger sample size required for the primary effectiveness endpoint, this approximation should be reasonable, and the planned sample size provide a high degree of power. A margin of 5.8% is approximately 38% of the value of the expected rate, reflecting a clinically reasonable non-inferiority margin given the underlying expected event rate.

14.2 Analysis Populations

Section 8.8 describes the different subject classifications in the study. The ITT Randomized population will be used to analyze the Primary Safety and Efficacy Endpoints. Additional analyses of different populations (Attempted and Implanted) will be considered supportive in nature for the Primary Safety and Efficacy Endpoints and will the utilized to examine other

Secondary Endpoints. Additional analyses of populations who receive the Initial CLAAS System vs. the Next Generation CLAAS System will be performed.

14.3 Method of Analysis & Reporting

All endpoints will be reported using appropriate descriptive statistics. Statistics for continuous variables will include sample size, mean, standard deviation, median, interquartile range, minimum, and maximum. Binary variables will be summarized using sample size, frequencies, and percentages.

Analysis will be conducted using SAS (version 9.4 or greater), unless otherwise noted. Additional details will be pre-specified in the formal Statistical Analysis Plan (SAP).

14.4 Baseline Characteristics

The following data will be summarized using descriptive statistics and presented:

- Baseline demographics
- Baseline comorbidities, risk factors, and medical and surgical history, including NYHA and if applicable, anginal status (may be done per standard of care up to 30 days prior to consent)
- Cardiac risk factors and cardiac history
- Procedural characteristics
- Device details

14.5 Study Hypothesis

14.5.1 Primary Effectiveness

The primary effectiveness endpoint will be assessed with the following non-inferiority hypothesis:

H_0: Pt - Pc ≥ 0.032
H_A: Pt - Pc < 0.032

where Pt and Pc are the proportion of subjects with primary effectiveness endpoints in the treatment and control groups respectively at 18 months (study day 547) and 0.032 represents the non-inferiority margin. The hypothesis will be evaluated using a one-sided 97.5% confidence interval for the difference in event rates based on the Kaplan-Meier estimate based on a linear transformation. If the one-sided upper confidence bound for the difference is less than the non-inferiority margin, the objective will be met, and the treatment group will be non-inferior to the control group for the primary effectiveness endpoint.

14.5.2 Primary Safety

The primary safety endpoint will be tested with the following non-inferiority hypothesis test:

H_0: St - Sc ≥ 0.058
H_A: St - Sc < 0.058

where St and Sc are the proportion of subjects with primary safety endpoints in the treatment and control groups respectively at 12 months (study day 365) and 0.058 represents the non-inferiority margin. The hypothesis will be evaluated using a one-sided 97.5% confidence interval for the difference in event rates based on the Kaplan-Meier estimate. If the one-sided upper confidence bound for the difference is less than the non-inferiority margin, the objective will be met, and the treatment group will be non-inferior to the control group for the primary safety endpoint.

14.5.3 Secondary Endpoints

The secondary endpoints defined in Section 8.3.3 will be summarized with descriptive statistics. Hypothesis tests for secondary endpoints are planned to use a gatekeeping approach for specific performance endpoints listed below. All other secondary endpoints will be summarized with descriptive statistics for completeness.

14.5.3.1 Specific Secondary Effectiveness Endpoints with Statistical Hypothesis Testing

Secondary endpoints, along with plans for formal hypothesis testing with type I error control will be described in the Statistical Analysis Plan.

The following endpoints will have formal statistical hypothesis tests with a gatekeeping approach to control the Type I error rate. Each endpoint will be based on a comparison of the treatment and control arms.

1. **Non-inferior closure success** (≤5 mm) **at 45 days**, defined as peri-device residual leak ≤5 mm by TEE as evaluated by an independent core lab. A 3% margin will be used.
2. **Non-inferior closure success** (≤3mm) **at 45-days**, defined as peri-device residual leak ≤3mm on TEE as evaluated by an independent core lab. A 5% margin will be used.
3. **Non-inferior complete closure success at 45 days,** defined as lack of any detectable (>1mm) peri-device residual leak on TEE as evaluated by an independent core lab. A 5% margin will be used.
4. **Superior closure success at 45 days,** defined as peri-device residual leak ≤3mm based on TEE as evaluated by an independent core lab.
5. **Superior closure success at 45 days, device subgroup test:** CLAAS vs. specific control device: defined as lack of any detectable (>3mm) peri-device residual leak on TEE as evaluated by an independent core lab. Tests associated with this endpoint will be performed in descending order of specific control devices (device testing will be performed only for control devices that are used > 20% of cases).
6. **Superior complete closure success at 45 days,** defined as lack of any detectable (>3 mm) peri-device residual leak on TEE as evaluated by an independent core lab.
7. **Superior closure success at 45 days, device subgroup test:** CLAAS vs. specific control device: defined as lack of any detectable (>1mm) peri-device residual leak on TEE

as evaluated by an independent core lab. Tests associated with this endpoint will be performed in descending order of specific control devices (device testing will be performed only for control devices that are used > 20% of cases).

14.6 Additional Analyses

The following data will be summarized using descriptive statistics presented by treatment group in the ITT Randomized, Attempted, and Implanted populations, as applicable:

- Subject enrollment and data compliance by site and visit (data compliance at each visit is the percentage of subjects whose data forms have been collected and entered divided by the percentage of subjects whose forms should have been collected and entered).
- Frequency (number and percentage of subjects) with each type of concomitant medication.
- Frequency (number and percentage of subjects) with each site-reported Treatment Emergent AE overall and by MedDRA system organ class and preferred term (a treatment emergent AE is an AE that started or worsened during or after the index procedure).
- Frequency (number and percent of subjects) with each site-reported Treatment Emergent Serious AE overall and by MedDRA system organ class and preferred term.
- Frequency (number and percent of subjects) with each site-reported Treatment Emergent AE or SAE, by CEC-adjudicated relationship to the investigational device or procedure and CEC-adjudicated sub-classification as implant-related or delivery system-related.
- Protocol deviations (number and percentage of subjects with each deviation type).

Detailed listings on primary and secondary endpoints, site-reported AEs, and protocol deviations will be provided, as necessary.

14.7 Poolability and Subgroup Analyses

All investigational sites will follow the requirements of a common protocol and standardized data collection procedures and forms. Poolability of the primary effectiveness and primary safety endpoints across investigational sites will be evaluated using Cox regression models with fixed effects for treatment, site, and treatment by site interaction. If a p-value for the interaction effect is <0.15, additional exploratory analyses will be performed to understand any variations in outcome by site.

Similar analysis will be performed for geography (US vs. outside of the US) as well as subject subgroups defined by the following baseline characteristics: age, sex, race, ethnicity, CHA2DS2-VASc, HAS-BLED, device type (i.e., Initial CLAAS System, Next Generation CLAAS System, Watchman, Amulet), implant size, and AF pattern, examining the potential interaction of subgroup and treatment group.

14.8 Missing Data Handling

All attempts will be made to limit the amount of missing data. The number of evaluable observations will be reported in analysis so that extent of missing data can be assessed. In addition, survival methods will be used to capture the extent of follow-up data available for subjects who are lost or withdrawn from the study.

Tipping point sensitivity analyses will be performed to assess the impact of missing endpoint status for each of the primary effectiveness and primary safety endpoints. These will be based on a Cox regression model with the imputed endpoint rate for censored subjects varied to determine results that would change the study conclusions. This will incorporate multiple imputation, based on randomly imputing events for censored subjects from the on randomized group specific Kaplan-Meier estimated survival distribution after the censoring time.

14.9 Administrative Analyses

An Administrative Analysis of the 1-year safety data and TEE assessments are planned. Access to this information will be restricted under Confidentially Agreements to prevent disclosure of data from introducing bias. The Administrative Analysis will be performed by an independent unblinded statistician separate from the personnel involved with anything related to study operations. There are no planned sample size or study modifications for the administrative analysis.

14.10 Measures to Minimize Bias

Randomization assignment provides protection against confounders, both measured and unmeasured. Pre-specified endpoints and analysis plans also minimize bias. To decrease the variability of clinical outcome measurements, all site-reported cardiovascular adverse events and all potential endpoint events will be adjudicated by an independent CEC according to standardized endpoint definitions, and the relationship of these events to the study device will also be adjudicated and sub-classified as implant-related or delivery system-related. The CEC will be blinded to the treatment assignment to the extent possible to further minimize bias. In addition, independent imaging core laboratory analysis will provide objective determination of peri-device residual leak, and the presence of thrombus.

15 Publication Policy

Conformal and the Principal Investigator(s) are committed to the publication and widespread dissemination of the results of the study in the scientific community. This study represents a joint effort between the Sponsor and the Principal Investigator(s); as such, the parties agree that the recommendation of any party concerning manuscript or text shall be taken into consideration in the preparation of final scientific documents for publication or presentation. Conformal will submit trial results for publication (regardless of trial outcome) following the conclusion or termination of the trial.

A Publication Agreement will be signed between the principal investigator and the sponsor either as a separate Publication Agreement or within the Clinical Trial Agreement.

The investigator or site may not publish any information that the sponsor believes to be confidential information. The publication of the initial results of the CONFORM Pivotal Trial shall be subject to the review and release of sponsor’s publication committee, which shall confer with the site regarding such publication.

Publication guidelines will be followed according to the International Committee of Medical Journal Editors (ICMJE). Within 21 days of enrollment of the first subject into the CONFORM Pivotal Trial, this clinical trial will be registered on ClinicalTrials.gov. A full report of the pre-specified outcomes, regardless of trial results, will be made public through the ClinicalTrials.gov website according to

the requirements of Section 801 of the FDA Amendments Act. If this clinical trial is terminated early, Conformal will make every effort to hasten the release of the pre-specified outcomes through the ClinicalTrials.gov website.

16 Data Collection and Monitoring

16.1 Data Collection and Monitoring

All required data for this study will be collected on standardized Case Report Forms (CRFs) using an electronic data capture system (EDC). The verification, validations and security of the EDC may be noted in the Data Management Plan and/or related documents. 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.

The investigator (or designated hospital staff) will ensure primary data collection based on source-documented hospital chart reviews.

Monitoring will be performed by the Sponsor and/or its designee(s) to ensure that the investigator and his/her study team conduct the clinical investigation in accordance with contract specifications, this protocol, the Declaration of Helsinki, ICH-GCP, ISO 14155:2020, 21 CFR Part 812, and other applicable FDA (and other regulatory authorities, as applicable) and local regulations, and to ensure adequate protection of the rights and safety of subjects and the quality and integrity of the resulting data. All monitors will receive study-specific training on the Clinical Investigation Plan, the eCRF, and the use of the investigational device in accordance with Sponsor SOPs.

Submitted trial data will be verified against subject charts and other sources containing original records of subject data. Source document verification will occur in accordance with the pre-specified study-specific Monitoring Plan. All study endpoints will be 100% source data verified. The Investigator/institution will permit direct access to source data/documents for trial-related monitoring, audits, IRB/REB/EC review and regulatory inspections to be performed. The frequency of monitoring will be based upon enrollment, study duration and compliance,

Progress of the trial will be monitored by:

- On-site or remote review, as deemed appropriate by the Sponsor
- Telephone communications between site personnel (e.g., Site Investigator, Trial Coordinator) and trial monitors, as appropriate

- Review of CRFs and associated clinical records
- Review of regulatory documents

If a monitor becomes aware of a significant non-compliance with the requirements mentioned above, the Sponsor will be notified by the monitor. The Sponsor will evaluate the non-compliance and may assess if a corrective and preventative action plan is applicable to secure compliance. Immediate actions may be taken to secure compliance and should be documented. If necessary, the Sponsor may halt shipments of the investigational device to the Investigator and terminate the Investigator's participation and enrollment in the investigation. The Investigator will be required to return all unused devices to the Sponsor.

After each monitoring visit, the Monitor will send to the Investigator a letter summarizing the monitoring visit. A monitoring report will be provided to the Sponsor. The report will include the date of the monitoring visit, the site name, the name of the monitor, the name of the Investigator, the names of other individuals present for the monitoring visit, items reviewed during the visit, findings, and any required follow-up action items. The Investigator will be responsible for ensuring that follow-up actions needed to resolve issues at the site are completed in an accurate and timely manner.

Final monitoring visits at the investigational sites will be conducted at the close of the study at the site. The purpose of the final visit is to collect any outstanding study documents, ensure that the Investigator's files are accurate and complete, review record retention requirements with the Investigator, make a final accounting of all study supplies, provide for appropriate disposition of any remaining supplies, and ensure that all applicable requirements are met for the study.

16.2 Source Documentation

Auditors, monitors, IRB/REB/ECs, the Sponsor, and the FDA and other regulatory authorities may have access to the medical records related to this study. Original or certified copies of all relevant clinical findings, observations, and other activities throughout the clinical investigation must be recorded and maintained in the medical file of each enrolled subject (no source documentation will be recorded directly on the CRF). At a minimum, the following must be included in each subject's file:

- Sufficient medical and surgical history and current physical condition, including any medication(s) the subject is taking at the time of the procedure to assess the subject's eligibility;
- The medical file should reveal the subject's participation in this study, including documentation of written informed consent;
- Dated report of the index procedure including medication, material usage, and complications, if applicable;
- Dated reports of the post-procedure / pre-discharge and follow-up assessments;
- Dated results of required laboratory tests;
- Any adverse event(s), the resultant action or treatment, and outcome, if applicable; and

- In the case of withdrawal of informed consent, the reason and subject status at time of withdrawal.

The Site Investigator will permit study-related monitoring, audits, IRB/REB/EC review, and FDA and other applicable regulatory authority inspections by allowing direct access to the source data.

In case of electronic source data, access will be necessary for full safety review. The review will be specific to study subjects and the records that would contain potential safety data.

16.3 Auditing

As a quality assurance measure, investigational sites may be audited during the trial or following trial completion. The purpose of an audit is to provide an independent evaluation of trial conduct and protocol and GCP compliance, separate from routine monitoring or other quality control functions. An audit may be conducted by Conformal Medical personnel (or designee), the IRB/REB/EC, the FDA, or another regulatory body.

Site Investigators are requested to notify the Sponsor if an audit is requested for this study. The site investigator and/or institution shall permit Conformal Medical (or designee) personnel, the IRB/REB/EC and regulatory body representatives' direct access to source data and all other relevant study documents during an audit.

16.4 Data and Record Retention

Study records (i.e., subject records, investigational site file documents, etc.) shall be maintained for a period of at least 15 years or as specified in the Clinical Trial Agreement and local regulations after the clinical investigation with the investigational device in question has ended; or, in the event that the device is subsequently placed on the market, and at least 10 years after the last device has been placed on the market.

17 Device Accountability

Information regarding opened, introduced, and implanted CLAAS devices will be recorded on the applicable CRF. Information regarding opened and introduced delivery systems will also be recorded on the applicable CRF.

Investigational devices will be shipped (or hand-carried) after documentation of site activation is completed and a clinical release form is completed in accordance with Conformal Standard Operating Procedures.

Access to investigational devices will be controlled and the investigational devices will be used only in the clinical investigation and in accordance with the clinical investigation plan. The sponsor will keep records to document the physical location of all investigational devices from shipment of investigational devices to the investigation sites until return or disposal. The sponsor shall have instructions in place and make packaging materials available, if applicable, for the safe return or disposal of investigational devices, including potentially hazardous devices.

The principal investigator, or an authorized designee, shall keep records documenting the receipt, use, return and disposal of the investigational devices, which shall include:

a) name(s) of person(s) who received, used, returned or disposed the device,
b) the date of the receipt, identification and quantity of each investigational device (batch number/serial number or unique code),
c) the expiry date, if applicable,
d) the date or dates of use,
e) subject identification,
f) date on which the investigational device was returned/explanted from subject, if applicable,
g) the date of return of unused, expired or malfunctioning Investigational devices, if applicable.
h) the date and documentation of disposal of the investigational devices as per instructions of the sponsor, if applicable

18 Ethical and Regulatory Considerations

18.1 Applicable Regulations

This trial will be conducted in compliance with this protocol, the Sponsor's standard operating procedures and/or guidelines, FDA regulations concerning the protection of human subjects, e.g., 21 CFR parts 50, 56, and 812, EU MDR (2017/745) Annex XV, ICH GCP guidelines, the Declaration of Helsinki, ISO 14155:2020, or other laws or regulations, if applicable. In the event of conflict between provisions of the cited regulations, the applicable regional or national law or regulation shall prevail.

18.2 IRB/REB/EC

Prior to initiation of the study, the investigator (or designee) will forward copies of the protocol, Investigators Brochure (if applicable), informed consent form and all other appendices to be used for the study to the relevant Institutional Review Board (IRB)/ Research Ethics Board (REB)/Ethics Committee (EC) for review and approval. A copy of the written IRB/REB/EC approval must be provided to the Sponsor (or designee) and should include the following:

- A statement of IRB/ REB/EC approval for the proposed study at the institution;
- The date the study was approved and the duration of approval (if applicable);
- Identification of the approved documents including version dates and/or other references. At a minimum, the following documents should be listed:
    - Study protocol
    - Subject informed consent form
    - Any additional written information to be provided to the subject
- A listing of any conditions attached to the approval (if applicable);
- Identification of the approved Principal Investigator; and
- The signature of the IRB/ REB/EC chairperson.

Any amendments to the protocol, as well as possible associated information and consent form changes, will be submitted to the IRB/REB/EC and written approval obtained prior to implementation. The IRB/REB/EC may request additional requirements, in which case the Sponsor shall review and assess if implementation is applicable. Substantive changes will be submitted to the FDA and other regulatory authorities for approval prior to implementation, and the FDA and other regulatory authorities will be notified of any changes not requiring approval according to applicable guidelines.

18.3 Regulatory Approval

The Sponsor is responsible for obtaining FDA and other regulatory authority approval where applicable to conduct the study according to regulatory requirements. Investigators may not commence enrollment of subjects until they have met any local IRB/REB/EC and hospital management requirements and have received confirmation from the Sponsor that the appropriate regulatory approvals have been obtained.

18.4 Records and Reports

Sponsor and investigator will maintain records related to this study for a period of at least 15 years or as specified in the Clinical Trial Agreement and local regulations after the clinical investigation with the investigational device in question has ended, or, if the device is subsequently placed on the market, and at least 10 years after the last device has been placed on the market.

Records maintained by the Sponsor will include:

- All essential correspondence related to the clinical trial
- Investigator Signature Page
- Curriculum vitae for each Investigator
- Records of device shipment and disposition (shipping receipts, material destruct records, etc.)
- Adverse event and complaint information
- All data forms prepared and signed by the Investigators, and all received source documentation and core laboratory reports
- Clinical Investigation Plan (CIP) and any amendments
- Site monitoring reports
- Financial disclosure information
- Investigator/Clinical Trial Agreement(s), which may outline specific roles and obligations of the investigator, site and the Sponsor, etc.

Records maintained by each site Principal Investigator (the investigator may delegate responsibility for record maintenance to a member of his/her study team, but remains the ultimate responsible person) will include:

- All essential correspondence related to the clinical trial

- Device use/disposition records
- Records of each subject's case history and exposure to the device. Case histories include the CRFs and supporting data (source documentation).
- Investigator Signature Page
- Curriculum vitae
- Clinical Investigation Plan (CIP) and any amendments
- Informed Consent documentation

The Sponsor and Site Investigators are each responsible for the preparation, review, and submission of all required reports in accordance with local laws and regulations, the requirements of the FDA and other regulatory authorities as applicable, and the requirements of local IRB/REB/ECs.

18.5 Protocol Amendments

Any protocol amendments will be approved by the Sponsor, the IRB/REB/EC and any necessary regulatory body before it can be implemented. Substantive changes will be submitted to the FDA (and other regulatory authorities, as applicable) for approval prior to implementation, and the FDA (and other regulatory authorities as applicable) will be notified of any changes not requiring approval in accordance with relevant guidelines.

18.6 Informed Consent

Informed consent will be obtained and documented as described previously prior to the performance of any study-specific procedures or assessments in accordance with 21 CFR Part 50, other applicable laws and regulations, and local IRB/REB/EC requirements.

18.7 Termination of the Study

The Sponsor reserves the right to terminate the study but intends only to exercise this right for valid scientific or administrative reasons and reasons related to protection of subjects. Possible reasons for early trial termination include:

- Unanticipated Adverse Device Effects (UADEs) present an unreasonable risk to subjects
- Recommendation from the DSMB
- Sponsor decision to suspend or discontinue development of the device

If the trial is terminated early, the Sponsor will provide a written statement to the Investigators to enable notification of the IRB/REB/ECs. The Sponsor will also inform the FDA (and other regulatory authorities where required). In the case of early termination of trial enrollment, follow-up visits will continue for all enrolled subjects.

The Sponsor may terminate an investigators or site's participation in the study if there is evidence of an investigator's failure to maintain adequate clinical standards or evidence of an investigator or staff's failure to comply with the protocol. Should investigator or site participation be considered for termination, the Sponsor (or designee) will ensure appropriate follow-up for any subjects enrolled, including transferal to the supervision of an approved investigator and approval of

transfer of subject oversight and follow-up by the appropriate IRB/REB/EC. Notification of study site suspension or termination will occur no later than five (5) working days after the Sponsor makes the determination. A suspended or terminated study site may not be reinitiated without approval of the reviewing IRB/REB/EC. The investigator should notify the IRB/REB/EC in writing as soon as possible but no later than within 10 days if the premature termination is related to safety or compliance issues. The same procedure will be applied to other applicable regulatory authorities where required.

18.8 Subject Privacy

The Sponsor affirms and upholds the principle of subject confidentiality. Throughout this study, all data provided to Conformal, or its designee(s) will only be identified by a study-specific subject identification number. “Protected Health Information” will be maintained in compliance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and applicable local regulations.

The investigator agrees that representatives of Conformal, its designee(s), and regulatory authorities may inspect included subjects’ records to verify trial data, provided the data are treated as confidential and that the subject’s privacy is maintained.

18.9 Clinical Trial Insurance

Clinical trial insurance will be secured prior to investigation initiation in accordance with local/national requirements, as applicable.

19 Site and Investigator Selection and Training

19.1 Selection of Study Sites and Investigators

The Sponsor will select Investigators who are qualified by training and experience. Sites will be selected based upon review of a recent site feasibility questionnaire and the qualifications of the Principal Investigator at the site.

Each site will have an interventional cardiologist and/or a cardiac electrophysiologist willing and able to participate in the study. All participating Investigators must have performed ≥25 interventional cardiac procedures that involve transeptal puncture through an intact septum and ≥25 LAAO procedures. Each site will have at least one delegated Echocardiographer (a non-implanting physician) willing and able to participate in the study. All participating investigators will be trained to the protocol and study procedures prior to enrolling subjects.

19.2 Training of Investigators and Research Staff

All Investigators, Echocardiographers, and research staff are required to attend Sponsor training sessions, which may be conducted at an Investigator's meeting, a site initiation visit, or another appropriate venue. Training by telephone, read and acknowledge format, or self-training format may take place per Sponsor’s discretion, as required. Training of Investigators/research staff will include but is not limited to:

- the Clinical Investigation Plan (including imaging acquisition protocols),
- investigational device Instructions for Use,

- eCRF completion,
- adverse event documentation and reporting requirements, and
- investigator and research staff responsibilities.

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.

Neurological assessments may be performed by a non-delegated neurology professional (e.g., board-certified or board-eligible neurologist, neurology fellow, neurology physician assistant, or neurology nurse practitioner, or NIHSS- and/or mRS-certified staff where applicable), as long as assessments are completed as part of standard of care and documentation of current certification is maintained in site Regulatory files.

19.2.1 Specific Investigator Training Requirements

Comprehensive Investigator training will be conducted to ensure that Investigators have a thorough knowledge of the investigational device Instructions for Use, the proper technique for implantation of the CLAAS Implant, and the Clinical Investigation Plan. All participating implanting physicians will receive formal device training prior to their first implant.

All participating investigators will receive formal training on the device prior to first subject in. At a minimum, implanting investigators must receive the following training, unless otherwise noted in site-specific training records:

- CLAAS System Device Training (including review of the Instructions for Use)
    - Device preparation, use and handling
    - Device positioning and deployment
    - Implantation procedure steps and training
- Clinical Investigation Plan Review
    - General procedural and data collection requirements
    - Imaging acquisition requirements and data transfer procedures (Angiography and TEE)

19.2.2 Training Documentation

A training log must be maintained at each site that documents the Investigators and research staff who have completed study-specific training, the training modules completed, and the date the training was completed. No trial-related activities (other than those considered standard of care at the study site) may be performed by investigators or research staff who have not completed study-specific training.

Other training requirements may be specified in the CONFORM Pivotal Manual of Procedures (MOP).

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21 Appendices

21.1 Appendix A: Definitions

<table>
<tr><td>Adverse Device Effect (ADE)</td><td colspan="2">An adverse device effect is an adverse event related to the use of a medical device. This includes:
Any adverse event resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the medical device
Any event that is a result of a use error or intentional misuse</td></tr>
<tr><td rowspan="5">Adverse Event Classifications</td><td colspan="2">21.2 Intensity or Severity
Intensity of an adverse event to be used:</td></tr>
<tr><td>Mild</td><td>Awareness of a sign or symptom that does not interfere with the subject’s usual activity or is transient, resolved without treatment and with no sequelae.</td></tr>
<tr><td>Moderate</td><td>Interferes with the subject’s usual activity and/or requires symptomatic treatment.</td></tr>
<tr><td>Severe</td><td>Symptom(s) causing severe discomfort and significant impact of the subject’s usual activity and requires treatment.</td></tr>
<tr><td colspan="2">21.3 Relatedness
Relationship to the study device or procedure:</td></tr>
<tr><td></td><td>Not related</td><td>Relationship to the device, comparator or procedures can be excluded when:
the event has no temporal relationship with the use of the investigational device, or the procedures related to application of the investigational device;
the serious adverse event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
the discontinuation of medical device application or the reduction of the level of</td></tr>
</table>

		activation/exposure - when clinically feasible -and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious adverse event; - the event involves a body-site or an organ that cannot be affected by the device or procedure; - the serious adverse event can be attributed to another cause (e.g., an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors); - the event does not depend on a false result given by the investigational device used for diagnosis, when applicable; In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious adverse event.
	Possible	The relationship with the use of the investigational device or comparator, or the relationship with procedures, is weak but cannot be ruled out completely. Alternative causes are also possible (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.
	Probable	The relationship with the use of the investigational device or comparator, or the relationship with procedures, seems relevant and/or the event cannot be reasonably explained by another cause.
	Causal Relationship	The serious adverse event is associated with the investigational device, comparator or with procedures beyond reasonable doubt when:

		- the event is a known side effect of the product category the device belongs to or of similar devices and procedures; - the event has a temporal relationship with investigational device use/application or procedures; - the event involves a body-site or organ that • the investigational device or procedures are applied to; • the investigational device or procedures have an effect on; - the serious adverse event follows a known response pattern to the medical device (if the response pattern is previously known); - the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious adverse event (when clinically feasible); - other possible causes (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out; - harm to the subject is due to error in use; - the event depends on a false result given by the investigational device used for diagnosis10, when applicable; In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious adverse event.

21.4 Outcome

The clinical outcome of the AE or SAE will be characterized as follows:

Death/Fatal	The SAE CRF must be completed for this outcome

	<table><tr><td>Recovered/Resolved</td><td>The subject returned to baseline status</td></tr><tr><td>Ongoing</td><td>Subject did not recover, and symptoms continue</td></tr><tr><td>Recovered/Resolved with sequelae</td><td>The subject has recovered but with clinical sequelae from the event</td></tr><tr><td>Unknown</td><td>The subject outcome is unknown</td></tr></table> **21.5 Treatment or Action Taken** Action taken after the occurrence of an AE or SAE will be reported as: <table><tr><td>Interventional Treatment</td><td>Surgical, percutaneous or other procedure</td></tr><tr><td>Medical Treatment</td><td>Medication dose reduction/interruption or discontinuation, or medication initiated for event</td></tr><tr><td>None</td><td>No action is taken</td></tr></table>
Anticipated Serious Adverse Device Effect (ASADE)	An anticipated serious adverse device effect is a serious adverse device effect which by its nature, incidence, severity, or outcome has been identified in the investigational plan or application (including a supplementary plan or application).
Atrial septal defect (ASD)	Atrial septal defect is defined as a hole in the septum that divides the chambers of the heart. Iatrogenic ASDs that do not warrant closure do not meet adverse event reporting criteria.
Attempted Population	A Randomized subject that has a LAAO Access Sheath inserted into the body to implant the device, but eventually does not receive a device.
Bleeding complications	Defined according to the following BARC definitions(30), and classified as major bleeding (Type 3, 4, or 5) and minor bleeding (Type 2) Type 0: no bleeding Type 1: bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies,

	hospitalization, or treatment by a healthcare professional; may include episodes leading to self-discontinuation of medical therapy by the patient without consulting a healthcare professional Type 2: any overt, actionable sign of hemorrhage (e.g., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for type 3, 4, or 5 but does meet at least one of the following criteria: (1) requiring nonsurgical, medical intervention by a healthcare professional, (2) leading to hospitalization or increased level of care, or (3) prompting evaluation Type 3 Type 3a Over bleeding plus hemoglobin drop of 3 to <5 g/dL* (provided hemoglobin drop is related to bleed) Any transfusion with over bleeding Type 3b Overt bleeding plus hemoglobin drop ≥5 g/dL* (provided hemoglobin drop is related to bleed) Cardiac tamponade Bleeding requiring surgical intervention for control (excluding dental/nasal/skin/hemorrhoid) Bleeding requiring intravenous vasoactive agents Type 3c Intracranial hemorrhage (does not include microbleeds or hemorrhagic transformation, does include intraspinal) Subcategories confirmed by autopsy or imaging or lumbar puncture Intraocular bleed comprising vision Type 4: CABG-related bleeding Perioperative intracranial bleeding within 48 h Reoperation after closure of sternotomy for the purpose of controlling bleeding Transfusion of ≥5 U whole blood or packed red blood cells within a 48-h period (NOTE: cell saver products are not counted) Chest tube output ≥2L within a 24-h period

<table>
<tr><td></td><td>Type 5: fatal bleeding

Type 5a

Probable fatal bleeding; no autopsy or imaging confirmation but clinically suspicious

Type 5b

Definite fatal bleeding; overt bleeding or autopsy or imaging confirmation

NOTES:

Platelet transfusions should be recorded and reported but are not included in these definitions until further information is obtained about the relationship to outcomes. If a CABG-related bleed is not adjudicated as at least a type 3 severity event, it will be classified as not a bleeding event. If a bleeding event occurs with a clear temporal relationship to CABG (i.e., within a 48-h time frame) but does not meet type 4 severity criteria, it will be classified as not a bleeding event.

* Corrected for transfusion (1 U packed red blood cells or 1 U whole blood = 1 g/dL hemoglobin)</td></tr>
<tr><td>Cardiac Perforation</td><td>Puncture or migration of device or accessory through cardiac structure requiring intervention for treatment</td></tr>
<tr><td>Cardiac tamponade</td><td>Evidence of a new pericardial effusion associated with hemodynamic instability and clearly related to the LAA closure</td></tr>
<tr><td>CHA_2DS_2-VASc Score</td><td>A clinical risk stratification scheme for predicting stroke and thromboembolism in patients with nonvalvular AF(31), updated from the earlier $CHADS_2$ score. Patients are assigned a score from 0 to 9 by adding the points for each applicable risk factor below to obtain a total score:

<table>
<tr><th>Risk Factors</th><th>Score</th></tr>
<tr><td>Congestive Heart Failure</td><td>1</td></tr>
<tr><td>Hypertension</td><td>1</td></tr>
<tr><td>Age ≥ 75 years</td><td>2</td></tr>
<tr><td>Diabetes mellitus</td><td>1</td></tr>
<tr><td>Stroke/TIA/thromboembolic event in the past</td><td>2</td></tr>
</table>
</td></tr>
</table>

		Vascular disease (prior MI, PAD, or aortic plaque)	1
		Age 65 to 74 years	1
		Sex **c**ategory (female gender)	1
Closure success	Defined as closure or peri-device residual leak ≤ 5 mm in width on TEE as evaluated by an independent core lab [evaluated at 45 days and 12 months post procedure]		
CNS hemorrhage	NeuroARC defined (29) as any brain, spinal cord, or retinal hemorrhage on the basis of imaging or pathology, not caused by trauma (includes symptomatic intracerebral hemorrhage [Type 1.b], symptomatic subarachnoid hemorrhage [Type 1.c], and covert CNS hemorrhage [Type 2.b])		
CNS infarction	NeuroARC defined (29) as any brain, spinal cord, or retinal infarction on the basis of imaging, pathology, *or* clinical symptoms persisting for ≥24 h (includes ischemic stroke [Type 1.a], ischemic stroke with hemorrhagic conversion [Type 1.a.H], stroke not otherwise specified [Type 1.d], symptomatic hypoxic-ischemic injury [Type 1.e], covert CNS infarction [Type 2.a], and covert CNS infarction with hemorrhagic conversion [Type 2.a.H])		
Complete Closure Success	Defined as closure or lack of any peri-device residual leak on TEE as evaluated by an independent core lab [evaluated at 45 days and 12 months]		
Composite efficacy	Defined as all-cause mortality, all stroke, TIA, and systemic thromboembolism; individual components will also be reported		
Covert CNS injury	Acutely asymptomatic brain or spinal cord injury detected by neuroimaging (NeuroARC Type 2) (29), including: Type 2.a Covert CNS infarction Brain, spinal cord, or retinal cell death attributable to focal or multifocal ischemia, on the basis of neuroimaging or pathological evidence of CNS infarction, without a history of acute neurological symptoms consistent with the lesion location Subtype 2.a.H Covert CNS infarction with hemorrhagic conversion Covert CNS infarction includes hemorrhagic conversions. These should be subclassified as Class A or B when CNS infarction is		

	the primary mechanism and neuroimaging or pathology confirms a hemorrhagic conversion. Class A (Petechial hemorrhage): Petechiae or confluent petechiae within the infarction or its margins, but without a space-occupying effect Class B (Confluent hemorrhage): Confluent hemorrhage or hematoma originating from within the infarcted area with space-occupying effect Type 2.b Covert CNS hemorrhage Neuroimaging or pathological evidence of CNS hemorrhage within the brain parenchyma, subarachnoid space, ventricular system, spinal cord, or retina on neuroimaging that is not caused by trauma, without a history of acute neurological symptoms consistent with the bleeding location
Death	See “mortality”
Device deficiency	Inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance. NOTE: Device deficiencies include malfunction, use error, and inadequate labeling. They may or may not affect device performance or lead to an adverse event.
Device Embolization	Device exiting the LAA without an attachment to tether or cable requiring open surgical removal or additional percutaneous procedure. Devices which embolize during the index procedure are NOT considered device embolization unless they require emergency open surgical procedure.
Device malfunction	Failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the Instructions for Use or protocol. *NOTE: A device malfunction occurs when the device is used in compliance with the Instructions for Use but does not perform as described in the Instructions for Use.*
Device migration	Movement of the LAAO device from its intended position within the left atrial appendage post release.
Device misuse	Any use of the investigational device by an investigator that is contradictory to the application described in the Instructions for

<table>
<tr><td></td><td>Use will be categorized as device misuse. This is a form of Use Error.</td></tr>
<tr><td>Device related thrombus (DRT)</td><td>Thrombus formation on the left atrial face of the LAAO device.</td></tr>
<tr><td>Device success</td><td>Defined as LAAO device deployed and implanted in correct position</td></tr>
<tr><td>DOAC</td><td>Direct oral anticoagulants (DOACs) are a group of direct coagulation factor inhibitors including both direct thrombin inhibitors and direct factor Xa inhibitors. These medications may cause hemostasis assay interference by falsely increasing or decreasing measured values, depending on the analyte (includes: dabigatran, rivaroxaban, apixaban, edoxaban, betrixaban).</td></tr>
<tr><td>Embolic events</td><td>Defined as ischemic stroke as defined by NeuroARC (29) and systemic thromboembolism characterized as any thromboemboli in the arterial system</td></tr>
<tr><td>HAS-BLED Score</td><td>A scoring system to assess the risk of major bleeding in patients with atrial fibrillation receiving oral anticoagulation (OAC) therapy.(32) Patients are assigned a score from 0 to 9 by adding the points for each applicable clinical characteristic below to obtain a total score:
<table>
<tr><th>Clinical Characteristic</th><th>Score</th></tr>
<tr><td>Hypertension (uncontrolled, > 160 mmHg systolic)</td><td>1</td></tr>
<tr><td>Abnormal renal and liver function (1 point each)</td><td>1 or 2</td></tr>
<tr><td>Stroke</td><td>1</td></tr>
<tr><td>Bleeding history or predisposition</td><td>1</td></tr>
<tr><td>Labile INRs in patients taking warfarin</td><td>1</td></tr>
<tr><td>Elderly (> 65 years)</td><td>1</td></tr>
<tr><td>Drugs (concomitant antiplatelet agents or NSAIDs) or alcohol abuse (1 point each)</td><td>1 or 2</td></tr>
</table>
</td></tr>
</table>

Implanted Patient (IP) Population	All subjects who leave the catheterization laboratory after the index procedure with an implanted (Study or Control) device
Intended Population	A Randomized subject that does not have an implant attempt (i.e., a LAAO Access Sheath is never inserted into the body)
Intention to Treat (ITT) Randomized Population	All subjects that sign an informed consent form. In the RCT cohort, the Randomized Population includes all subjects who have signed the Informed Consent who at the time of randomization meet eligibility criteria and are randomly assigned to a Treatment Group
Ischemic stroke	NeuroARC-defined (29) Type 1.a or 1.a.H overt CNS injury: Type 1.a Ischemic stroke Sudden onset of neurological signs or symptoms fitting a focal or multifocal vascular territory within the brain, spinal cord, or retina, that: 1) Persist for ≥24 h or until death, with pathology or neuroimaging evidence that demonstrates either: a) CNS infarction in the corresponding vascular territory (with or without hemorrhage); *or* b) Absence of other apparent causes (including hemorrhage), even if no evidence of acute ischemia in the corresponding vascular territory is detected or 2) Symptoms lasting <24 h, with pathology or neuroimaging confirmation of CNS infarction in the corresponding vascular territory. *Note:* When CNS infarction location does not match the transient symptoms, the event would be classified as covert CNS infarction (Type 2a) and a TIA (Type 3a), but not as an ischemic stroke. Signs and symptoms consistent with stroke typically include an acute onset of 1 of the following: focal weakness and/or numbness; impaired language production or comprehension; homonymous hemianopia or quadrantanopsia; diplopia; altitudinal monocular blindness; hemispatial neglect; dysarthria; vertigo; or ataxia. Subtype 1.a.H Ischemic stroke with hemorrhagic conversion Ischemic stroke includes hemorrhagic conversions. These should be subclassified as Class A or B when ischemic stroke is the

	primary mechanism and pathology or neuroimaging confirms a hemorrhagic conversion. Class A (Petechial hemorrhage): Petechiae or confluent petechiae within the infarction or its margins, but without a space-occupying effect Class B (Confluent hemorrhage): Confluent hemorrhage or hematoma originating from within the infarcted area with space-occupying effect
Major endovascular intervention	Major endovascular intervention includes pseudoaneurysm repair, AV fistula repair, and other major endovascular repair. The following interventions are not considered major endovascular interventions: percutaneous catheter drainage of pericardial effusions, percutaneous retrieval of an embolized device, thrombin injection to treat femoral pseudoaneurysm, and nonsurgical treatments of access site complications.
Major procedure-related complications	Includes any of the following specific events (see individual definitions for each component) (identified within 12 months of procedure and adjudicated as procedure related): • cardiac perforation, • pericardial effusion requiring drainage, • ischemic stroke, • device embolization, • and major vascular complications
Major safety events	Defined as the composite of all-cause mortality, overt CNS injury defined in NeuroARC (29), and major bleeding defined as Barc Type 3-5 (30)
Mortality	Classified as cardiovascular and all-cause mortality through 18 months according to the following ARC definitions. All deaths are considered cardiac unless an unequivocal noncardiac cause can be established. Specifically, any unexpected death even in patients with coexisting potentially fatal noncardiac disease (e.g., cancer, infection) should be classified as cardiac. • Cardiac death: Any death due to proximate cardiac cause (e.g., MI, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, and all procedure-related

	deaths, including those related to concomitant treatment, will be classified as cardiac death. • Vascular death: Death caused by noncoronary vascular causes, such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular diseases. • Noncardiovascular death: Any death not covered by the above definitions, such as death caused by infection, malignancy, sepsis, pulmonary causes, accident, suicide, or trauma.
Myocardial infarction	As defined by VARC-3 (33)and MVARC (34) as described below. These definitions are developed from SCAI (35) and the Fourth Universal MI Definitions (36) evaluating MI in the post procedure as well as follow-up timeframe [evaluated through 7 days post procedure for the purposes of the Primary Safety Endpoint: Peri-procedural MI (≤72 h after the index procedure): • New ischemic symptoms (e.g., chest pain or shortness of breath), or new ischemic signs (e.g., ventricular arrhythmias, new or worsening heart failure, new ST-segment changes, hemodynamic instability, new pathological Q waves in at least two contiguous leads, imaging evidence of new loss of viable myocardium or new wall motion abnormality) AND • Elevated cardiac biomarkers (preferably CK-MB) within 72 h after the index procedure consisting of at least one sample post-procedure with a peak value exceeding 15x upper reference limit for troponin or 5x for CK-MB. If cardiac biomarkers are increased at baseline (>99th percentile), a further increase of at least 50% post-procedure is required AND the peak value must exceed the previously stated limit. Spontaneous MI (>72 h after the index procedure). Any one of the following criteria: • Detection of rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile URL, together with evidence of myocardial ischemia with at least one of the following: ○ Symptoms of ischemia

	○ ECG changes indicative of new ischemia [new ST-T changes or new left bundle branch block (LBBB)] ○ New pathological Q waves in at least two contiguous leads ○ Imaging evidence of new loss of viable myocardium or new wall motion abnormality • Sudden, unexpected cardiac death, involving cardiac arrest, often with symptoms suggestive of myocardial ischemia, and accompanied by presumably new ST elevation, or new LBBB, and/or evidence of fresh thrombus by coronary angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood. • Pathological findings of an acute myocardial infarction.
Neurologic dysfunction without CNS injury	Acutely symptomatic (NeuroARC Type 3 (29)) without CNS injury, including: Type 3.a TIA Transient focal neurological signs or symptoms (lasting <24 h) presumed to be due to focal brain, spinal cord, or retinal ischemia, but without evidence of acute infarction by neuroimaging or pathology (or in the absence of imaging) Type 3.b Delirium without CNS injury Transient nonfocal (global) neurological signs or symptoms (variable duration) without evidence of cell death by neuroimaging or pathology
Neurologic events	See “ischemic stroke,” “Overt CNS Injury,” “Covert CNS Injury,” “Neurological dysfunction without CNS injury,” “CNS infarction,” and “CNS hemorrhage”
NYHA (New York Heart Association) functional capacity	Classified as(37): <u>Class I.</u> Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain. <u>Class II.</u> Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

	Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain. Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.
OAC	Oral Anticoagulant (Coumadin or DOAC)
Overt CNS injury	Acutely symptomatic brain or spinal cord injury (NeuroARC Type 1) (29), including: Type 1.a Ischemic stroke Sudden onset of neurological signs or symptoms fitting a focal or multifocal vascular territory within the brain, spinal cord, or retina, that: 3) Persist for ≥24 h or until death, with pathology or neuroimaging evidence that demonstrates either: a) CNS infarction in the corresponding vascular territory (with or without hemorrhage); *or* b) Absence of other apparent causes (including hemorrhage), even if no evidence of acute ischemia in the corresponding vascular territory is detected Or 4) Symptoms lasting <24 h, with pathology or neuroimaging confirmation of CNS infarction in the corresponding vascular territory. *Note:* When CNS infarction location does not match the transient symptoms, the event would be classified as covert CNS infarction (Type 2a) and a TIA (Type 3a), but not as an ischemic stroke. Signs and symptoms consistent with stroke typically include an acute onset of 1 of the following: focal weakness and/or numbness; impaired language production or comprehension; homonymous hemianopia or quadrantanopsia; diplopia; altitudinal monocular blindness; hemispatial neglect; dysarthria; vertigo; or ataxia. Subtype 1.a.H Ischemic stroke with hemorrhagic conversion

	Ischemic stroke includes hemorrhagic conversions. These should be sub classified as Class A or B when ischemic stroke is the primary mechanism and pathology, or neuroimaging confirms a hemorrhagic conversion. Class A (Petechial hemorrhage): Petechial or confluent petechiae within the infarction or its margins, but without a space-occupying effect Class B (Confluent hemorrhage): Confluent hemorrhage or hematoma originating from within the infarcted area with space-occupying effect Type 1.b Symptomatic intracerebral hemorrhage Rapidly developing neurological signs or symptoms (focal or global) caused by an intraparenchymal, intraventricular, spinal cord, or retinal collection of blood, not caused by trauma Type 1.c Symptomatic subarachnoid hemorrhage Rapidly developing neurological signs or symptoms (focal or global) and/or headache caused by bleeding into the subarachnoid space, not caused by trauma Type 1.d Stroke, not otherwise specified An episode of acute focal neurological signs or symptoms and/or headache presumed to be caused by CNS ischemia or CNS hemorrhage, persisting ≥24 h or until death, but without sufficient evidence to be classified as either (i.e., no neuroimaging performed) Type 1.e Symptomatic hypoxic-ischemic injury Nonfocal (global) neurological signs or symptoms due to diffuse brain, spinal cord, or retinal cell death (confirmed by pathology or neuroimaging) in a nonvascular distribution, attributable to hypotension and/or hypoxia
Pericardial effusion	Pericardial effusion will be classified for severity and time of occurrence according to the following definitions (38): Clinically non-relevant: • Requiring no intervention • Treated pharmacologically Clinically relevant (sub-classified as with or without cardiac tamponade): • Treated with therapeutic pericardiocentesis

	• Treated with surgical intervention • Requiring blood transfusion • Resulting in shock and/or death Time of occurrence: • Intraprocedural: during the index procedure • Acute: <48 hours after the index procedure • Late: ≥48 hours after the index procedure • Very Late: ≥45 days after the index procedure Pericardial Effusion Grading • Small <10mm • Moderate 10-20mm • Large > 20mm Pericardial effusion deemed as small does not meet adverse event reporting criteria.
Patent Foramen Ovale	Patent foramen ovale [PFO] is a remnant of normal fetal anatomy which persists into adulthood and is defined as a communication between the left and right atria at the level of the fossa obalis. PFOs that do not warrant closure do not meet adverse event reporting criteria.
Procedure success	Defined as Technical Success without in-hospital major procedure-related complications (excluding minor device embolization) evaluated at hospitalization or at 7 days whichever is first.
Screen failure	Any subject that has signed informed consent but at any point during the process does not fulfill all eligibility criteria will be considered a Screen Failure.
Serious Adverse Device Effect (SADE)	A serious adverse device effect is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Adverse Event (SAE)	A serious adverse event is an adverse event that: 1. Led to a death 2. Led to a serious deterioration in the health of the subject that:

	a. Resulted in a life-threatening illness or injury b. Resulted in a permanent impairment of a body structure or a body function c. Required in-patient hospitalization or prolongation of existing hospitalization d. Resulted in medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to body structure or a body function 3. Led to fetal distress, fetal death or a congenital abnormality or birth defect.
Systemic Embolism	Acute vascular insufficiency or occlusion of the extremities or any non-CNS organ associated with clinical, imaging, surgical/autopsy evidence of arterial occlusion in the absence of other likely mechanism (e.g., trauma, atherosclerosis, or instrumentation). When there is presence of prior peripheral artery disease, angiographic or surgical or autopsy evidence is required to show abrupt arterial occlusion.(38)
Technical Success	Defined as device success, complete closure or peri-device residual leak ≤5 mm in width on TEE, as evaluated by independent imaging core lab without device-related complications [evaluated post-procedure].
Transient ischemic attack (TIA)	NeuroARC defined (29) as transient focal neurological signs or symptoms (lasting <24 h) presumed to be due to focal brain, spinal cord, or retinal ischemia, but without evidence of acute infarction by neuroimaging or pathology (or in the absence of imaging).
Unanticipated Adverse Device Effect (UADE)	An unanticipated adverse device effect is any serious adverse effect on the health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety or welfare of subjects. NOTE: An anticipated serious adverse device effect (ASADE) is a serious adverse device effect which by its nature, incidence, severity, or outcome has been identified in the investigational plan or application (including a supplementary plan or application).

Use Error	Act or omission of an act that results in a different medical device response than intended by the manufacturer or expected by the user. NOTE 1: Use error includes slips, lapses and mistakes. NOTE 2: An unexpected physiological response of the patient does not itself constitute a use error.
Vascular complications	Based upon VARC-3(33) definitions, classified as major or minor and sub-classified as access site-related or non-access site-related **Major Vascular Complications** **Includes One of the Following:** • Aortic dissection or aortic rupture • Vascular (arterial or venous) injury (perforation, rupture, dissection, stenosis, ischemia, arterial or venous thrombosis including pulmonary embolism, arteriovenous fistula, pseudoaneurysm, hematoma, retroperitoneal hematoma, infection) or compartment syndrome resulting in death, VARC type ≥2 bleeding, limb or visceral ischemia, or irreversible neurologic impairment • Distal embolization (non-cerebral) from a vascular source resulting in death, amputation, limb or visceral ischemia, or irreversible end-organ damage • Unplanned endovascular or surgical intervention resulting in death, VARC type ≥2 bleeding, limb or visceral ischemia, or irreversible neurologic impairment • Closure device failure‡ resulting in death, VARC type ≥2 bleeding, limb or visceral ischemia, or irreversible neurologic impairment **Minor Vascular Complications** **Includes One of the Following:** • Vascular (arterial or venous) injury (perforation, rupture, dissection, stenosis, ischemia, arterial or venous thrombosis including pulmonary embolism, arteriovenous fistula, pseudoaneurysm, hematoma, retroperitoneal hematoma, infection) *not* resulting in death, VARC type ≥2 bleeding, limb or visceral ischemia, or irreversible neurologic impairment

	• Distal embolization treated with embolectomy and/or thrombectomy, *not* resulting in death, amputation, limb or visceral ischemia, or irreversible end-organ damage • Any unplanned endovascular or surgical intervention, ultra-sound guided compression, or thrombin injection, *not* resulting in death, VARC type ≥2 bleeding, limb or visceral ischemia, or irreversible neurologic impairment • Closure device failure‡ *not* resulting in death, VARC type ≥2 bleeding, limb or visceral ischemia, or irreversible neurologic impairment
Vitamin K Inhibitor	Coumadin/warfarin

21.6 Appendix B: Questionnaire for Verifying Stroke-Free Status (QVSFS)

21.7 Appendix C: National Institutes of Health Stroke Scale (NIHSS)

21.8 Appendix D: Modified Rankin Scale (mRS)

21.9 Appendix E: Conscious Sedation Sub-Study Protocol

The Conscious Sedation Single Arm Sub-Study is designed to evaluate the safety and performance of the CLAAS System implantation procedure using conscious sedation.

A. Sub-Study Design

The Sub-Study is a prospective single arm trial evaluating a conscious sedation protocol. The Sub-Study will evaluate the safety and performance of the CLAAS System using conscious sedation in comparison with the device delivery safety and performance observed in the CLAAS arm of the RCT. The Sub-Study will be performed in accordance with all protocol requirements and all subjects will be evaluated for Primary Endpoint based on the product performance at the 45 days post procedure assessment. Enrollment in the Sub-Study will not commence until enrollment in the randomized cohort is complete, initial safety of the CLAAS system is confirmed by the DSMB and FDA approval of the Sub-Study has been granted through an IDE Supplement. All subjects enrolled in the conscious sedation single arm study will follow the same clinical protocol requirements and follow-up as the randomized subjects. The Sub-Study will be identified by an NCT that is separate from the RCT with Roll-in.

B. Eligibility Criteria

The Sub-Study will enroll subjects with the same inclusion and exclusion criteria utilized in the RCT study cohort. These enrollment criteria are provided in Section 8.5 of the RCT protocol.

C. Procedural Requirements

The Sub-Study will be performed using the same procedural and follow up assessments through 45 Days post procedure as outlined in the RCT phase of the study.

D. Screening/Baseline

The following tests and examinations must be performed prior to the index procedure to verify eligibility and to collect baseline study data. Assessments performed as part of standard medical care prior to study enrollment are valid sources of data for verifying study eligibility and collecting baseline study data, provided that the previously performed assessments comply with applicable protocol requirements.

- History and Physical (may be done per standard of **care up to 30 days prior to consent**). Physical assessment to include Height, Weight, Pulse and Blood Pressure.
    - Atrial fibrillation stroke risk assessment with the CHA_2DS_2-VASc scores
- Major bleeding risk assessment with the HAS-BLED score
- Neurological assessment (**within 14 days of index procedure**), to include:
    - Questionnaire for Verifying Stroke-Free Status (QVSFS)
    - NIH Stroke Scale (NIHSS); the NIHSS must be performed by a neurologist or NIHSS-certified research staff
    - Modified Rankin Scale (mRS) to establish the disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological

disability at baseline; the mRS must be performed by a neurologist or research staff who have completed mRS training

- Patients in whom an incident neurologic event is suspected on the basis of the QVSFS, NIHSS, or other signs or symptoms, will require a neurologic examination and evaluation be performed by a neurologist or clinical designee (e.g., neurology fellow).

- Female patients of childbearing potential must have a pregnancy test (by site standard, either serum or urine) performed within 7 days of index procedure
- Laboratory testing per site standard practice as part of a catheterization procedure. Recording of the following Standard of Care labs shall be included as part of the study database: Serum Creatinine or GFR/eGFR; platelet count, HCT/HgB. Lab testing must be collected within 24 hours prior to the index procedure.
- A 12-lead electrocardiogram (ECG). An ECG performed within 30 days prior to the index procedure may be used as the baseline ECG, provided there have been no signs or symptoms of myocardial ischemia between the time of the ECG and the screening assessment (in which case the ECG should be performed within 24 hours prior to the index procedure).
- Brain imaging. For patients with a history of TIA/Stroke, a Brain Scan with MRI or CT is required within 6 months prior to consent. For all subjects with brain MRI scans performed in the 24-month period prior to consent, a repeat the MRI may be required by the Sponsor as a baseline reference, only if there is a suspected neuro event.
- Baseline TTE will be done to confirm subject eligibility and to serve as baseline for any potential adverse event assessments. Cardiac CT or MRI performed within 6 months prior to consent may be used in place of TTE only if all the exclusion criteria can be evaluated with this study. If not, a TTE is required at baseline. If a significant cardiac event occurs after the cardiac imaging which is potentially related to a change in cardiac status (e.g., CHF decompensation), the TTE must be repeated prior to randomization. All cardiac CT images shall be uploaded to the image portal for review by the CT Imaging Core lab. See instructions for the CT imaging guidelines provided by the Core Lab in the Study Manual of Procedures.
- Medication assessment including the use of antiplatelet, anticoagulation, antibiotic medication
- Relevant levels of INR.
- Eligibility Criteria Imaging will be performed to confirm subject eligibility (size, depth, presence of thrombus). Imaging must be performed within 14 days of index procedure.
- Patient must be maintained on anticoagulation during eligibility criteria imaging assessment until index procedure

E. Index Procedure

Trained Conformal representatives may be present during the CLAAS Implant procedure. Site personnel should contact Conformal to schedule the implant procedure with proctor, as necessary.

E.1) Pre-Procedure Medical Therapy

Pre-procedure oral anticoagulation should be managed as per site protocol. Warfarin should be discontinued in accordance with site standard of care practices including INR levels on the day of the procedure.

The following loading doses should be administered prior to the index procedure:

- Aspirin
  - ASA 81-100 mg (administered 1 day prior to procedure), or
  - ASA 325 mg (chewed 1 hour prior to procedure)
- **Antibiotic Prophylaxis**
  - Pre-procedure antibiotic for endocarditis prophylaxis should be administered prior to the procedure as per local standard of care.

E.2) Intraprocedural Medical Therapy

Intraprocedural anticoagulation with heparin should be administered per physician standard practice in accordance with published guidelines and local standards of care, with a goal of maintaining an activated clotting time (ACT) of 250-350 sec throughout the procedure. The highest and lowest intraprocedural ACT measurements shall be recorded in the CRF for all subjects.

Total heparin dose and prophylactic antibiotics administered, including the dose and timing, shall be recorded in the subject's medical record, and recorded on the eCRF.

E.3) Transseptal Puncture

Percutaneous femoral vein access and transseptal puncture should be performed per physician standard practice using a standard commercially available transseptal access system.

E.4) Study Imaging

Eligibility Criteria Imaging, procedural angiographic and ultrasound images will be uploaded using the image submission guidelines outlined in the Study Manual of Procedures.

At any time during the study, ultrasound imaging obtained during a repeat procedure or for diagnostic purposes should also be uploaded for analysis.

E.5) Implant Deployment

Implantation of the CLAAS device should be performed as per the IFU.

Procedural details will be captured as appropriate on the procedural worksheets and subsequently recorded on the eCRF. Any Adverse Events observed, or Device Deficiencies shall also be recorded in the EDC.

The procedure is considered complete once the last venous access sheath is removed or the subject has been discharged from the catheterization lab, whichever is first.

E.6) Anticoagulation/Antiplatelet Therapy Requirements – CLAAS

i) Post-Procedure

- If the final post procedural, post tether release imaging demonstrates adequate seal (residual leak ≤5 mm) and there is no evidence of thrombus, subjects *shall* receive DAPT (ASA 81-100 mg QD and clopidogrel* 75 mg QD) until 45 days post-procedure imaging.
- **If the 45-day TEE demonstrates adequate closure:** DAPT *should* be continued to 6 months; unless deemed unsafe by the subject's physician.

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.

ii) Additional Considerations:

Inadequate seal: Subjects with inadequate seal (residual leak >5 mm) at the post-deployment imaging (or any subsequent imaging) 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 the follow up imaging. Antithrombotic therapy should be individualized to the patient 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 imaging (or any subsequent imaging), the subject should be evaluated for treatment with OAC 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 patient based on clinical (risk of anticoagulation) considerations

iii) Endocarditis Prophylaxis

Appropriate endocarditis prophylaxis is recommended for 6 months following device implantation. The decision to continue beyond 6 months is at the discretion of the principal investigator.

F. Pre-discharge Follow-up

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:

- Physical assessment (Weight, Pulse and Blood Pressure)
- TTE to evaluate for pericardial effusion
- Current concomitant medications documentation. If DAPT has been interrupted or terminated the stop date (and resumption date, if applicable) and the reason for interruption/termination should be recorded.

- A neurological assessment to evaluate neuro status of patient. If the assessment is indicative of a potential neurological deficit, further evaluation by a board-certified neurologist or designee (e.g., neurology fellow) must be performed.
- Adverse event assessment

Prior to hospital discharge, research staff should review the follow-up requirements with the subject to ensure compliance with the subsequent follow-up assessment.

G. 7-day Follow-up + 2 Days (Telehealth Visit)

All subjects must undergo a follow-up assessment on day 7 to 9 post-procedure to enable timely documentation of safety endpoint events.

If the subject has not yet been discharged from the index procedure hospitalization at day 7 post-procedure, the 7-day follow-up may be conducted in-hospital, and no separate telehealth visit is necessary. In clinic visit will satisfy the telehealth visit, if appropriate.

The 7-day follow-up assessment must include:

- Questionnaire for Verifying Stroke Free Status (QVSFS). If any question is answered "Yes," a formal neurologic examination and evaluation must be performed by a board-certified neurologist or clinical designee (e.g., neurology fellow).
- Current concomitant medications documentation. If DAPT has been interrupted or terminated, the stop date (and resumption date, if applicable) and the reason for interruption/termination should be recorded.
- Adverse event assessment.

H. 45-day Follow-up ± 7 Days (Telehealth Visit and Imaging)

All subjects will complete an assessment at 45 days (± 7 days) post-procedure with imaging (TEE) \and clinical evaluation through a minimum of a telehealth visit. The 45-day follow up visit will include the following assessments:

- Questionnaire for Verifying Stroke Free Status (QVSFS) If any question is answered "Yes," a formal neurologic examination and evaluation must be performed by a board-certified neurologist or clinical designee (e.g., neurology fellow).
- A transesophageal echocardiogram (TEE) must be performed in all subjects who left the index procedure with an implanted device. Subjects in whom the TEE demonstrates significant residual leak (>5 mm), or thrombus must undergo a repeat TEE at 6 months. The TEE images will be required to be uploaded in accordance with Core Lab instructions provided in the Study Manual of Procedures.
- Current concomitant medications documentation.
- Adverse event assessment

Prior to concluding the visit, research staff should also review the follow-up requirements with the subject to help ensure study compliance.

NOTE: For subjects who did not leave the index procedure with an implanted device and/or did not have an implant attempt, the 45-day clinic follow-up is the final required follow-up assessment for this protocol, and the TEE imaging assessment is not required. The study exit form should be completed for these subjects at this time.

I. Primary Endpoints:

i) Primary Efficacy:

Successful implantation of the LAAO Device in the LAA with acceptable position, and complete closure or peri-device residual leak ≤5 mm in width on TEE, as evaluated by independent core lab at 45 days post-procedure and without in-hospital major procedure-related complications during hospitalization or at 7 days whichever is first.

ii) Primary Safety:

A composite of Major Procedure-related complications assessed through 45 days (listed below) as adjudicated by an independent Clinical Events Committee as related to either the study device or procedure.

Major Procedure-Related Complications includes any of the following specific events with the specific definitions outlined in Appendix A for each component:

- cardiac perforation,
- pericardial effusion requiring drainage,
- ischemic stroke,
- device embolization,
- major vascular complications

Statistical Considerations:

The sub-study is designed to demonstrate non-inferiority in CLAAS Implant success compared to the CLAAS arm of the RCT, based on the 45-day endpoint assessment. It is estimated that a total sample size of 130 subjects (including 6% attrition) is required to demonstrate non-inferiority. This estimated sample size will be verified and adjusted, if necessary, based on the observed rate of CLAAS Implant success rate in the RCT, prior to initiation of the sub-study.

J. Sample Size Determination

Subjects are enrolled in the Conscious Sedation Sub-Study when the subject has signed informed consent and has the procedure scheduled.

The Conscious Sedation Sub-Study will be analyzed by comparing subjects from the sub-study with subjects who receive the CLAAS Implant from the randomized cohort. The primary endpoint for the Sub-Study is Procedure Success at 45-days, defined as:

- successful implantation of the LAAO Device in the LAA with acceptable position, and complete closure or peri-device residual leak ≤5 mm in width on TEE, as evaluated by independent core lab [at 45 days post-procedure] and without in-

hospital major procedure-related complications during hospitalization or at 7 days whichever is first.

The goal of the Sub-Study will be to demonstrate non-inferiority between the two procedural techniques based on the Procedure Success at 45-day endpoint.

The endpoint will be assessed with the following non-inferiority hypothesis:

H_0: Pt - Pc ≤ -0.10
H_A: Pt - Pc > -0.10

where Pt and Pc are the proportion of subjects with Procedure Success at 45-days in the treatment and control groups respectively and 0.10 represents the non-inferiority margin. The hypothesis will be evaluated using a one-sided 95% confidence interval for the difference in proportions based on a Farrington-Manning non-inferiority test. If the one-sided upper confidence bound for the difference is less than the non-inferiority margin, the objective will be met, and the treatment group will be non-inferior to the control group for the primary effectiveness endpoint.

It is anticipated that the Procedure Success for the CLAAS procedure with general anesthesia will be between 90-95%. As such, using a non-inferiority margin of 10%, and a one-sided 0.05 alpha level, a total of 130 subjects (including attrition of 6%, e.g., 122 evaluable subjects) in a conscious sedation sub study versus approximately 600 CLAAS subjects from the overall randomized RCT would provide greater than 90% power. Calculations are based on a Farrington-Manning test of non-inferiority for binomial proportions.

The final statistical details will be confirmed as an amendment to the Statistical Analysis Plan prior to the enrollment of Sub-Study subjects.

Tab Name: 6 Informed Consent Templates

No documents behind this tab

Tab Name: 7 IRB Documents

No documents behind this tab

Tab Name: 8 Training Materials

CONFORM Pivotal Trial

CLAAS® LAAO Implant

INVESTIGATOR'S BROCHURE

Conformal Medical, Inc.

Revision History:

Revision	Date	Description
A	15-Aug-2023	Initial Release
B	27-Nov-2023	• Added Section 7, summary of procedures and assessments, and protocol deviation language. • Contract manufacturer information added to section 1.2 and section 8.

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1 GENERAL INFORMATION

1.1 Sponsor Information

Name:	Conformal Medical, Inc.
Address:	15 Trafalgar Square, Suite 101 Nashua, NH 03063 USA
Telephone Number:	+1 (603) 718-8742

1.2 Manufacturer Information

Legal Manufacturer Name:	Conformal Medical, Inc.
Address:	15 Trafalgar Square, Suite 101 Nashua, NH 03063 USA
Telephone Number:	+1 603-718-8742

Contract Manufacturer Name:	Biomerics Advanced Catheter
Address:	10351 Xylon Avenue N. Suite 100/150 Brooklyn Park, MN 55445
Telephone Number:	+1 763-428-0010

1.3 Device Name, Risk Classification and Classification Rule

Device Trade Name:	CLAAS® System
Risk Classification:	Class III
Applicable Rule:	Implantable Device. Rule 8
Rule Description:	Class III - All implantable devices and long-term-surgically invasive devices (including those intended to be used in direct contact with the heart, the central circulatory system or the central nervous system)

1.4 Intended use / Indications for Use

The CLAAS® System is intended to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who:

- Are at increased risk for stroke and systemic embolism based on CHADS2 or CHA2DS2-VASc scores and are recommended for oral anticoagulation (OAC) therapy; AND
- Are deemed by their physician to be suitable for OAC; AND
- Have an appropriate rationale to seek a non-pharmacological alternative to OAC, taking into account the safety and effectiveness of the device compared to OAC

1.5 Confidentiality Statement

This Investigator's Brochure contains confidential information for use by the principal investigators and their designated representatives participating in this clinical investigation. It should be held confidential and maintained in a secure location. It should not be copied or made available for review by any unauthorized person or firm.

1.6 General Principle for Conduct of Clinical Research

The investigation is in compliance with the Good Clinical Practice (GCP) standards for clinical studies and conforms with:

- ISO 14155:2020
- The Declaration of Helsinki

2 EXECUTIVE SUMMARY AND BACKGROUND

Atrial fibrillation (AF) is the most common, clinically significant, cardiac tachyarrhythmia, affecting more than 33 million patients worldwide, with a projected incidence of 5 million patients per year.(1) In the United States alone, approximately 6 million individuals suffer from AF and over one million new cases are diagnosed annually; due to the aging population, the number is expected to double by the year 2030.(2, 3)

AF is associated with a substantially increased risk of stroke and thromboembolic events, primarily due to the Left Atrial Appendage (LAA) serving as a site for thrombus formation(4). Untreated patients with AF have a 2-5% annual incidence of stroke, with a history of stroke or thromboembolic events conferring an even higher risk.(5, 6) Strokes that occur with AF are large and can be quite debilitating, leading to death or costly and painful rehabilitation as well as adding significant financial burden to the medical system.

2.1 Current Standard of Care to Treat Atrial Fibrillation

The standard treatment for stroke prevention in subjects with AF is oral anticoagulant (OAC) therapy to reduce the likelihood of clot formation, which is recommended regardless of the management strategy of the underlying rhythm disorder.(7) Options include warfarin and the direct oral anticoagulants (DOACs) (dabigatran, rivaroxaban, apixaban, and edoxaban).(8-11) While pharmacotherapy can reduce stroke incidence in AF by approximately 60%,(12) OAC therapy is associated with an increased risk of bleeding complications,(13) an issue of significant concern due to the high bleeding risk of many AF patients. In addition, management of OAC therapy is burdensome and long-term compliance is poor, leaving patients at risk for embolic events.

Echocardiographic evidence that the LAA is the source of thrombi in more than 90% of patients with AF has prompted the development of novel transcatheter therapies to occlude the LAA, (14-18) The WATCHMAN® Left Atrial Appendage Closure Device (Boston Scientific Corporation, Marlborough MA) was the first Left Atrial Appendage Occlusion (LAAO) device to be extensively studied in patients. The WATCHMAN device is a self-expanding nitinol structure with a polyethylene face. The device is constrained within the delivery system until deployment within the LAA. Randomized clinical trials demonstrated the WATCHMAN to have acceptable benefit to risk ratios for LAA closure in patients with non-valvular AF and a high risk for stroke or systemic embolism and an appropriate rationale to seek a non-pharmacologic alternative to oral anticoagulation.(7, 19) The WATCHMAN device received FDA approval in March 2015 on the basis of data from the PROTECT-AF(20) and PREVAIL (19) randomized clinical trials and associated continued access registries that demonstrated that the device was non-inferior to warfarin for the primary composite endpoint of stroke, systemic embolism, or cardiovascular death. In addition, when compared to the warfarin control arm, patients receiving the WATCHMAN device had approximately 80% reduction in hemorrhagic strokes and a >50% reduction in cardiovascular death. (7, 19)

A second-generation WATCHMAN Device, the WATCHMAN FLXTM, was developed to simplify LAAO and was studied in the Pinnacle Study, a single arm study which showed comparable performance0F. (21) Based on the Pinnacle study results, the WATCHMAN FLX received FDA approval in July 2020.(22)

Recently, Abbott Laboratories (Abbott Park, IL) received FDA Approval for the Amplatzer Amulet Left Atrial Appendage Occluder.(23) The Amulet consists of a lobe and disk connected by a flexible waist and is constructed from a nitinol mesh and a polyester patch. The Amulet is deployed using a similar procedure as the WATCHMAN and comes in 8 sizes3F.(24)

While LAA closure with the WATCHMAN and Amplatzer devices represents an important advance in stroke prevention for patients with AF, important limitations remain. These include the need for precise measurement of LAA diameter and depth, precision coaxial delivery, frequent residual leaks and anatomic features which make LAAO difficult to achieve.

The stroke risk for patients with AF has been extensively studied. The Swede AFib study examined the stroke risk in 180,000 untreated AF patients from 2005-2008 and further validated the CHA2DS2-VASc as seen in Figure 1 below.(25)

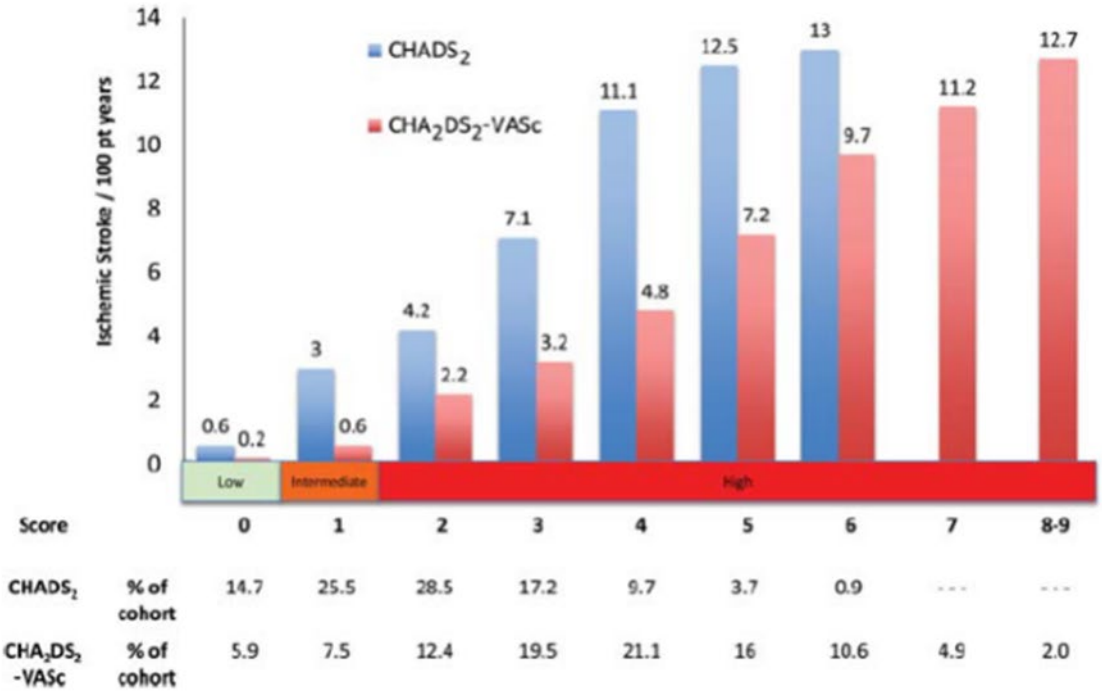

Figure 1: Extracted from European Heart Journal (2012) 33, 1500–1510(25)

These data have allowed prediction of the rate of strokes for patients enrolled in the CONFORM Trial if untreated medically or without LAAO. Assuming a CHA2DS2-VASc score of 4.5 (the observed score reported for patients recruited to the AMULET(26) and Pinnacle Trials(21)) the stroke risk is ~6% per year based upon the Swede Study. We expect the stroke risk to be similar in patients who are enrolled in the CONFORM Trial. The poor acceptance of OAC was also highlighted by the Swedish study which showed

that >45% of patients with indication for OAC (CHA2DS2-VASc ≥2) were untreated. This data underscores the need for alternatives to traditional pharmacologic treatment such as LAAO. Presently, there are only two LAAO implantable devices available that have the limitations listed above. Therefore, additional options for patients and caregivers are needed.

3 DEVICE AND PROCEDURE RISKS

The device and procedure are both associated with risks. Below is a summary of the expected risks that may occur. They are divided between those events associated with the procedure versus those associated with the CLAAS system. There may be additional risks that are unknown at this time.

Procedural Risks: The risks of delivery of the CLAAS device are like those of other procedures that require a transseptal puncture, TEE and transcatheter delivery of an implant through the venous system, across the interatrial septum, and into the left atrium using a large bore catheter (e.g., EP procedures and/or other LAA devices such as WATCHMAN and Amulet). These risks are well recognized and experienced clinicians that are well versed in the use of large bore catheters have mitigated these risks to the extent possible in their standard of care. The recognized procedural risks observed in prior studies with CLAAS and other LAAO products include (in alphabetical order):

- Acute Kidney Injury potentially requiring need for dialysis
- Air embolus
- Allergic reaction to contrast media necessary for imaging during procedure
- Anesthesia risks (e.g., nausea/vomiting, aspiration pneumonia)
- Arrhythmia
- Bleeding/anemia requiring transfusion
- Cardiac Perforation, Puncture, Tamponade, and/or Effusion requiring drainage and/or "open heart" surgery
- Chest pain/angina
- Damage to cardiac structure (e.g., valve, chordae)
- Death
- Deep Vein Thrombosis or Pulmonary Embolism
- Dyspnea
- Electrolyte imbalance
- Fever
- Heart Failure
- Hematuria
- Hemodynamic Instability (hypotension/hypertension)
- Hemothorax
- Iatrogenic ASD requiring treatment
- MI including ST segment elevation
- Pericardial Effusion/tamponade
- Pleural Effusion
- Pulmonary Edema
- Respiratory failure
- Stroke/TIA or Systemic embolization
- Systemic Infection including pneumonia
- TEE/intubation risks including throat pain, trauma to airway or esophagus with or without bleeding
- Thrombocytopenia
- Thromboembolic event

- Venous access site complications including pain, AV fistula, pseudoaneurysm, infection, hematoma, bleeding requiring transfusion and/or the need for surgical repair

Device Risks: In addition to the risks of undergoing an interventional procedure, there should be consideration to the risks which are specific to the CLAAS implant and CLAAS Delivery System. Conformal Medical has identified a set of risks that the rates of may be different due to the design of the CLAAS system as outlined below. A number of the risks have been determined to be present with other interventional (e.g., WATCHMAN or Amulet) as well as surgical implants designed to occlude the LAA. These risks include but are not limited to:

- Arrhythmias
- Cardiac perforation, puncture, tamponade, and/or effusion caused by device
- Chest pain
- Deep Vein Thrombosis or Pulmonary Embolism
- Death
- Device embolization or thrombosis
- Device malfunction/breakage resulting in the inability to reposition, recapture or retrieve requiring further intervention
- Device manipulation resulting in the inability to reposition, recapture or retrieve requiring further intervention
- Device migration requiring intervention
- Infection
- Heart Failure
- Major bleed requiring transfusion
- Myocardial Erosion
- Prolonged procedure time risk
- Re-intervention due to incomplete seal
- Re-intervention to remove device
- Residual leak in LAA
- Stroke/TIA or Systemic embolization
- Thrombus formation

3.1 Methods to Minimize Risks

Extensive risk management activities have been conducted during the development of the CLAAS device to identify and analyze known and foreseeable hazards and reasonably foreseeable sequences or combinations of events that could result from using this product and the risks associated with each hazard. Mitigations have been implemented in the design, processes, and/or labeling and Instructions for Use of the product to reduce the residual risk of each hazard as far as possible.

The clinical investigational plan is specifically designed to manage and minimize risks through the selection of qualified and experienced investigators, thorough training of investigators and the investigational team, careful subject selection, adherence to pre-determined time points to assess subject clinical status, and regular clinical monitoring visits by Sponsor-appointed monitoring personnel. In addition, an independent Data Safety Monitoring Board will review accumulating safety data at

regular intervals to monitor for the incidence of serious adverse events that would warrant modification or termination of the trial. Also, an independent Clinical Events Committee will meet regularly to adjudicate the relationship of site-reported adverse events to the investigational device and procedure.

3.2 Potential Benefits

The targeted patient population consists of patients presenting with non-valvular atrial fibrillation, and who are at increased risk for stroke and systemic embolism and are recommended for OAC therapy but have an appropriate rationale to seek a non-pharmacological alternative to OAC, and who have been deemed appropriate for LAA closure by the Site PI and a physician not on the interventional team or an advanced provider using a shared decision-making process. Compared with LAA closure with a commercially available device, LAA closure with the CLAAS device may offer a simpler, safer implantation procedure and an increased likelihood of achieving successful closure.

Subjects in the CONFORM Pivotal Trial may not derive any direct benefit from their participation in the trial; however, subjects may gain satisfaction from having made an altruistic contribution to medical science, and the results of the trial may contribute to improved treatments that could benefit future patients who require LAA occlusion for the prevention of stroke and systemic embolism.

3.3 Benefit-Risk Assessment

A risk analysis of the CLAAS device has been performed and concluded that the identified risks have been reduced as far as possible. When combined with the risk management measures incorporated into the design of the clinical trial, the potential benefits of the clinical use of the CLAAS device in the CONFORM Pivotal Trial are judged to justify the potential risks to study participants. The potential benefits and risks of study participation will be evaluated on an individual basis and discussed with each patient prior to enrollment in the study.

4 DEVICE DESCRIPTION

4.1 Overview

The CLAAS® System delivers a plug to the ostia of the Left Atrial Appendage (LAA) and is designed to occlude the appendage to eliminate blood flow (Figure 2). The CLAAS Implant is designed to conform to the geometry of the LAA and is delivered via a percutaneous Delivery System. The system includes the following components:

- CLAAS Delivery Catheter, including Implant and Loading Cone
- Access Sheath with Dilator

The Implant is pre-attached to the Delivery Catheter and loaded by the user into the Delivery Catheter at the time of the procedure. The Delivery System consists of: 1) CLAAS Delivery Catheter with Implant and Loading Cone (Figure 3), 2) Access Sheath with Dilator (Figure 4), and is designed to track through the vascular anatomy from the femoral vein to the LAA. The system includes an Access Sheath with Dilator to accommodate vascular access using a standard femoral vein approach to the right atrium, across the atrial septum, and into the LAA. Echocardiography and fluoroscopy are used during the procedure to verify sizing and to aid in deployment of the Implant to the target location.

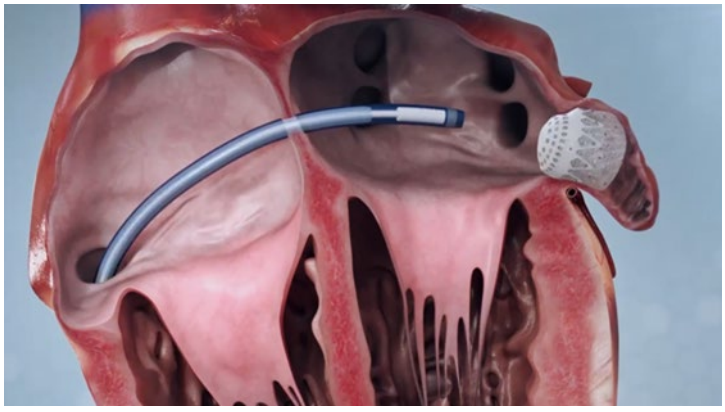

Figure 2: CLAAS Delivery System and Implant in LAA anatomy

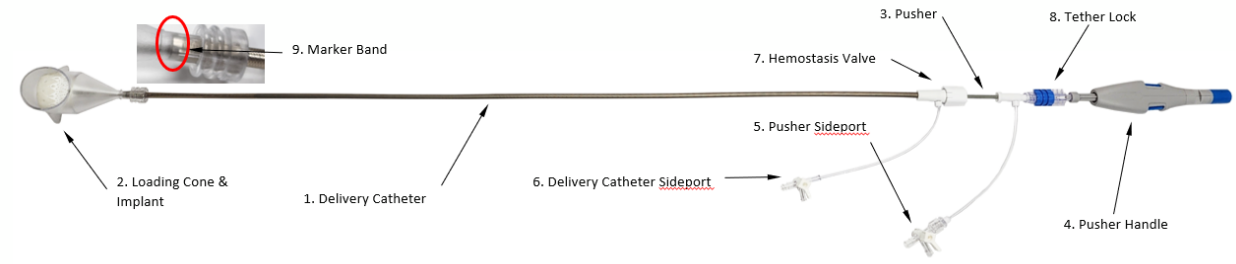

Figure 3: CLAAS Delivery Catheter, Loading Cone, Pusher, and Implant

Figure 4: CLAAS Access Sheath with Dilator

4.2 System Components

The CLAAS system component part numbers are listed in Table 1.

Table 1: CLAAS System Catalog Numbers

Catalog No.	Description
30-00214	Regular (27mm) Implant with Delivery Catheter
30-00269	Large (35mm) Implant with Delivery Catheter
30-00215	Regular (27mm) Access Sheath, Dilator Single Curve
30-00216	Regular (27mm) Access Sheath, Dilator Double Curve
30-00270	Large (35mm) Access Sheath, Dilator Single Curve
30-00271	Large (35mm) Access Sheath, Dilator Double Curve

4.3 Principles of Operation

The CLAAS is designed to provide optimal occlusion of the LAA to eliminate blood flow into, and clot passage from, the LAA using a cylindrical Nitinol endoskeleton with foam cover. The system is designed to provide a controlled, precise deployment. The device may be recaptured and repositioned during the implantation procedure.

4.3.1 Access

The CLAAS system is delivered to the target location at the LAA ostium using standard interventional techniques and imaging to ensure appropriate placement and sizing. Under echocardiographic guidance, a transseptal puncture is performed with standard techniques. A pigtail catheter may be advanced over a guidewire, through the septum and into the LAA to perform an angiogram of the LAA. Alternatively, echocardiography may be used to determine the LAA ostium diameter to properly select the Implant size (Table 2).

Table 2: CLAAS Implant Sizing

Implant Size	Mean LAA Ostium Dia (Dmax + Dmin) / 2	LAA Ostium Diameter Range	Min Landing Zone Depth
Regular	≤ 25 mm	10 – 33 mm	10 mm
Large	≤ 32 mm	20 – 40 mm	10 mm

The appropriate size Access Sheath is prepped with saline and then advanced over a guidewire, through the septum, and into the LA.

4.3.2 Implant Loading

The Delivery Catheter is prepared in accordance with the Instructions for Use. The CLAAS Implant is loaded into the Delivery Catheter by hand. The user grasps the handle and pulls it, which advances the Implant into the Loading cone and into the Delivery Catheter.

4.3.3 Delivery

With the Implant loaded into the Delivery Catheter, the system can be introduced into the Access Sheath and advanced until the Access Sheath and Delivery Catheter hubs engage. The Delivery Catheter is shorter than the Access Sheath. The implant is initially advanced from the Delivery Catheter into the Access Sheath. Then the implant is positioned at the desired location.

The Implant is deployed by withdrawing the Access Sheath and Delivery Catheter while holding the Pusher Handle in place (de-sheath). The Implant Proximal (Shoulder) radiopaque (RO) marker is used to confirm proper placement. The Implant may be partially recaptured into the Access Sheath for repositioning, or fully recaptured into the Delivery Catheter to withdraw the Implant from the body. (*NOTE: A fully recaptured Implant cannot be reused)*. A contrast injection is performed through the Pusher side port to evaluate the LAA seal. Echocardiography may also be used.

Once the Implant is in place, a tug test is performed to ensure that the Implant is secure in the tissue. This is done by first providing slack in the tether as shown in Figure 5 (initial position panel A to slack position, panel B). To provide slack, the two buttons of the handle are depressed, and the handle is advanced forward (distal). This allows for the evaluation of implant position and provides the slack necessary for the tug test (Figure 6).

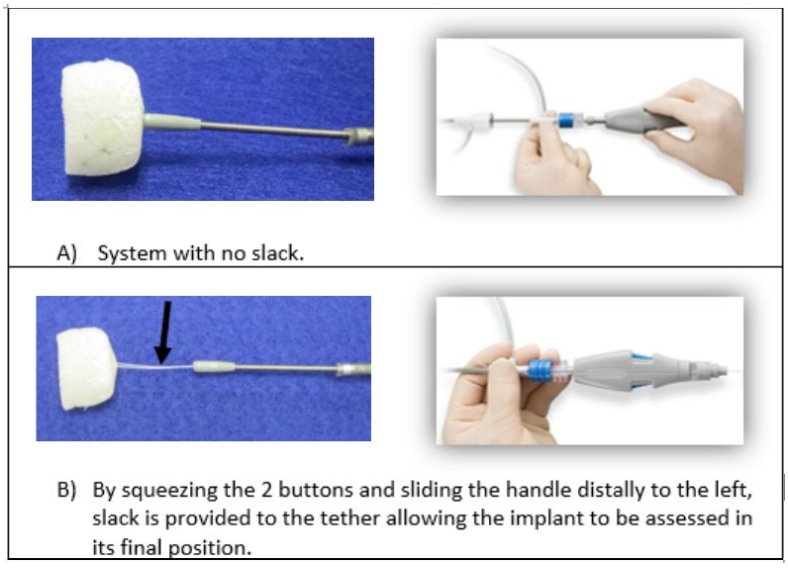

Figure 5: Preparing the System for the tug test

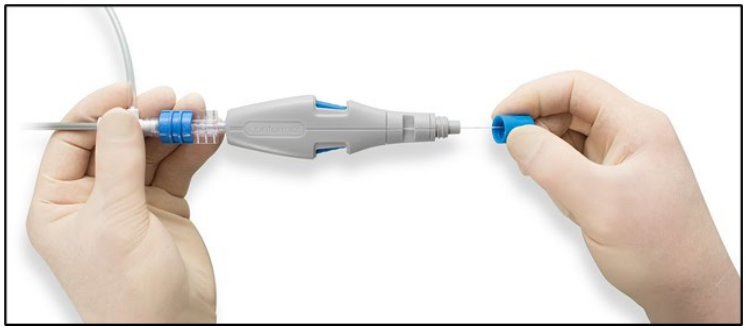

Figure 6: Tug test

4.3.4 System Removal

Once the Implant is in position with seal and anchoring confirmed, one of the two exposed tethers between the handle and the tug test cap is cut and the tether withdrawn from the Delivery Catheter. The Delivery Catheter and Access Sheath can then be removed, and the access site managed in accordance with standard of care.

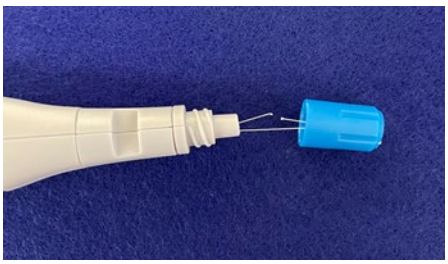

Figure 7: Tether cut prior to system removal

4.4 Implant (P/N 20-00158 (Regular) and 20-00255 (Large))

The CLAAS Implant is designed to conform to the LAA geometry to permanently seal off the LAA. The Implant components are shown in Figure 8.

The Implant consists of a cylindrical inner Nitinol endoskeleton (frame) that provides the mechanical base structure. The Implant is available in two different sizes (Figure 9), referred to as Regular (27mm) and Large (35mm), to accommodate the range of clinical ostia diameters described in Table 2.

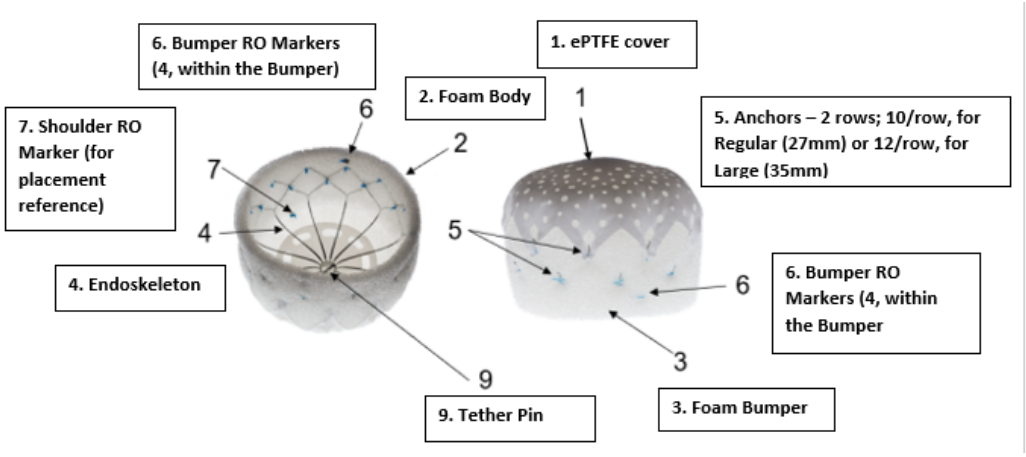

Figure 8: CLAAS Implant components of construction

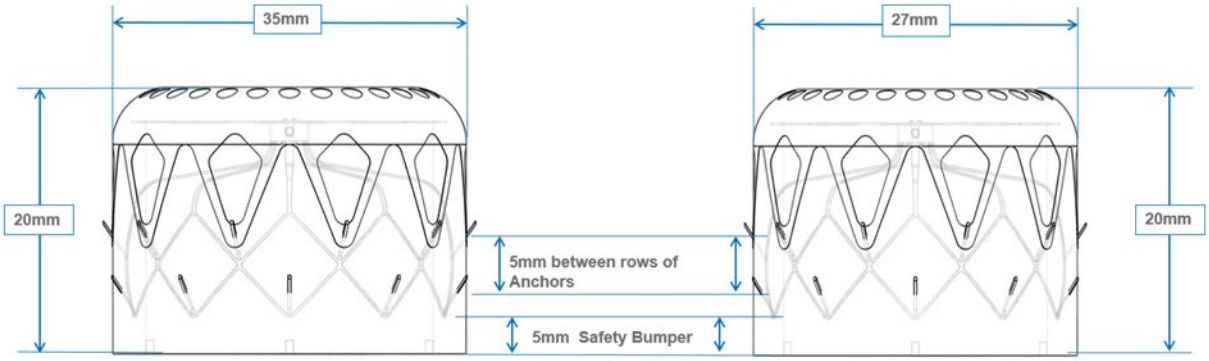

Figure 9: CLAAS Implant Dimensions

The Nitinol endoskeleton contains 10 face struts and 20 anchors in the Regular size and 12 struts and 24 anchors in the Large size. The anchors face proximally to engage the tissue to resist movement. The endoskeleton also provides the conformable structure to enable the foam cylinder to compress against the LAA tissue to facilitate sealing. Refer to Table 3 for Implant characteristic and nominal dimensions.

Table 3*:* CLAAS Implant Characteristics and nominal dimensions

	Regular (27mm)	Large (35mm)
NiTi tube thickness	0.203mm (0.008in)	0.203mm (0.008in)
NiTi tube OD	3.15mm (0.1240in)	3.50mm (0.1378in)
Struts	10	12
Anchors	20	24
NiTi pin diameter	0.635mm (0.025in)	0.635mm (0.025in)
Foam cup length	20mm	20mm
OD	27mm	35mm
Foam Thickness	2.5mm	2.5mm

	Regular (27mm)	Large (35mm)
Overall length	21mm	22.25mm
Minimum LAA depth	10mm	10mm
Venous access sheath	18F	20F
Foam bumper (distal) depth	5mm	5mm

4.4.1 Implant – Materials

The materials used to fabricate the Implants and contact duration are listed in Table 4.

Table 4*:* CLAAS Implant components and contact duration

Component	Material Chemical Name	Patient Contact Information (type and duration)
Nitinol Endoskeleton and Pin	Nickel Titanium	Implant, permanent
Foam Cup	Polycarbonate Polyurethane Urea	Implant, permanent
RO Marker Bands	Platinum-Iridium (90% Pt 10%Ir)	Implant, permanent
ePTFE Face and Inner Cover	Expanded polytetrafluoroethylene (ePTFE)	Implant, permanent
6-0 Polypropylene Monofilament Suture (Blue)	Polymer: Polypropylene Colorant: [phthalocyaninato (2-)] copper, < 1% by weight, CAS 147-14-8, 99.35%	Implant, permanent

4.5 Implant Component – Nitinol Endoskeleton (Frame with Pin) (P/N's 20-00147 (Regular) and 20-00248 (Large))

The Nitinol endoskeleton (also referred to as the frame) is laser cut from a single Nitinol tube and then heat treated to set its shape and to ensure super-elasticity at body temperature. The frame includes a proximal nipple, tether pin, front face with arms, a diamond pattern cylindrical body and anchors. The assembly is electropolished to enhance performance and improve corrosion resistance.

The anchors are approximately 2.5mm long and formed to rest at a 35^{o} angle to the central axis of the implant. The anchors are placed through the foam walls and ePTFE cover during assembly. Two (2) rows of anchors are incorporated into the middle of the implant to ensure engagement with the LAA tissue distal to the ostium (Figure 10). The foam is affixed to the frame at the anchor sites using 6-0 polypropylene non-resorbable suture material. Attaching the frame to the foam compresses the foam, exposing the anchors to the tissue. A Nitinol tether pin is welded inside the proximal nipple and serves to engage the removable tether, which is wrapped around the pin and used to load and recapture the Implant.

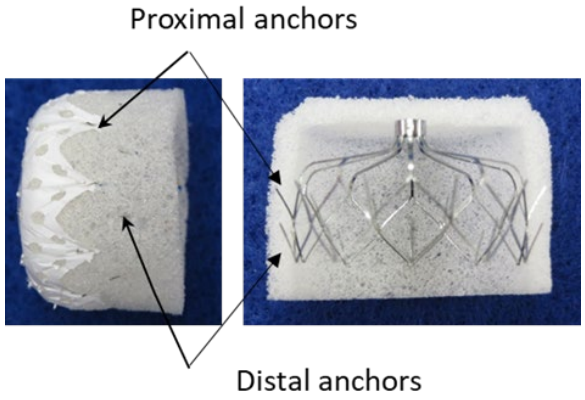

Figure 10: Location of the proximal and distal anchors at the middle of the Implant (left) and foam penetration (right)

4.5.1 Implant Component – Foam Cup (P/N's 10-00016 (Regular) and 10-00044 (Large))

The Implant consists of a foam covering that provides the conformability needed to ensure sealing of the LAA. The foam material is a non-resorbable, reticulated, cross-linked, polycarbonate polyurethane-urea material that is highly porous.

4.5.2 Implant Component – ePTFE Face (P/N's 10-00156 (Regular) and 10-00243 (Large))

The proximal face of the Implant is covered with a perforated, ePTFE cover. The cover is designed to enhance the ability to recapture the implant in-vivo by distributing the forces applied by the catheter as the foam itself does not have sufficient strength to enable recapture. The ePTFE is much stronger than the foam and can withstand the forces necessary to facilitate recapture. Perforations in the cover facilitate blood to flow through the implant as a mitigation for potential implant embolization.

4.5.3 Implant Component – ePTFE Inner Cover (P/N 10-00209)

A disc of ePTFE is placed between the foam and the Nitinol frame nipple. This serves to minimize erosion of the metal nipple into the foam. The ePTFE disc is compressed between the frame and foam, which are assembled using high strength sutures to maintain position without the need for any additional fastening.

4.5.4 Implant Component – 6-0 Polypropylene Attachment Sutures (P/N 40-00135)

Polypropylene, 6-0 monofilament sutures are used throughout the implant to attach the foam, proximal cover, and RO markers to the foam and frame.

4.6 Delivery System

4.6.1 Overview

Delivery of the Implant is achieved with a customized coaxial delivery system. Vascular access is achieved with the Conformal Access Sheath with Dilator. The Implant is loaded into the distal end of the Delivery Catheter by hand. The system is designed with sufficient length to access the LAA from a right femoral vein puncture. The Delivery Catheter working length is designed such that when it is locked to the Access Sheath, its distal tip is about 3cm short of the Access Sheath tip. This allows the user to advance the Implant from the Delivery Catheter into the Access Sheath prior to deploying it into the patient. The Delivery System includes the Access Sheath with Dilator, and the Delivery Catheter. The Delivery System components and configurations are depicted in Figure 17 - 18.

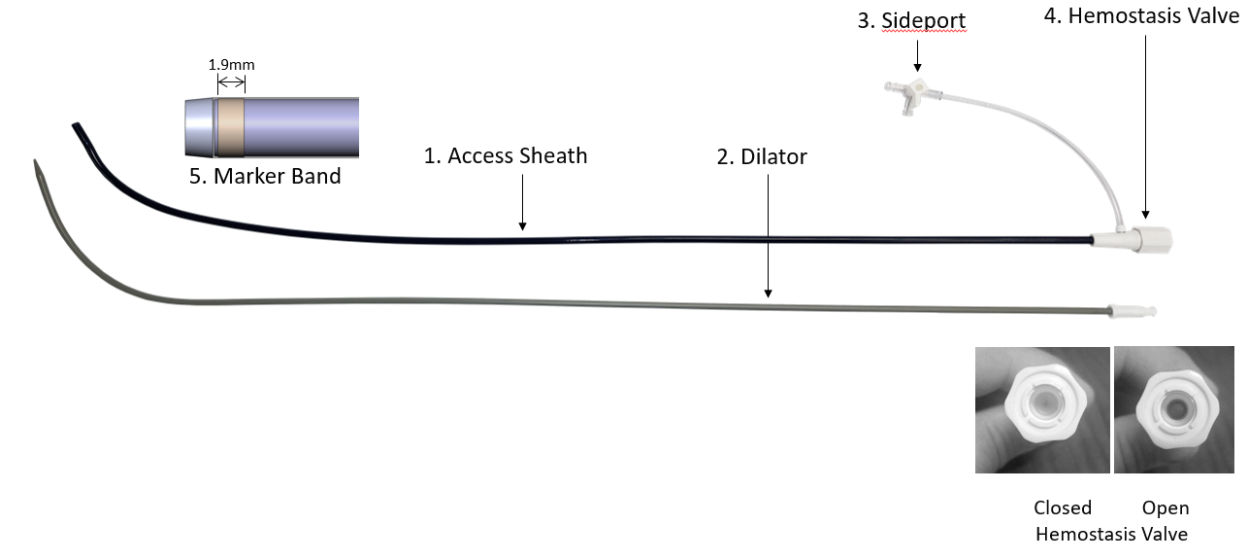

Figure 11: Single curve Access Sheath with Dilator components

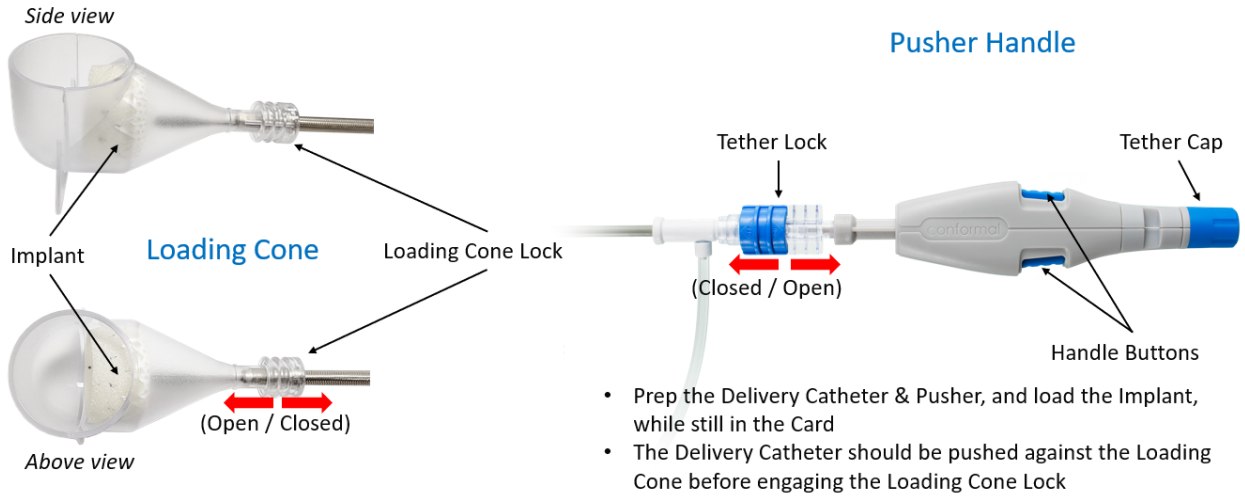

Figure 12: Loading Cone, Pusher Handle, and Implant

An alternate Pusher Handle, shown in Figure 13, may be introduced to improve ergonomics of delivery. The buttons and slide valve are eliminated in this design. All other functions and materials are similar to the current design.

Figure 13: Alternate Pusher Handle

4.6.2 CLAAS Access Sheath with Dilator

Access to the left atrium through the atrial septum is obtained via a standard transseptal puncture using commercially available equipment and standard of care techniques. The CLAAS Access Sheath with Dilator comes in four (4) configurations to accommodate femoral vascular access and variations in vascular geometry:

- Regular Single Curve Access Sheath and Dilator (P/N 30-00215)
- Regular Double Curve Access Sheath and Dilator (P/N 30-00216)
- Large Single Curve Access Sheath and Dilator (P/N 30-00270)
- Large Double Curve Access Sheath and Dilator (P/N 30-00271)

Once a guidewire is placed across the septum and into the left atrium (LA) using standard of care techniques, the Access Sheath with Dilator is advanced over the wire, through the septum and into the LA. The Dilators fit inside the Access Sheaths and serve to smoothly guide the Access Sheaths across the septum with their tapered tips. The Access Sheath has an embedded RO marker band at the distal tip to facilitate visualization during the procedure. The Single Curve Access Sheath has a single, 90-degree bend at its distal end with a radius of 3.5 inches (Figure 14). The Double Curve Access Sheath has a double curve, which is an anterior curve distal to the primary curve.

Figure 14: Single Curve Access Sheath with Dilator

Nominal dimensions of the Access Sheaths and Dilators are listed in Table 5.

Table 5: Access Sheath and Dilator nominal dimensions

Component	Regular	Large
Access Sheath		
Outer diameter	17.8F	19.8F
Inner diameter	15.7F	17.6F
Working length	77.5cm	77.5cm
Access Sheath Dilator		
Outer diameter	15.5F	17.4F
Working length	83.8cm	83.8cm
Optional Vascular Access Sheath (not provided)	18F	20F

4.6.3 Access Sheath and Dilator – Materials

The materials used to fabricate the Access Sheath and Dilator, and the contact duration are listed in Table 6.

Table 6*:* Access Sheath and Dilator materials and contact duration

Component	Description	Chemical Name	Patient Contact Information (type and duration)
Access Sheath	Liner	PTFE	Blood contact < 24 hrs.
	Braid	304 stainless steel	Blood path < 24 hrs.
	Shaft	Polyether block amide 55D, 20% BaSO4, 295c blue	Blood path < 24 hrs.
	Valve Body and Cap	Polyether block amide 72D, white color	Blood path < 24 hrs.
	Hemostatic Valves	Silicone	Fluid path < 24 hrs.
	Side Arm Tubing	PVC	Fluid path < 24 hrs.
	Sidearm Stopcock	Polycarbonate housing Polypropylene switch	Fluid path < 24 hrs.
	RO Marker	90% Platinum / 10%Iridium	Blood path < 24 hrs.
Dilator	Shaft	Regular: HDPE, BaSO4, Grey 422c Large: Blend 50% HDPE, 20% BaSO4, Grey 422c and 50% LDPE 20% BaSO4 Grey 7544	Blood path < 24 hrs.
	Hub	HDPE	Fluid path < 24 hrs.

NOTE: PTFE = polytetrafluoroethylene, TPE=thermoplastic elastomer, TPU=thermoplastic polyurethane, ABS = acrylonitrile butadiene styrene, PVC = polyvinyl chloride, COPE=Copolyester, HDPE=high density polyethylene.

The Access Sheath has a hemostatic (Touhy) valve at its proximal end. This is the same valve used on the Delivery Catheter. Clockwise rotation of the cap squeezes the silicone gland and closes the valve (Figure 15).

Figure 15: Hemostatic (Touhy) valves open (left) and closed (right)

4.6.4 CLAAS Delivery Catheter (P/N 600138-001) and Pusher (P/N 600139-01)

The Delivery Catheter (Figure 16) is a straight, braided shaft catheter that passes through the Access Sheath to deliver the Implant to the LAA. The Pusher passes through the center of the Delivery Catheter and serves to push the Implant from the Delivery Catheter. There is an RO marker band at the distal tip of the Delivery Catheter that may be used as a guide to ensure the Delivery Catheter is fully loaded into the Access Sheath.

Figure 16: Delivery Catheter

Table 7 lists the nominal dimensions for the delivery Catheter, The working length is 3cm short of access sheath tips when engaged.

Table 7: Delivery Catheter Nominal Dimensions

Component	Regular	Large
Outer diameter	15.2F	17.1F
Inner diameter	13.3F	15.3F
Working length	79.2cm	79.2cm

Table 8 summarizes the materials and contact duration of the Delivery Catheter components. The Implant is provided attached to the Delivery Catheter with a UHMWPE suture material that passes through the center of the Pusher. The Implant is loaded into the distal tip of the Delivery Catheter at the time of the procedure by pulling the handle.

The Delivery System has a handle attached to the Pusher part of the Delivery Catheter to facilitate Implant deployment (Figure 17). The handle assembly is made from Acrylonitrile butadiene styrene (ABS) with Nitinol (NiTi) springs and is non-patient contacting.

Table 8: Delivery Catheter materials and contact duration

Component	Description	Chemical Name	Patient Contact Information (type and duration)
Delivery Sheath (P/N 600138-001)	Liner	PTFE	Fluid path < 24 hrs.
	Braid	304 stainless steel	Fluid path < 24 hrs.

Component	Description	Chemical Name	Patient Contact Information (type and duration)
	Shaft, distal	Polyether block amide 40D, Natural	Fluid path < 24 hrs.
	Shaft, proximal	Vestamid ML21, Natural	Fluid path < 24 hrs.
	Valve Body & Cap	Polyether block amide 72D with white color	Fluid path < 24 hrs.
	Hemostatic Valve Seals	Silicone	Fluid path < 24 hrs.
	Side Arm Tubing	PVC	Fluid path < 24 hrs.
	Sidearm Stopcock	Polycarbonate housing Polypropylene switch	Fluid path < 24 hrs.
	RO markers	90% Platinum / 10%Iridium	Fluid path < 24 hrs.
Pusher (P/N 600139-01)	Shaft	HDPE, 20%BaSO4, Grey 422c	Fluid path < 24 hrs.
	Pusher tip	HDPE, 20% BaSO4, Grey 422c	Blood path < 24 hrs.
	Pusher Spring	304 Stainless Steel	Blood path < 24 hrs.
	Pusher Hub	HDPE	Fluid path < 24 hrs.
	Pusher flow switch	PC Colorant Acetal Colorant ABS Silicone	Fluid path < 24 hrs.
Delivery Handle (P/N 30-00282)	Buttons and Cap Parts	ABS & Colorant	Non-patient contacting
	Body halves, Suture covers and Slider	ABS & Colorant	
	Dowel Pins	Steel	
	Spring Pins	Nitinol	
	Flow Switch body	PC & Colorant	
	Flow Switch Slider	Acetal & Colorant	
	Flow Switch Plunger	ABS	
	Flow Switch Valve	Silicone	

NOTE: PTFE = polytetrafluoroethylene, TPU=thermoplastic polyurethane, ABS = acrylonitrile butadiene styrene, PVC = polyvinyl chloride, PC=polycarbonate, COPE=Copolyester, HDPE=high density polyethylene, UHMWPE=ultrahigh molecular weight polyethylene

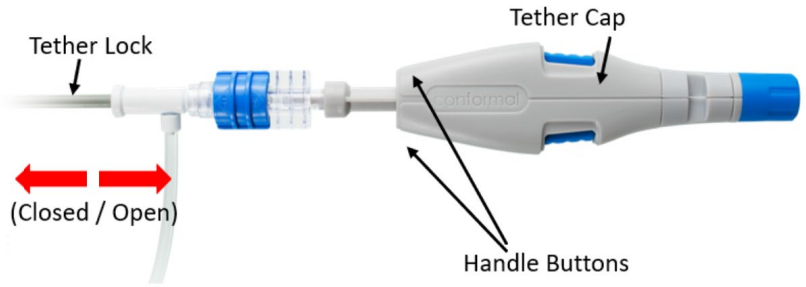

Figure 17: Delivery Handle

4.6.5 CLAAS Delivery System – Tether (P/N 40-00136)

A removable tether attaches the Implant to the Delivery Catheter and is used to load and recapture the Implant. The tether is made of braided, ultra-high-molecular-weight polyethylene (UHMWPE) suture material which has demonstrated strength to withstand the forces to both load and recapture the CLAAS Implant. Tether material and contact duration information is provided in Table 9. The tether forms a loop (Figure 18) that passes from the proximal end of the Delivery Catheter, through the Delivery Catheter Pusher, around the Implant tether pin and back through the Delivery Catheter where the tether is tied to the handle. The tether is released by cutting one of the tethers and pulling the other end out of the implant.

Table 9: Tether material and contact duration

Component	Chemical Name	Patient Contact Information (type and duration)
Tether	UHMWPE	Blood contact <24 hrs.

Figure 18: Tether Routing

4.6.6 CLAAS Delivery System – Loading Cone (30-00324 (Regular) and 30-00328 (Large))

The Implant is provided tethered to the Delivery Catheter, inside a Loading Cone which is attached to the Delivery Catheter. The Implant is loaded into the Delivery Catheter in the catheterization lab at the time of the procedure. The loading cone is a polycarbonate funnel-shaped component that compresses and guides the Implant into the Delivery Catheter.

The Implant is pulled through the Loading Cone (Figure 19) and into the Delivery Catheter manually by pulling on the handle. The Loading Cone is attached to the Delivery Catheter with a locking feature. Once loaded, the Loading Cone is unlocked by pushing the locking feature distal so it may be removed. The Loading Cone material and contact duration are listed in Table 10.

Table 10: Loading cone material and contact duration

Component	Material	Patient Contact Information (type and duration)
Loading Cone	Polycarbonate, clear	Contacts Implant During Loading

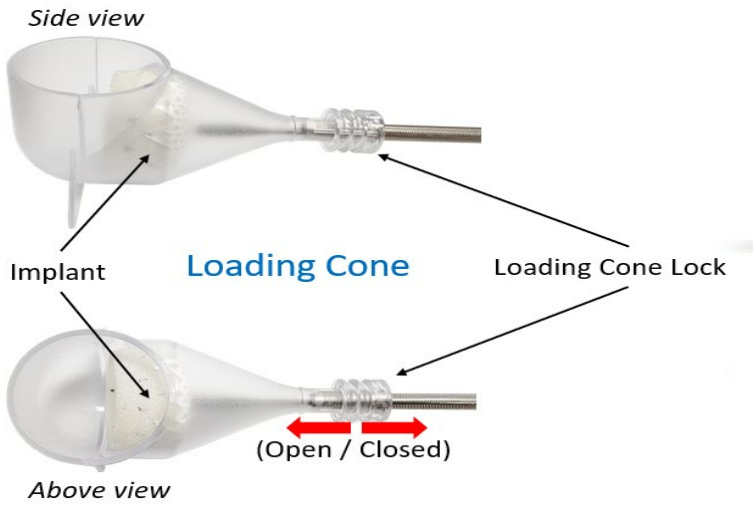

Figure 19: Loading Cone

5 PRECLINCIAL TESTING

Extensive preclinical testing has been performed on the CLAAS System including bench, biocompatibility, fatigue, particulate and animal testing to demonstrate safety and performance requirements in accordance with international and device-specific standards. The sterile barrier system and packaging was also evaluated after exposure to EO sterilization, environmental conditional and distribution simulation. All testing passed the pre-specified acceptance criteria and was found suitable for investigational use.

All testing was done in accordance with international and device-specific standards. Table 11 provides a list of all applicable standards.

Table 11: Standards List

Standard	Title
ISO 10993-1:2018	Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing Within a Risk Management Process
ISO 10993-3:2014	Biological Evaluation of Medical devices – Part 3: Tests for Genotoxicity, Carcinogenicity and Reproductive Toxicity
ISO 10993-4:2017	Biological Evaluation of Medical Devices – Part 4: Selection of Tests for Interaction with Blood
ISO 10993-5:2009	Biological Evaluation of Medical Devices – Part 5: Tests for In Vitro Cytotoxicity
ISO 10993-6:2016	Biological Evaluation of Medical devices – Part 6: Tests for Local Effects After Implantation
ISO 10993-10:2021	Biological Evaluation of Medical Devices – Part 10: Tests for Irritation and Skin Sensitization
ISO 10993-11:2017	Biological Evaluation of Medical devices – Part 11: Tests for Systemic Toxicity
ASTM F2052-21	Standard Test Method for Measurement of Magnetically Induced Displacement Force on Passive Implants in the Magnetic Resonance Environment
ASTM F2213-7	Standard Test Method for Measurement of Magnetically Induced Torque on Passive Implants in the Magnetic Resonance Environment
ASTM F2182-19e2	Standard Test Method for Measurement of Radio Frequency Induced Heating Near Passive Implants During Magnetic Resonance Imaging
ASTM F2119-07(2013)	Standard Test Method for Evaluation of MR Image Artifacts from Passive Implants
ASTM F2516-22	Standard Test Method for Tension Testing of Nickel-Titanium Superelastic Materials
ASTM F2129-19a	Standard Test Method for Conducting Cyclic Potentiodynamic Polarization Measurements to Determine the Corrosion Susceptibility of Small Implant Devices
ASTM F1980-21	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices

Standard	Title
ISO 10555-1:2013/Amd 1:2017	Intravascular catheters – Sterile and single-use catheters Part 1: General Requirements
ISO 11070:2014	Sterile single-use Intravascular Introducers, Dilators and guidewires
ISO 11135:2014	Sterilization of health-care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices
ISO 10993-7: 2008	Biological evaluation of medical devices – Part 7: Ethylene oxide sterilization residuals
AAMI TIR14:2016 (R2020)	Contract sterilization using ethylene oxide
AAMI TIR15:2016 (R2020)	Physical aspects of ethylene oxide sterilization
AANI TIR16:2017 (R2020)	Microbiological aspects of ethylene oxide sterilization
ISO 14971:2019	Medical devices - Application of risk management to medical devices
ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labeling, and information to be supplied
ISO 80369-7:2021	Small-bore connectors for liquids and gases in healthcare applications -- Part 7: Connectors for intravascular or hypodermic applications
ISO 11607-1:2019	Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems
ASTM D4169-22	Standard Practice for Performance Testing of Shipping Containers and Systems
ASTM F2063-18	Standard Specification for Wrought Nickel-Titanium Shape Memory Alloys for Medical Devices and Surgical Implants
ASTM F2096-11(2019)	Standard Test Method for Detecting Gross Leaks in Packaging by Internal Pressurization (Bubble Test)
ASTM F2477-23	Standard Test Methods for in vitro Pulsatile Durability Testing of Vascular Stents
ASTM F756-17	Standard Practice for Assessment of Hemolytic Properties of Materials
ASTM F88/F88M-23	Standard Test Method for Seal Strength of Flexible Barrier Materials
ISO 25539-1:2017	Cardiovascular Implants - Endovascular Devices - Part 1: Endovascular Prostheses
ISO 25539-2:2020	Cardiovascular implants — Endovascular devices — Part 2: Vascular stents
ISTA 3A:2018	General Simulation Performance Test Procedure

Table 12: Preclinical Bench Testing

Test Description	N	Acceptance Criteria
Material Composition	N/A	ASTM F2063
Shape Memory and Superelasticity	N=1 frame radio per lot	Active A_f of finished frame 20±5°C
Mechanical Properties	N=15 (3 lots of 5 samples)	There are no acceptance criteria since the purpose of these tests is to characterize the mechanical properties of the Nitinol tubing.
Corrosion Resistance		
Corrosion Resistance (Breakdown Potential) ASTM F2129	N=10 implants per size	**Regular (27mm)**
		Average breakdown potential Eb > 500mV
		Probability that pitting will occur (Eb-Er< 0) is <1%
		Large (35mm)
		Average breakdown potential Eb > 500mV
		Probability that pitting will occur (Eb-Er< 0) is <1%
Implant Functional Attributes		
Radiopacity & Echogenicity	N=8	GLP Animal Study
Stress/Strain Analysis (FEA)	N/A	FEA conducted for characterization purposes only
Fatigue Analysis (FEA)		FEA conducted for characterization purposes only
Endurance Limit Testing	N=3 groups of 16 samples and 1 group of 8	Endurance Limit Testing conducted for characterization purposes only
Accelerated Durability (400 Mil cycles) Testing	N=30	No fatigue failures at 400 million cycles.
Animal Testing		
GLP Study in Canine Model	N=8 4@90d 4@150d	Overall Animal Health (moribundity)
		Device (Implant) Performance including Thrombogenicity and Tissue Response
		Delivery System & Implant Thrombogenicity
		System Usability including Radiopacity and Echogenicity
		Subchronic and Chronic Toxicity
Biocompatibility		
Implant	N/A	ISO 10993-1:2009, See section 5.4.1
Simulated Use		
Implant loading force	N=60	< 15 lbs.
Implant deployment force	N=60	< 10 lbs.
Implant partial recapture force	N=59	< 10 lbs.
Implant full recapture force	N=30	< 15 lbs.
Implant diameter recovery	N=30	> 25 mm (for 27mm implant) > 33 mm (for 35mm implant)

Test Description	N	Acceptance Criteria
Implant dislodgement force	N=30	> 0.5 lbs.
Fluid Flow Through Implant	N=3	>1.0 L/min
Access Sheath Dimensions	N=46	Meets specification
Delivery Catheter Dimensions	N=46	Meets specification
Tether release force	N=29	< 0.5 lbs.
Packaging Validation		
Visual Inspection	N=30	Inspect pouches for visible damage (i.e., seal failures, holes, tears, and voids).
Visual Inspection	N=30	No obvious physical damage to any of the components of the access system.
Bubble Leak	N=30	ASTM F2096-11
Seal Strength	N=30	ASTM F88/F88-15
Destructive Testing		
Catheter joint forces	N=10	> 10 lbs. (main catheter) > 3.4 lbs. (side ports)
Access Sheath Torque	N=30	90 degrees without failure
Access Sheath Kink	N=30	Must fit 1.5-inch radius without kinking
Delivery Catheter Kink	N=30	Must fit 1.5-inch radius without kinking
Leak Test (Access Sheath, dilator and Delivery Catheter hubs & fittings)	N=30	> 45 psi
Leak Test (Pusher Side Port)	N=30	> 100 psi
Air Ingress (all catheter joints)	N=30	No ingress
Ultimate System Strength	N=30	95%/99% LCL > Implant full recapture force 95%/99% UCL which was 16.7 lbs.
Implant Partial Recapture Cycle Testing	N=60	> 4 cycles without failure (95%/95%)
Tether tensile force	N=30	95%/99% LCL > Implant full recapture force with 95%/99% UCL of both systems which were 16.7 and 13.9 lbs.
Particulates		
Simulated Use Particulates	N=10	For characterization >10 micron: <6000 particles >25 micron: <600 particles >50 micron: <100 particles

5.1 Animal Testing

5.2 Acute Animal Study

5.2.1 Purpose

The purpose of the acute animal study was to evaluate the ability to deliver and maintain position of the LAA Closure device during a 1-hour period and to analyze the seal and blood interactions with the device during and after completion of the study. The study was performed to confirm the final design of the product.

5.2.2 Study Procedure

The device was implanted using standard transseptal techniques utilized in standard clinical practice. Intracardiac echocardiography (ICE) and fluoroscopy (fluoro) were used to guide the delivery system to the target location and deploy the implant.

5.2.3 Results

The acute study demonstrated the ability of the implant to be located appropriately in the target location with adequate sealing. Both immediately following implantation and prior to sacrifice, echocardiography confirmed the presence of complete sealing with no leaks. At termination, the implant was well positioned with good apposition and sealing around the ostium of the appendage. There was no visible thrombus attached to the surface of the implant, and no observable thrombus embolized to the downstream organs including brain, lungs, liver, spleen, and kidneys. The implant was well visualized with echo (ICE) and fluoroscopy. At termination, the LAA was visually inspected and palpated for anchor protrusion and none was observed or felt.

5.3 Chronic Animal Study

5.3.1 Purpose

The purpose of this study was to evaluate the ability to deliver and maintain position the LAA closure device over a 60-day period and to analyze the seal, thrombogenicity, and healing response of the device at 3 and 45 days (via transthoracic echocardiography) and at 60 days based on echocardiography, fluoroscopy, gross examination, and histopathological analysis. Gross and histopathology were conducted to evaluate the explanted specimens for LAA seal, tissue ingrowth, re-reendothelialization, inflammation, presence of loose thrombus, and to assess the animal for distal organ emboli.

5.3.2 Pharmacologic Post-Procedure Management

All animals received DAPT (Aspirin 81mg & clopidogrel 75mg) for 45 days following implantation. After 45 days, each animal continued to receive aspirin (81mg) until termination.

5.3.3 Study Procedure

The device was implanted using standard transseptal techniques utilized in standard clinical practice. Intracardiac echocardiography (ICE) and fluoroscopy (fluoro) were used to guide the delivery system to the target location and deploy the implant.

5.3.4 Results

All devices were successfully placed, and all animals survived without any adverse events noted in the follow up time frame. Immediately following implantation, all devices were observed to be in a stable position with no clots present. No leaks past the implant were identified at delivery, however, there were three devices with gutters flowing up to the implant shoulder. No thrombus was noted on any of the delivery system or access sheath elements following the placement procedures nor was there any indication of pericardial effusion. Post-implant angiography was performed on all animals to demonstrate device position and LAA occlusion.

Follow-up TTE procedures 2 days and 42-44 days post-implant were performed to evaluate device position and function. For all animals, the device was assessed to be in stable position and showed no indication of clot formation at day 2 and day 44. No flow around the device was observed for all animals and time points, except for one animal which had a possible tiny leak into the LAA per echocardiography on Day 42 post-implant. In addition, two animals showed signs of pericardial effusion by echocardiography, one had a small effusion at day 2 post-implant, while a second had tiny pericardial effusion at day 2 post-implant. All other animals showed no signs of pericardial effusion.

Prior to termination, both TTE and fluoroscopy evaluations showed the device to be in a stable position. Additionally, there were no negative findings in any downstream organs. TTE showed no signs of clot formation for all animals and good occlusion of the LAA with no pericardial effusion noted in any of the animals. A small leak path was originally noted in the TTE examination for 2 animals, however, further review of the TTE video along with review of the histopathology concluded that the leak was a small gutter that did not extend into the distal LAA beyond the implant shoulder. Gross analysis and histopathology review of the implant within the LAA confirmed complete healing of the LA face and no leak in all devices. It is important to note that while the use of TTE provides valuable input regarding the general position of the implant, however, it may be technically challenging to use this imaging modality as a reasonable surrogate for evaluating LAA sealing. It is believed that the evaluation in animals of sealing is most appropriately determined at the time of explant with visual confirmation.

5.3.5 Summary

The chronic animal results demonstrate LAA sealing and favorable tissue response to the implant. There has also been no identification of distal emboli to either local or distal organs. This data confirmed the initial safety profile of the product. The favorable histopathology outcomes from the animals at 60 days provides supports that healing is complete.

Table 13: Animal testing summary

Duration	n	Results
Acute – 1 hour	1	Pass
Chronic – 60 Days	6	Pass

5.4 Biocompatibility

5.4.1 Implant Biocompatibility

Implant biocompatibility, including subchronic and chronic toxicity, implantation, genotoxicity, carcinogenicity plus an additional evaluation for implant thermogenicity was conducted at North American Science Associates, Inc. (NAMSA) in accordance with ISO 10993-1:2009 (Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing within a Risk Management Process). In accordance with ISO 10993-1, the implant is in permanent contact (>30 days) with circulating blood. Table 14 summarizes biocompatibility testing performed on the CLAAS implant. All testing passed specifications and concluded there was no biocompatibility risk.

5.4.1.1 Chronic Toxicity, Genotoxicity, and Carcinogenicity Risk Assessment

A comprehensive risk assessment was conducted regarding chronic toxicity, genotoxicity, and carcinogenicity. Based on the complete comprehensive data reviewed, it was concluded that, within the scope of this evaluation, there are no component materials or materials related to manufacturing process residue identified as toxicological risks of systemic toxicity (acute, subchronic or chronic), genotoxicity or carcinogenicity.

Table 14: Implant Biocompatibility Summary

Test	Result	Supporting Evidence
Cytotoxicity Study Using the ISO Elution Method	Pass	NAMSA Testing
ISO Maximization Sensitization Study	Pass	
ISO Intracutaneous Study	Pass	
ISO Systemic Toxicity Study	Pass	
Pyrogen Study – Material Mediated	Pass	
ASTM Hemolysis	Pass	
SC5b-9 Compliment Activation Assay	Pass	
Thrombogenicity	Pass	Chronic Animal Studies
Thrombogenicity	Pass	GLP Animal Study
Subchronic Toxicity	Pass	
Implantation	Pass	
Chronic Toxicity	Pass No significant risk	GLP Animal Study Scientific Rationale
Genotoxicity	No significant risk	Scientific Rationale

Test	Result	Supporting Evidence
Carcinogenicity	No significant risk	Scientific Rationale

5.4.2 Delivery System

Biocompatibility testing was performed by NAMSA, in accordance with ISO 10993-1:2009 (Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing within a Risk Management Process). Testing included Cytotoxicity, Sensitization, Intracutaneous, Systemic Toxicity, Pyrogen (material mediated), Hemolysis, SC5b-9 Complement Activation, and Thrombogenicity. All testing passed specifications and concluded the delivery system and access sheath are biocompatible and safe for use in a clinical trial.

In accordance with ISO 10993-1, the Delivery System is characterized as limited exposure (A) circulating blood external communicating devices. The limited exposure (A) category is for devices that contact circulating blood whose cumulative, single or repeated use or contact is up to 24 h.

6 CLINCIAL EXPERIENCE

6.1 Early Feasibility Clinical Summary Information

Conformal has conducted two early feasibility clinical studies, one EFS IDE study was performed in the US (ongoing) and a second feasibility study performed in the Czech Republic. The aim of both studies was to confirm the safety of the device and procedure to support further use of the product in a pivotal clinical study design.

The two studies enrolled consistent subjects that are at high risk for stroke based on CHA2DS2-VASc scores. The major difference between the two studies is that the EU trial subjects were all treated using Monitored Anesthesia Care (MAC) methods versus General Anesthesia which is typically used in the US. In addition, TEE was not used in the EU trial during the CLAAS delivery but was used to check positioning at the end of the procedure prior to implant release.

A total of eighty-four (84) subjects were enrolled in the combined two clinical studies: sixty-four (64) subjects in the US EFS IDE study and twenty (20) in the EU study. There have been no unanticipated events reported and the AE/SAEs were all consistent with those expected with LAA occlusion procedures. The results from these studies confirm the safety profile of the CLAAS® device and procedure.

6.1.1 EFS (US) Results

As of July1, 2022, a total of sixty-nine (69) subjects were enrolled and consented. Sixty-four (64) patients enrolled in Conformal EFS, five (5) subjects did not receive a CLAAS® Implant but completed their 45-day visit at the time of reporting, and six (6) patients have exited the study due to death.

Table 15 presents a summary of the demographics and baseline status for all subjects. The characteristics are consistent with the anticipated population for the product intended use.

Table 15: Demographics and Baseline Characteristics (n=69)

Variable	Statistics	% (n/69)
Age at Implant (Years)		
Mean ± SD	73.6 ± 7.75	
Median	73	
Gender (n, %)		
Female	19	27.5%
Male	50	72.5%
NYHA Classification		
N/A	43	62.3%
I	8	11.6%
II	18	26.1%
III	0	0%
IV	0	0%
CHA2DS2-VASc		
0-1	0	0%

Variable	Statistics	% (n/69)
2	13	19%
3	17	25%
4	13	19%
5	13	19%
6	7	10%
7	4	6%
8	2	3%
Mean ± SD	4.06 ± 1.62	
Median	4	
HAS-BLED		
0	3	4%
1	3	4%
2	16	23%
3	27	39%
4	18	26%
5	2	3%
Mean ± SD	2.87 ±1.08	
Median	3	
Reason for LAAC		
Fall Risk	20	29%
Gastrointestinal Bleed	17	25%
Intracranial Bleed	2	3%
Other bleed	10	14%
Stroke	6	9%
Other	14	20%

The Conformal EFS experience includes fifty-nine (59) patients who received a CLAAS implant. Forty-seven (47) patients received a Regular implant and twelve (12) received a Large implant. One (1) subject had a leak >5mm as of the 45-day follow-up. TEE core lab review indicated the leak was due to a secondary lobe, which was not appreciated by the procedural team at the time of implant. This leak was subsequently closed by placement of a Watchman device which was implanted 546 days after the index procedure. No patients had thrombus at the end of the procedure. Additional procedure information is summarized in Table 16.

Table 16: Procedural Information

Variable	Statistic
Implantation (N=64)	
Yes	59
No	5
Implants (N=59)	
Regular (27 mm)	47 (79.6%)
Large (35mm)	12 (20.3%)
Leak (N=58)	

Variable	Statistic
No	53
1-3mm	2
3-5mm	2
>5mm	1
Thrombus (N=59)	
Yes	0
No	59
Recapture (number of times)	
Full	14
Partial	51
Duration of Hospitalization for the Index Procedure (days)	
Min-Max	0-3
Mean	1.05

A total of five (5) subjects were categorized as failure to implant. In four (4) subjects, the device was deployed without difficulty but was found not to provide an adequate seal and the LAA was considered too large for the implant size and the Large device was not available. In all cases, the device was recaptured and withdrawn successfully without apparent sequalae.

No unanticipated adverse device effects (UADEs) have been reported in the Conformal EFS Study to date. A Clinical Events Committee (CEC) was established for the study to review target AE/SAEs in an ongoing manner and the committee determined that the events are consistent with the descriptions reported by the site. The CEC Board has convened for adjudication meetings five (5) times since the start of the Conformal EFS Study.

As of July 1, 2022, a total of one hundred thirty-seven (137) adverse events have been reported in sixty-four (64) enrolled subjects. Of these, a total of seventy-three (73) were reported to be SAEs (73/137; 53.3%).The EFS IDE demonstrated a reasonable safety profile. The initial cohort of subjects have been evaluated for the one-year endpoint and the events have been adjudicated by an Independent Clinical Events Committee. This data has been reviewed by an Independent Medical Monitor and determined there were no safety concerns identified regarding the product or procedure and the technical performance of the product has been demonstrated.

6.1.2 EFS (EU) Results

A total of twenty (20) subjects at one (1) center were targeted for this feasibility study. Twenty (20) subjects were consented in the Conformal Prague study, of which nineteen (19) were implanted. One (1) subject was a screen failure and exited the study; and two (2) subjects died. Seventeen (17) subjects completed study follow-up as expected and have exited the study. Subject demographics and baseline characteristics are listed in Table 17 below.

Table 17: Patient Demographics and Baseline Characteristics

Characteristic (n = 19)	Statistics
Age at Implant (Years)	
Mean ± SD	72.3 ± 9.9
Age ≥ 75	10 (53%)
Gender (n, %)	
Men	8 (42%)
CHA2DS2-VASc	
Mean ± SD	4.1 ± 1.7
HAS-BLED	
Mean ± SD	3 ± 1.5
Reason for LAAC	
Ocular Bleed	1
Fall Risk	1
Stroke	2
GI Bleed	4
Stroke/TIA	3
LAA thrombus	1
Epistaxis	2
Other	5
Antithrombotic Agents	
ASA	2
ASA/Clopidogrel	4
ASA/Dabigatran	5
ASA/Apixaban	6
Dabigatran	1
ASA/Clopidogrel/Apixaban	1
Stroke Assessment	
Modified Rankin Scale	0.8 ± 1.2
NIH Stroke Scale	0.9 ± 1.5

Of the nineteen (19) subjects who were eligible for procedure, nineteen (19) received the investigational implant resulting in 100% procedural success. Fourteen (14) subjects were implanted with the Regular device and five (5) subjects were implanted with the Large device. See procedural data in Table 18 below.

Table 18: Procedural Data (n=19)

Characteristic		Value	Std. Dev.
Least LAA Depth		22.9	6.3
LAA Orifice		21.8	4.1
Device Size	Regular	14	
	Large	5	
Device Success		100 % (19/19)	
Number of devices / procedures		1.16	
Procedure duration H:mm		0:50	0:21
Fluoro Duration mm:ss		5:30	2:24
Contrast Vol cc		42.4	19.9
Peak ACT		302.5	45.8
Acute Complications		0	
Device Related Thrombus		0	

Table 19 outlines the TEE and CT imaging follow-up from 45 days to 6 months. The primary performance endpoint of closure success was met in 100% of reported subjects. There were no leaks greater than 3mm at 12 months.

Table 19: TEE and CT Imaging Follow-Up Findings

Characteristic	N
LAA Seal at 45 Days	15*
No residual flow	12
1-2 mm	3
3-4 mm	0
>5mm	0
DRT	0
Pericardial effusion with tamponade	0
LAA Seal at 6 Months	13**
No residual flow	11
1-2 mm	2
3-4 mm	0
>5mm	0
DRT	1
Pericardial effusion with tamponade	0
LAA Seal at 12 Months	16^
No residual flow	14
1-2 mm	2
3-4 mm	0
>5mm	0
DRT	1^^
Pericardial effusion with tamponade	0

Characteristic	N
*4 missed visit due to COVID restrictions ** 5 missed imaging due to COVID restrictions ^2 deaths, 1 did not complete imaging ^^Same subject, DRT persisted despite OAC	

There was a total of two deaths reported in the cohort of treated subjects. There was one subject death between the 45-day and 6-month assessment. This death was attributed to underlying heart failure and was determined to be unrelated to the investigational device or procedure. A second death was noted in a subject approximately 10 months post index procedure. This event was also reported to be unrelated to the device or procedure and was attributed to underlying heart failure.

The only device related SAE was in the subject reported to have a device related thrombosis. This subject, on day 162 (~6 months) post procedure, demonstrated a thin fibrous strand ~2 mm in length emanating from the device which was reported by the site as a device related thrombus (DRT) and confirmed by an independent imaging Core Lab. This patient was subsequently treated with DOAC with repeat TEE performed at 18 months which showed persistence of this finding. There has been no clinical sequalae reported in this subject related to this event.

6.1.2.1 Conclusion

The final subject completed their 12 month visit on 11 October 2022. The investigational site completed their study close out visit on 30 November 2022. Ethics Committee submission and acknowledgement of study closure is complete.

This study demonstrates the feasibility of LAA closure with the CLAAS device using a conscious sedation ICE guided protocol.

- 100% Freedom from major adverse events, evaluated at hospital discharge or at 7 days post-procedure
- 100% Closure success, defined as device success followed by complete closure or peri-device residual leak ≤5 mm in width on TEE

7 STUDY PROCEDURE AND ASSESMENTS

The following study procedures and assessments will occur throughout the duration of the study:

- History and Physical which may be performed as a Review of Systems
- Atrial fibrillation stroke risk assessment with the CHA_2DS_2-VASc or $CHADS_2$ scores
- Major bleeding risk assessment with the HAS-BLED score
- Vital signs (includes Height, Weight, Pulse, Blood Pressure)
- Neurological assessments to include:
- Questionnaire for Verifying Stroke-Free Status (QVSFS).
- NIH Stroke Scale (NIHSS); the NIHSS must be performed by a neurologist or NIHSS-certified research staff.
- Modified Rankin Scale (mRS) to establish the disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability at baseline; the mRS must be performed by a neurologist or research staff who have completed mRS training.
- Patients in whom an incidental neurologic event is suspected on the basis of the QVSFS, NIHSS, or other signs or symptoms, will require a neurologic examination and evaluation performed by a neurologist or clinical designee (e.g., neurology fellow).
- Pregnancy test for Female patients of childbearing potential
- Laboratory testing per site standard practice as part of a catheterization procedure.
- A 12-lead electrocardiogram (ECG).
- CT/MRI for subjects with documented history of TIA/stroke (previous imaging done post-neurological event per standard of care is acceptable; otherwise, must be done after consent).
- The index procedure (LAAO)
- TEE, Cardiac CT imaging
- TTE imaging
- Medication and adverse event assessment

All deviations from the requirements of this Clinical Investigation Plan will be considered protocol deviations. For any protocol deviation, a Protocol Deviation form should be completed in the eCRF indicating the type and reason for the deviation in accordance with FDA requirements outlined CFR 812.140 (a) (4), ISO 14155:2020, and other applicable regulations.

8 MANUFACTURING

The CLAAS System is manufactured according to standard medical device manufacturing processes by qualified employees. Conformal Medical, Inc. is the legal manufacturer of the CLAAS System.

The Conformal facility address is:
Conformal Medical, Inc.
15 Trafalgar Square, Suite 101
Nashua, NH 03063

The components of the CLAAS System, inclusive of catheter manufacturing, final assembly, packaging, and labeling, are managed by the contract manufacturer, Biomerics Advanced Catheter.
Biomerics Advanced Catheter holds ISO 13485 certification for contract design, development, manufacture, packaging, and distribution of medical devices and components, as well as contract extrusion of medical devices, signifying their compliance and proficiency in these specialized domains within the medical device industry.

The Biomerics Advanced Catheter facility address is:
10351 Xylon Avenue N. Suite 100/150
Brooklyn Park, MN 55445

8.1 Manufacturing Overview

Conformal has established and maintains procedures to control the design of the CLAAS System and to ensure that its design is correctly translated into production specifications per 21 CFR 820.30. Conformal has established and maintains requirements for planning, conducting, controlling, and monitoring production processes in accordance with generally recognized good manufacturing practices. regulatory requirements, and international standards. These include completing the appropriate paperwork to ensure there is evidence that the device conforms to specification and was made according to the Device Master Record (DMR) prior to its release.

8.1.1 Manufacturing Controls

All steps in the manufacturing process are controlled and documented. Process control is maintained throughout the production of products using controlled work instructions and drawings; preventive maintenance of equipment, tools, and fixtures; and inspections. Documentation is of sufficient detail to ensure that products are consistently built and conform to specified requirements. Production tools, fixtures, and test equipment receive regular maintenance and calibration. Work environments are kept clean and are conducive to good manufacturing practices. Throughout production, care is taken to ensure device characteristics and performance are protected. Assembly documents and product specifications including the device history record (DHR) are developed, documented, and controlled to ensure product requirements are clearly communicated.

8.2 Identification & Traceability

Traceability requirements are defined during the Design Control process and designed into the assembly documents. The DMR includes or references specifications, assembly instructions (including packaging and labeling), inspection and testing instructions, and the supporting forms. Conformal assembles sub-assemblies and uses suppliers/contract manufacturers to produce the final product. Travelers or DHRs

are used to maintain traceability from materials to assemblies. Components and subassemblies are identified by part number and lot number, as applicable. The DHR or Traveler accompanies the sub-assemblies throughout the process and identifies the status of the Lot. A completed DHR includes assembly part numbers, and lot/serial numbers, and includes or references the date of assembly/inspection, the quantity manufactured, acceptance records showing the device was built according to its Device Master Record (DMR), the quantity released, and labeling. Finished devices are identified by catalogue number (REF) and lot number (LOT). The REF and LOT number combination are sufficient for product traceability in the case of product recalls or product notices. Product status with respect to monitoring and measurement is identified by assembly documents and specified locations throughout product realization. Product status is maintained to ensure only product that has passed the required inspections and tests or has been released under concession is released.
Components, raw material, subassemblies, and finished product to be used in the CLAAS System are inspected in accordance with inspection procedures and the applicable drawings and/or specifications. All components are given a unique lot number traceable to the supplier lot number. Records of traceability are maintained.

9 PACKAGING, SHELF LIFE, AND STERILIZATION

9.1 Packaging, Shelf life and Sterilization

The CLAAS Implant and Delivery System (P/N's 30-00214 and 30-00269) is placed on a polymer card, in a double barrier poly Tyvek pouch, and placed in a cardboard box.

The Access Sheath with Dilator (P/N's 30-00215, 30-00216, 30-00270, and 30-00271) is placed on a polymer card, in a single barrier poly Tyvek pouch, and placed in a cardboard box.

Packaging validation has been successfully completed and ensures device packaging systems will withstand worst case forces of sterilization, shipping, handling and storage while maintaining a sterile barrier and other predetermined quality requirements as required by ANSI/AAMI/ISO 11607-1:2019, including:

- Provide adequate protection to all sterile barrier systems and the sterile contents through the hazards of handling, distribution, and storage such as: shock and vibration, compression, temperature, humidity, mode of transportation, pressure changes.
- Provide adequate protection to all sterile barrier systems and the sterile contents through the hazards of storage such as temperature.
- Demonstration that the sterile barrier system maintains integrity over time.

The packaging system for the CLAAS System is depicted in Figure 20.

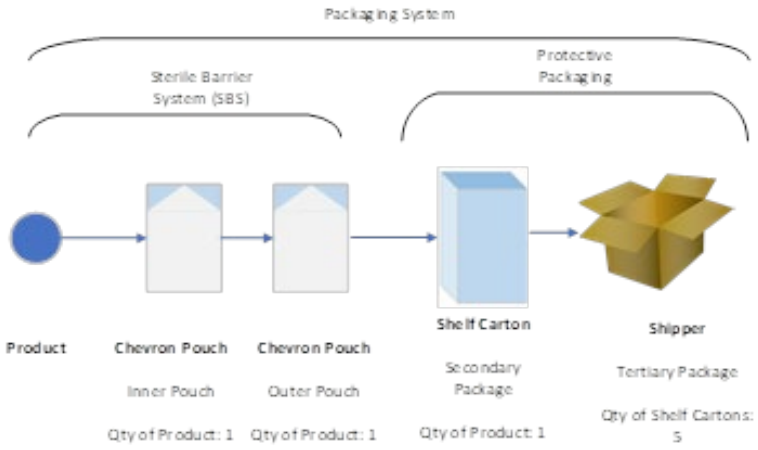

Figure 20: Packaging System Diagram

The CLAAS System has a shelf life of 13 months. CLAAS devices are sterilized using 100% ethylene oxide gas. Devices are sterilized to a sterility assurance level of 10^{-6} based on batch release sterilization performed under the guidelines of ISO 11135:2014/AMD1:2018 and AAMI TIR 16 utilizing the overkill approach.

10 LABELING

Refer to the CLAAS Instructions for Use (document No. 60-00430) for the necessary information on proper set up and deployment of the device.

A representative sample of the implant and access sheath labels are provided below.

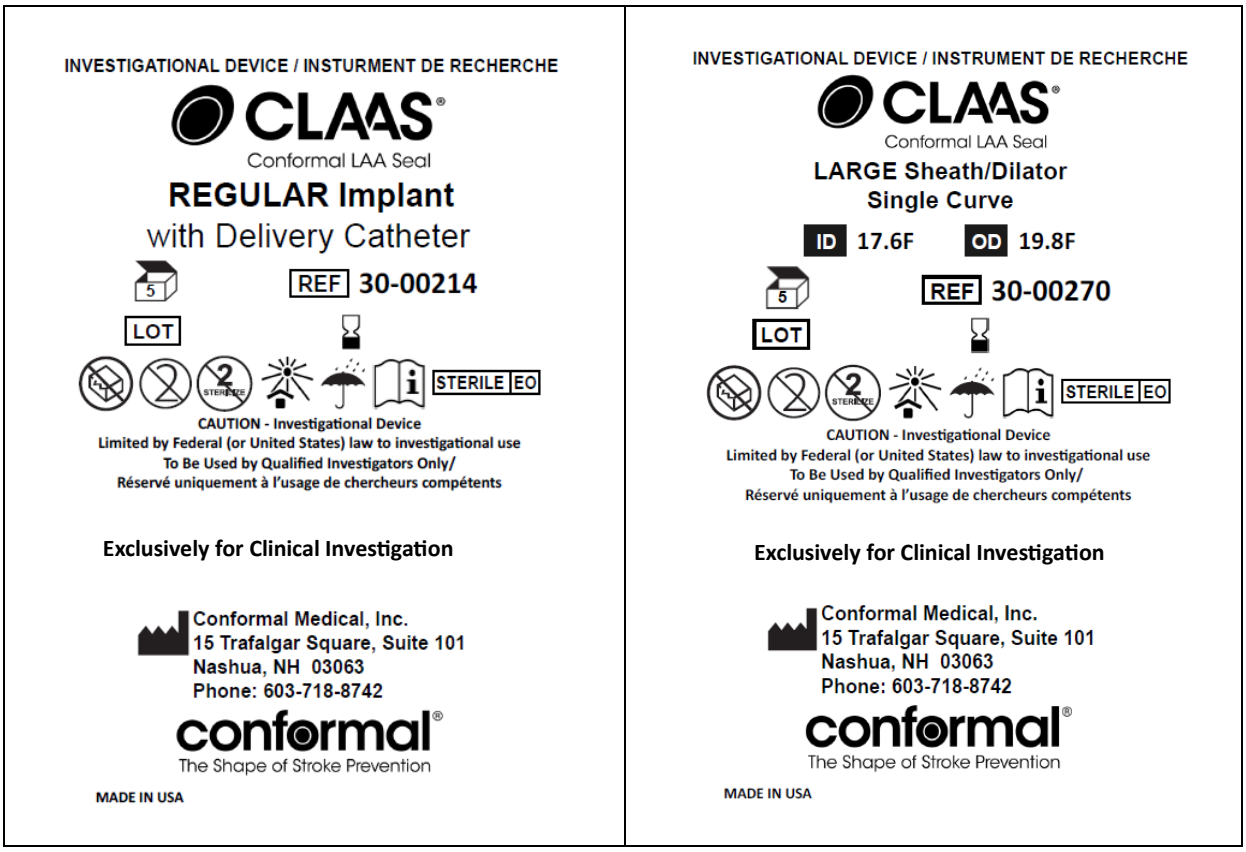

Figure 21: Representative image of product label

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Tab Name: 9 Imaging Protocols

Yale Cardiovascular Research Group
Yale Echocardiographic Core Lab

Transesophageal Echocardiography (TEE)

Image Acquisition Protocol Guidelines

The CONFORM Pivotal Trial

An Evaluation of the Safety and Effectiveness of the Conformal Left Atrial Appendage Seal for Left Atrial Appendage Occlusion

Sponsor: Conformal Medical, Inc.
15 Trafalgar Square, Ste.101
Nashua, NH 03063

Table of Contents

1.0 General Instructions to Site

The following TEE Imaging Protocol is guidance from the Yale Echocardiographic Core Lab that was written specifically for the CONFORM Trial to visualize the CLAAS device and control devices using transesophageal echocardiography (TEE). In order to obtain complete imaging of the device for patients in this trial, all efforts should be made to obtain images at every angle (0, 45, 90 & 135-degrees), as specified in this protocol.

- Confirm 3-beat loops for subjects in sinus rhythm. 3-second loops for arrhythmias and tachycardia.
- Color Flow Doppler: Optimize frame rate (>=20fps) for temporal resolution. Ensure gain setting is appropriate.
- Spectral Doppler: Sweep speed should be 75-100mm/s. 3-beat spectral acquisition for subjects in sinus rhythm, 5-beat acquisition for arrhythmias.
- Nyquist limit of LAA at 40cm/sec and valvular assessment at 60cm/sec.
- All images for the core lab should be recorded in single-plane, unless otherwise specified.
- **DICOM images *AND* Sonographer Worksheets for Index Procedure and Follow-Up should be uploaded to the EDC.**
- **PLEASE ENSURE ALL PHI HAS BEEN REMOVED FROM IMAGES PRIOR TO UPLOAD!**

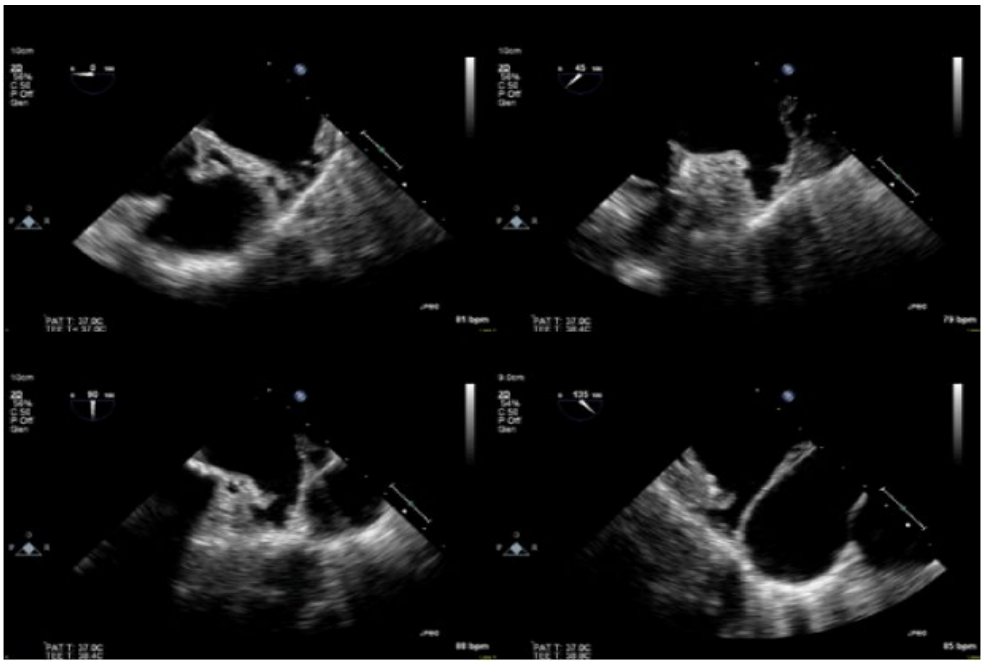
2.0 Two-Dimensional TEE Echocardiography Guide

2.1 Pre-Procedural Imaging (TEE 1: Baseline)

Note: In order to obtain complete imaging, all efforts should be made to obtain images at 0, 45, 90 & 135-degrees.

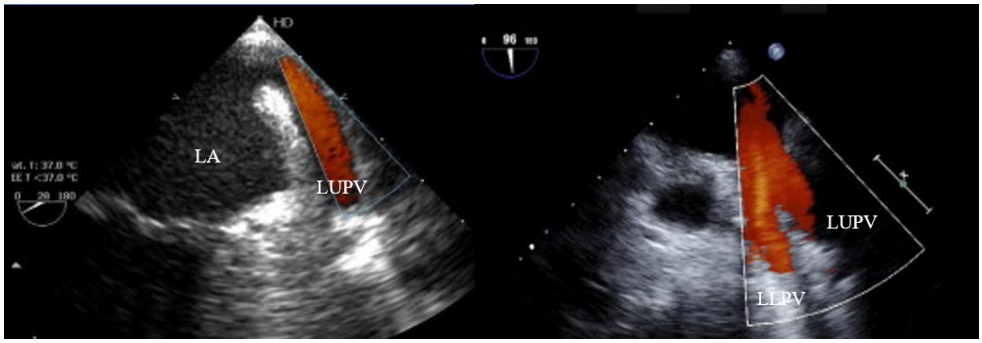
2.1.1 Two-Dimensional Imaging of Left Atrium/Left Atrial Appendage

Two-dimensional imaging of the left atrial appendage is at the level of the aortic valve (AoV). Once the AoV is visualized, anteflexion of the transducer is performed to obtain the LAA and evaluation is done from 0^0 – 180^0. Images of the LAA are acquired at 0^0, 45^0, 90^0, and 135^0.



2.1.2 Pulsed-Wave (PW) and Color Flow Doppler of Left Pulmonary Veins

Assess Left Upper Pulmonary Vein (LUPV) and Left Lower Pulmonary Vein (LLPV).
Increased maximum PV Doppler flow velocity (>1.1m/s) combined with color flow Doppler turbulence may be a reliable index[7] for diagnosing pulmonary vein stenosis.

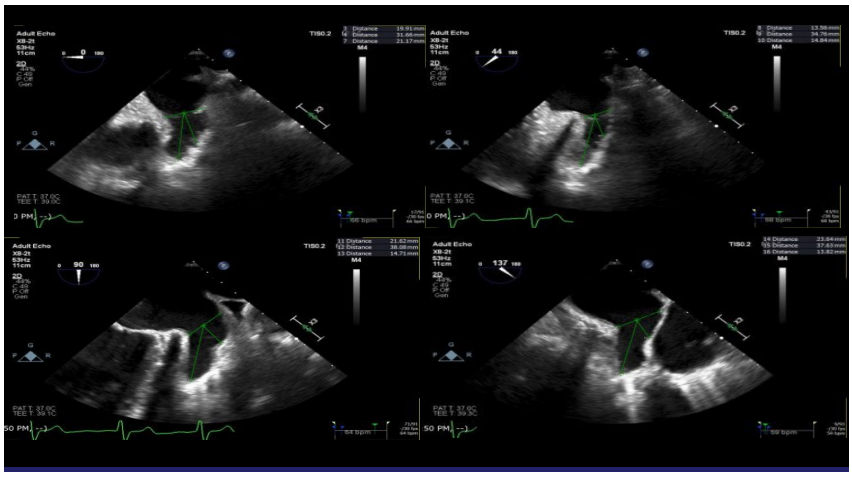


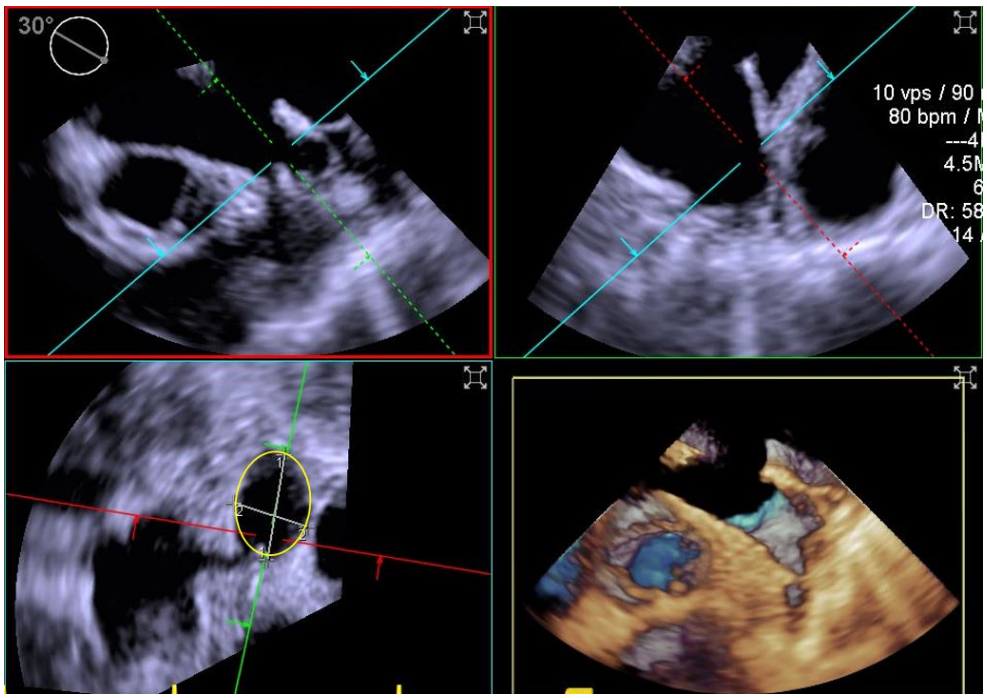
Cartwright, Bruce MBBS, et al Intraoperative Pulmonary Vein Examination by Transesophageal Echocardiography: An Anatomic update and Review of Utility. Journal of Cardiothoracic and Vascular Anesthesia. Volume 27, Issue 1, February 2013, Pages 111-120

2.1.3 LAA Ostium Diameter and LAA Depth

Sweep through LAA views to ascertain the largest diameter and longest depth of the LAA. Measurements are documented at 0^0, 45^0, 90^0, and 135^0. The 3D image of the LAA should be taken from a wide-angled view at 45^0. The perpendicular depth measurement should be made from the ostial plane to the shortest distance to any anatomic structure. The maximal depth is measured from the ostial plane to the most distal aspect of the LAA.

Implant Size	Mean LAA Ostium Diameter (D_{max} + D_{min}) / 2	LAA Ostium Diameter Range	Minimum Landing Zone
Regular	≤ 25mm	10 – 33mm	10mm
Large	≤ 32mm	20 – 40mm	10mm

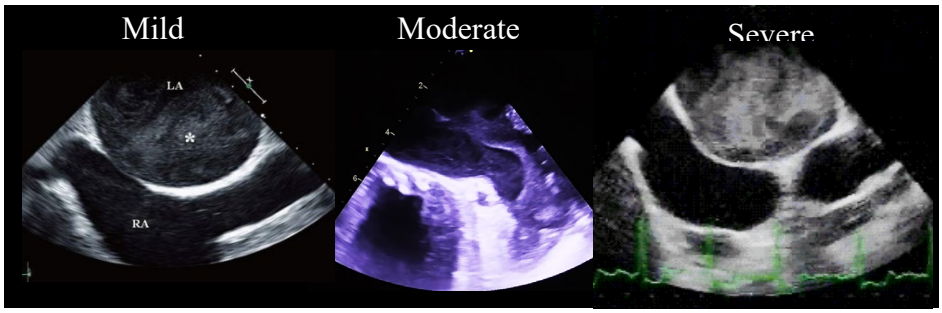




2.1.4 LAA Spontaneous Echocardiographic Contrast (SEC)

Will be assessed from the images acquired. Please optimize gains. The following grading will be used:

a. Absence of echogenicity
b. Mild (minimal echogenicity, only transiently detectable with optimal gain settings during the cardiac cycle)
c. Moderate (dense swirling pattern throughout the cardiac cycle)
d. Severe (intense echo density and very slow swirling patterns in the left atrial appendage, usually with similar density in the left atrium)[6]



Kim, Tae-Seok, MD Role of Echocardiography in Atrial Fibrillation J Cardiovasc Ultrasound. 2011 Jun; 19(2): 51–61.

Echocardiography step by step

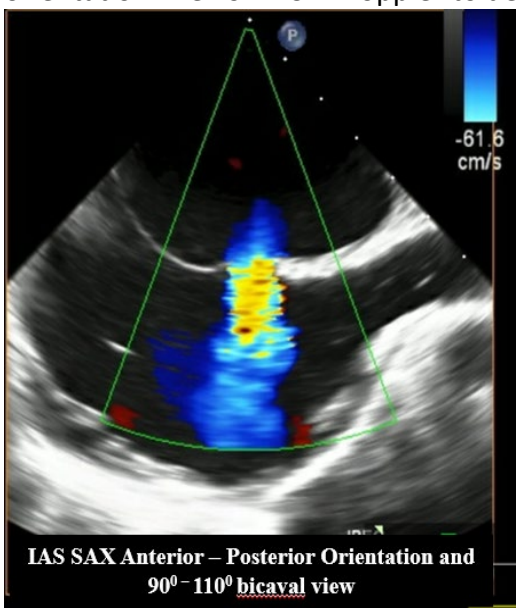
https://drsvenkatesan.com/2011/04/10/a-hurricane-inside-left-atrium/

2.1.5 Intracardiac Thrombus/Vegetation/Mass

A thorough investigation of all cardiac chambers, valves, structures with specific attention to LAA should be performed to rule out intracardiac thrombus, vegetation, or mass.

2.1.6 Atrial Septum

Image atrial septum in both LAX and SAX sweeping through planes. Document atrial septum with color flow Doppler and PW Doppler for atrial level shunting in $90^0 - 110^0$ bicaval view inferior to superior orientation. Perform CW Doppler to demonstrate direction of flow.

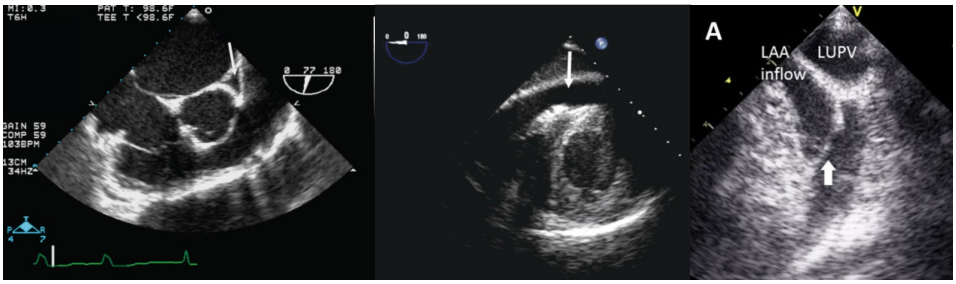


IAS SAX Anterior – Posterior Orientation and $90^0 - 110^0$ bicaval view

2.1.7 Pericardial Effusion

Image the pericardial space (transverse sinus, oblique sinus around the LAA) for effusion. The largest diameter in diastole will be documented and the degree of pericardial effusion will be decided.

a. Absent
b. Small (localized and <1cm width)
c. Moderate (circumferential and 1-2cm width)
d. Large (circumferential and >2cm width



https://thoracickey.com/wp-content/uploads/2016/06/B9781455707614000232_f23-02-9781455707614.jpg

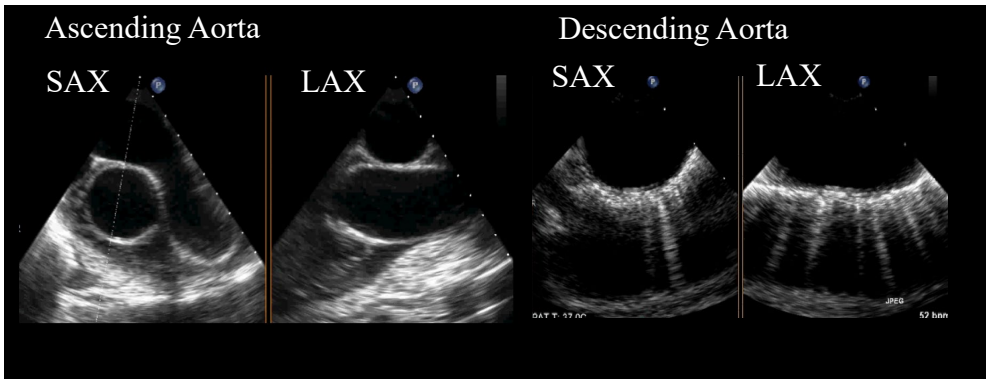
Kamperidis, V et al. "Left Atrial Appendage Pericardial Fluid: Contrast-Enhanced Transesophageal Echocardiography Makes It Visible." Hippokratia20.3 (2016): 235–237. Print.

2.1.8 Mitral Valve

Perform color flow Doppler and CW Doppler for quantitative assessment of the mitral valve. Image from ME4, ME3, and ME2.

2.1.9 Aortic Atheroma/Plaque

Image UE 120-150^0 to assess ascending Ao LAX, UE 0^0 ascending Ao SAX, ME 0^0 descending Ao SAX, ME 90^0 descending Ao LAX Document location and extent of atheroma if present.



2.2 Pre-Release Device Assessment (TEE 2: Pre-Release)

Note: In order to obtain complete imaging, all efforts should be made to obtain images at 0, 45, 90 & 135-degrees.

2.2.1 Assess Device

Scan ME 0^0-135^0 and acquire clips at 0^0, 45^0, 90^0, 135^0 with and without color flow Doppler over the device to determine whether there is residual flow through or around the LAAO device. For periodic follow up comparisons, leave the color flow settings at general/medium with color scale set at 30-40cm/s. Keep frame rates ≥ 20fps. Ensure to place the color flow region of interest over the device/LAA border.

2.2.1.1 Position

Identify and document the position of the LAAO device, prior to tug test.

Tug Test: Annotate “TUG”. Acquire dynamic clip(s) during the tug test showing tether insertion (device apex), in a dedicated viewing angle. Reassess the position of the LAAO device at the conclusion of the tug test.

2.2.1.2 Seal

Identify and document peri-device leaks if present. Demonstrate the vena contracta of the jet(s).

2.2.1.3 Thrombus

Perform a full cardiac scan to investigate for SEC and/or thrombus with specific attention to the implanted device. If thrombus is suspected, optimize imaging and zoom in when acquiring clip so an accurate evaluation of size can be performed. Utilize color flow and PW Doppler for further support.

2.3 Post-Release Device Assessment (TEE 3: Post-Release)

Note: In order to obtain complete imaging, all efforts should be made to obtain images at 0, 45, 90 & 135-degrees.

2.3.1 Assess for Pericardial Effusion

Image the pericardial space (transverse sinus, oblique sinus around the LAA) for effusion. The largest diameter in diastole will

be documented and the degree of pericardial effusion will be decided.

a. Absent
b. Small (localized and < 1cm width)
c. Moderate (circumferential and 1-2cm width)
d. Large (circumferential and >2cm width

2.3.2 Assess Device

Annotate "POST-RELEASE". Scan ME 0^0-135^0 and acquire clips at 0^0, 45^0, 90^0, 135^0 with and without color flow Doppler over the device to determine whether there is residual flow through or around the LAAO device. For periodic follow up comparisons, leave the color flow settings at general/medium with color scale set at 30-40cm/s. Keep frame rates ≥20fps. Ensure to place the color flow region of interest over the device/LAA border.

2.3.2.1 Position

Identify and document the position of the LAAO device.

2.3.2.2 Seal

Identify and document peri-device leaks if present. Demonstrate the vena contracta of the jet(s).

2.3.2.3 Thrombus

Perform a full cardiac scan to investigate for SEC and / or thrombus, with specific attention to the implanted device. If thrombus is suspected, optimize imaging, and zoom in when acquiring clip so an accurate evaluation of size can be performed. Utilize color flow and PW Doppler for further support.

2.3.2.4 Assess Device for 3D

The 3D image of the LAAO device should be taken from a wide-angled view at 45^0. If performed per SOC, please provide the 3D raw image file for Core Lab assessment.

2.3.3 Left Pulmonary Vein Assessment

Acquire loops of 2D and color flow Doppler of the LUPV and LLPV. Acquire PW spectral Doppler in the pulmonary vein (1cm inside the PV).

2.3.4 Assess Atrial Septum

Image Atrial Septum in both LAX and SAX sweeping through planes. Document atrial septum with color flow Doppler and PW Doppler for atrial level shunting in $90^0 - 110^0$ bicaval view inferior to superior orientation. Perform CW Doppler to demonstrate direction of flow.

2.3.5 Mitral Valve Assessment

Perform color flow Doppler and CW Doppler for quantitative assessment of the mitral valve.
Image from ME4, ME3, and ME2.

2.4 Follow-Up TEE:

2.4.1 Assess for Pericardial Effusion

Image the pericardial space (transverse sinus, oblique sinus around the LAA) for effusion. The largest diameter in diastole will be documented and the degree of pericardial effusion will be decided.

a. Absent
b. Small (localized and < 1cm width)
c. Moderate (circumferential and 1-2cm width)
d. Large (circumferential and >2cm width

2.4.2 Assess Device

Scan ME 0^0-135^0 and acquire clips at 0^0, 45^0, 90^0, 135^0 with and without color flow Doppler over the device to determine whether there is residual flow through or around the LAAO device. For periodic follow up comparisons, leave the color flow settings at general/medium with color scale set at 30-40cm/s. Keep frame rates ≥20fps. Ensure to place the color flow region of interest over the device/LAA border.

2.4.2.1 Position

Identify and document the position of the LAAO device.

2.4.2.2 Seal

Identify and document peri-device leaks if present. Demonstrate the vena contracta of the jet(s).

2.4.2.3 Thrombus

Perform a full cardiac scan to investigate for SEC and/or thrombus, with specific attention to the implanted device. If thrombus is suspected, optimize imaging and zoom in when acquiring clip so an accurate evaluation of size can be performed. Utilize color flow and PW Doppler for further support.

2.4.2.4 Assess Device for 3D

The 3D image of the LAAO device should be taken from a wide-angled view at 45^0. If performed per SOC, please provide the 3D raw image file for Core Lab assessment.

2.4.3 Left Pulmonary Vein Assessment

Acquire loops of 2D and color flow Doppler of the LUPV and LLPV. Acquire PW spectral Doppler in the pulmonary vein (1cm inside the PV).

2.4.4 Assess Atrial Septum

Image atrial septum in both LAX and SAX sweeping through planes. Document atrial septum with color flow Doppler and PW Doppler for atrial level shunting (ASD or PFO) in $90^0 - 110^0$ bicaval view inferior to superior orientation. Perform CW Doppler to demonstrate direction of flow.

2.4.5 Mitral Valve Assessment

Perform color flow Doppler and CW Doppler for quantitative assessment of the mitral valve. Image from ME4, ME3, and ME2.

3.0 Abbreviations

1. **2DE or 2D** - Two-Dimensional Echocardiography
2. **Ao** - Aorta
3. **AoV** - Aortic Valve
4. **ASD** – Atrial Septal Defect
5. **ASE** - American Society of Echocardiography
6. **CLAAS™** - Conformal Left Atrial Appendage Seal
7. **cm** – centimeter
8. **cm/s** – centimeters per second
9. **CW**- Continuous Wave Doppler
10. **DTG** – Deep Transgastric
11. **ePTFE** - expanded polytetrafluoroethylene
12. **fps** – frames per second
13. **IAS** - Interatrial Septum
14. **LA** - Left Atrium
15. **LAA** – Left Atrial Appendage
16. **LAAO** – left Atrial Appendage Occlusion
17. **LAX** – Long Axis
18. **LE** – Lower Esophageal
19. **LLPV** – Left Lower Pulmonary Vein
20. **LUPV** – Left Upper Pulmonary Vein
21. **LV** - Left Ventricle
22. **ME** – Mid Esophageal
23. **mm** – millimeter
24. **m/s** – meters per second
25. **PFO** – Patent Foramen Ovale
26. **PW** - Pulsed Wave Doppler
27. **s** - seconds
28. **SAX** – Short Axis
29. **SEC** – Spontaneous Echocardiographic Contrast
30. **TEE** – Transesophogeal Echocardiography
31. **TG** - Transgastric
32. **UE** – Upper Esophageal
33. **TEE** – Transesophogeal Echocardiography

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5.0 Contacts

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THE CONFORM PIVOTAL TRIAL -
AN EVALUATION OF THE SAFETY AND EFFECTIVENESS OF THE CONFORMAL CLAAS SYSTEM FOR LEFT ATRIAL APPENDAGE OCCLUSION

CT ACQUISITION PROTOCOL

Revision A

Study Sponsor:
Conformal Medical, Inc.
15 Trafalgar Square, Ste. 101
Nashua, NH 03063

Cardiac CT Core Lab:
St. Paul's Hospital/University of British Columbia
1081 Burrard Street
Vancouver, BC
V6Z 1Y6,
Canada

APPROVAL SIGNATURE

Signature Page

The undersigned hereby jointly declare that they have reviewed the CT Acquisition Protocol, understand the impacts associated with approving this Protocol, and agree to its form and content.

Name	Function	Signature & Date
David Pomfret	VP Clinical Affairs	DocuSigned by: David Pomfret Signer Name: David Pomfret Signing Reason: I approve this document Signing Time: 15-Jun-2022 | 17:43:29 EDT 1C87BCDC0C294C79BCA0276D6AC3D9CB
Philipp Blanke	Director CT Core Lab	DocuSigned by: Philipp Blanke Signer Name: Philipp Blanke Signing Reason: I am the author of this document Signing Time: 15-Jun-2022 | 06:18:06 PDT FB1A7E95968B408DB92FE4A022C9D797

Table of Contents

1 Purpose

The purpose of this protocol is to provide recommendations on CT data acquisition and reconstruction for the cardiac CT performed for the CONFORM Pivotal Trial sponsored by Conformal Medical Inc. The CT data may be used in the screening process to assess inclusion / exclusion criteria and subject suitability for enrollment. CT follow-up imaging provides information on device positioning, residual LAA perfusion and thrombotic appositions.

2 Scope

This protocol is limited to the aspects of the CT data acquisition.

3 Scanner Requirements

The CT exam must be performed using a multi-detector scanner with at least 64-detector rows.

4 CT Data Acquisition/Protocol Fundamentals

The CT examination should be comprised of two main elements. An ECG-assisted contrast enhanced cardiac CT scan covering the entire heart and including the entire LAA and a delayed phase ECG-assisted acquisition limited to the LAA. The latter serves the purpose to increase the specificity for LAA thrombus detection, in particular by decreasing false positive findings.

The following lists the main components to create a default protocol.

4.1 Preparation

- Placement of an IV access in an antecubital vein (an 18-gauge IV typically provides the highest safety).
- Positioning of the patient on the scanner table in supine position; positioning should be similar to patient positioning on the cath lab/hybrid OR table, although arms are routinely elevated above the head to reduce radiation absorption at the level of the cardiac structures.
- Placement of ECG-electrodes for subsequent ECG-assisted data acquisition
- Patient instruction on breath-holding to improve patient compliance

Beta-blockers can be considered in patients with a resting heart rate >75 beats per minute. Administration of beta-blockers must be in accordance with the institutional local guidelines. Contraindications to beta-blockers have to be considered. In patients with contraindications to beta-blockers alternative rate controlling medications may be used

4.2 Scouts (Topogram, Scanogram)

- Standard AP, plus lateral scouts (depending on the scanner system) of the thorax

4.3 Contrast administration

Contrast administration protocols should allow for sufficient contrast opacification of the left atrium and left atrial appendage. The delayed phase acquisition does require an additional contrast administration.

- **Bolus tracking**: In general, 'bolus tracking' is recommended to trigger data acquisition. The region of interest (ROI) for bolus tracking should be placed with in the ascending aorta for 64/128/192 detector row scanners (all scanners except GE Revolution and Toshiba Aquilion One) or in the left atrium for volume scanners (GE Revolution and Canon/Toshiba Aquilion One). The threshold to trigger data acquisition has to be selected while taking into account the time needed for automated breathing instructions and a potential pre-scan delay, with the aim to achieve sufficient contrast enhancement in the left atrium.
- **Contrast injection**: Contrast administration requires the use of a dual-head injector and is performed as a biphasic protocol, i.e. injection of non-diluted contrast followed by a saline chaser. The amount of contrast and injection time should be adjusted to the patient's body habitus and the scanner system and scan time. Iodine delivery rate (mg/sec) has to be increased in patients with larger body habitus. This can be achieved using higher flow rates. Commonly used rates are 60-90ml contrast media at 3.5-4cc/sec (depending on iodine concentration and body habitus), followed by 50cc saline at the same injection rate.

4.4 First-pass ECG-assisted contrast enhanced cardiac CT data acquisition (' First-pass Cardiac CT')

An ECG-assisted contrast enhanced CT data acquisition of the entire heart including the entire LAA is required in all patients in order to assess the cardiac structures.

- **Acquisition modes**: With all scanner types/vendors, data acquisition should be performed using axial/sequential, prospective ECG-triggering. Depending on the scanner geometry, data acquisition is either performed as a 'step&shoot' acquisition or as a gated 'one beat whole heart' acquisition (volume scanners).

Manufacturer	Scanner Geometry	Acquisition mode
GE	64-row family (750HD, Discovery)	Step&Shoot (prospective ECG-triggering; axial/sequential)

	Revolution (256 row)	Gated one beat acquisition (prospective ECG-triggering; axial/sequential)
Philips	All scanners	Step&Shoot (prospective ECG-triggering; axial/sequential)
Siemens	All scanners	Step&Shoot (prospective ECG-triggering; axial/sequential) Dual Source scanners: High-pitch helical
Canon/Toshiba	64/80-row family	Step&Shoot (prospective ECG-triggering; axial/sequential)
	Aquilion One	Gated one beat acquisition(prospective ECG-triggering; axial/sequential)

- **Tube and detector settings**: Tube voltage and tube current settings should reflect settings of routine cardiac CT protocols and should follow institutional guidelines. For LAA imaging, higher image noise and thus lower mAs/mA levels are acceptable compared to coronary cardiac CT. Tube voltage should be BMI adjusted.
- **Scan length**: The scan range should extend from the tracheal bifurcation to at least 2cm below the left ventricular apex and has to include the entire LAA. CAVEAT: The routine approach of starting 2cm below the carina for coronary cardiac CT may sometimes lead to incomplete imaging of the LAA.
- Axial/sequential data acquisition (Step&Shoot) should be performed in cranial to caudal direction. Data should be acquired at the smallest available collimation (ideally <0.75mm), based on individual system capabilities.
- **Cardiac cycle coverage**: The target phase for ECG-assisted imaging is end-systole. Common approaches for end-systolic imaging included target phases of e.g. 35% of the RR-interval or 300msec past R-peak.

4.5 Delayed phase ECG-assisted CT data acquisition of the LAA

An ECG-assisted delayed phase CT data acquisition, limited to the LAA should be performed in all patients immediately following the cardiac data acquisition to provide further image data for evaluation of LAA. This data acquisition does not involve additional contrast media administration.

- **Scan mode**: Identical scan mode as use for first-pass cardiac CT.
- **Scan length**: The scan length should cover the LAA but does not have to cover the entire left ventricle.

- **Cardiac cycle coverage**: Identical target phase as for the first-pass cardiac CT.

5 CT Data reconstruction

The first-pass and delayed phase ECG-assisted cardiac CT data sets should be reconstructed as follows

- Axial, thin sliced reconstructions, ≤ 1mm; e.g. 0.6mm, 0/4mm increment
- Field of View (FoV) limited to the heart.
- Filtered-back projections or iterative reconstructions using a soft tissue convolution kernel/filter

Yale Cardiovascular Research Group
Yale Echocardiographic Core Laboratory

CONFORM Pivotal Trial

TEE/TTE Sonographer Worksheet

Please submit completed TEE/TTE Sonographer Worksheet with image uploads

---

Site ID: _____ **Subject ID:** _____

Echo Study Date: _____/_____/_____
dd mon yyyy

Modality: ☐ TEE ☐ TTE

Procedure Type:

☐ Diagnostic/Screening ☐ 45-Day ☐ Unscheduled

☐ Index Procedure ☐ 6-Month ☐ Adverse Event

☐ Pre-Discharge ☐ 12-Month ☐ Optional TEE at Baseline

Ultrasound Manufacturer: **Transducer Type:**

_____ _____

Comments _____

_____

_____

Site personnel completing form:

_____ _____ ____/____/_____
Name (print) Sign dd mon yyyy

conformal™ The Shape of Stroke Prevention	CONFORM Pivotal Trial **TEE Checklist – ALL LAAO cases to be performed by Non-Implanting Physician**

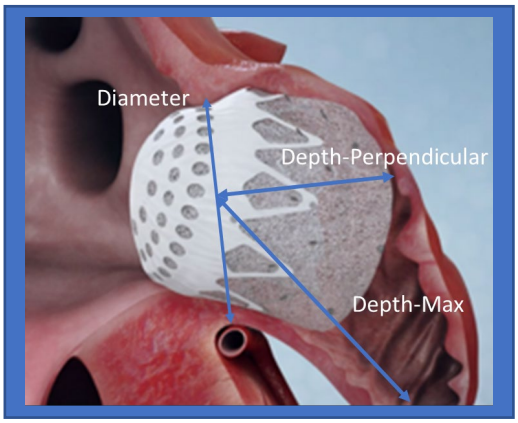
TEE BASELINE

General

- ☐ Confirm 3-beat loops for subjects in sinus rhythm. 3-second loops for arrhythmias and tachycardia
- ☐ Color Flow Doppler: Optimize frame rate (>=20fps) for temporal resolution. Ensure gain setting is appropriate
- ☐ Spectral Doppler: Sweep speed should be 75-100mm/S. 3-beat spectral acquisition for subjects in sinus rhythm, 5-beat acquisition for arrhythmias
- ☐ Nyquist limit of LAA at 40 cm/sec and valvular assessment at 60 cm/sec
- ☐ DICOM images AND Sonographer Worksheets should be uploaded to the EDC
- ☐ All images required for the core lab, should be recorded in single-plane unless otherwise specified
- ☐ **PLEASE ENSURE ALL PHI HAS BEEN REMOVED FROM IMAGES PRIOR TO UPLOAD!**

2D LAA

- ☐ 0°
- ☐ 45°
- ☐ 90° PW Doppler inside the LAA at 90°
- ☐ 135°



2D LAA Ostial and Depth Measurements (perpendicular to ostial plane and max depth, for both Treatment and Control cases)

- ☐ 0°
- ☐ 45°
- ☐ 90°
- ☐ 135°

3D Image of LAA

- ☐ Wide-angled acquisition at 45°

Left Pulmonary Veins (PW) and Color Flow Doppler

- ☐ 0-90° Assess LUPV by placing PW 1cm in the LUPV (adjust to scale)
- ☐ 90-110° Assess LLPV by placing PW 1cm in the LLPV (adjust to scale)

ASD/PFO

- ☐ 90-110° Bicaval view with and without color

Pericardial Effusion (Thorough evaluation at baseline is necessary)

- ☐ Trans gastric LV (biplane if possible)
- ☐ 4-Chamber LV biplane

Mitral Valve

- ☐ Biplane imaging of the mitral valve with and without color
- ☐ If suspicion of stenosis, formal evaluation with gradient is needed

Aortic Atheroma

- ☐ Upper-esophageal 120-150°
- ☐ Upper-esophageal 0°
- ☐ Mid-esophageal 0°
- ☐ Mid-esophageal 90°

IMPORTANT REMINDERS

- ☐ Imaging MUST be performed at 0, 45, 90 and 135 degrees
- ☐ Imaging MUST be performed at 0, 45, 90 and 135 degrees at PRE- and POST-Release with and without color
- ☐ Color sector must encompass the whole device
- ☐ Acquisition should be at least 3 seconds IF in AF

conformal™ The Shape of Stroke Prevention	CONFORM Pivotal Trial **TEE Checklist – ALL LAAO cases to be performed by Non-Implanting Physician**

TEE PRE-RELEASE

Tug Test

- ☐ Annotate "TUG"
- ☐ Acquire dynamic clip in view of tether insertion (device apex)

2D LAAO Device Assessment

- ☐ 0° Acquire clip with and without Color Flow Doppler
- ☐ 45° Acquire clip with and without Color Flow Doppler
- ☐ 90° Acquire clip with and without Color Flow Doppler
- ☐ 135° Acquire clip with and without Color flow Doppler

TEE POST-RELEASE AND FOLLOW-UP

General

- ☐ Confirm 3-beat loops for subjects in sinus rhythm. 3-second loops for arrhythmias and tachycardia
- ☐ Color Flow Doppler: Optimize frame rate (>=20fps) for temporal resolution. Ensure gain setting is appropriate
- ☐ Spectral Doppler: Sweep speed should be 75-100mm/s. 3-beat spectral acquisition for subjects in sinus rhythm, 5-beat acquisition for arrhythmias.
- ☐ Nyquist limit of LAAO at 40 cm/sec and valvular assessment at 60 cm/sec
- ☐ DICOM images AND Sonographer Worksheets should be uploaded to the EDC
- ☐ All images required for the core lab, should be recorded in single-plane, unless otherwise specified
- ☐ **PLEASE ENSURE ALL PHI HAS BEEN REMOVED FROM IMAGES PRIOR TO UPLOAD!**

Pericardial Effusion (if Pericardial effusion observed at baseline obtain similar images)

- ☐ Transgastric LV (biplane if possible)
- ☐ 4-Chamber LV biplane

2D LAAO Device Assessment

- ☐ Annotate "POST RELEASE"
- ☐ 0° Acquire clip with/without Color Flow Doppler
- ☐ 45° Acquire clip with/without Color Flow Doppler
- ☐ 90° Acquire clip with/without Color Flow Doppler
- ☐ 135° Acquire clip with/without Color Flow Doppler

ASD/PFO

- ☐ 90-110° Bicaval view with and without color

3D Image of LAAO Device

- ☐ Wide-angled acquisition (at 45°), 1-beat acquisition, 3-beat loop

Left Pulmonary Veins (PW) and Color Flow Doppler

- ☐ 0-90° Assess LUPV by placing PW 1cm in the LUPV (adjust to scale)
- ☐ 90-110° Assess LLPV by placing PW 1cm in the LLPV (adjust to scale)

Mitral Valve

- ☐ Biplane imaging of the mitral valve with and without color
- ☐ Confirm severity of MR has not changed

IMPORTANT REMINDERS

- ☐ Imaging MUST be performed at 0, 45, 90 and 135 degrees
- ☐ Imaging MUST be performed at 0, 45, 90 and 135 degrees at PRE- and POST-Release with and without color
- ☐ Color sector must encompass the whole device
- ☐ Acquisition should be at least 3 seconds IF in AF

Please upload the TEE images into the CONFORM Imaging Platform

Questions about Imaging? Please reach out to your Site Manager or Field Clinical Specialist or refer to the CONFORM Manual of Procedures Binder!

Tab Name: 10 Instructions for Use

conformal®
THE SHAPE OF STROKE PREVENTION

Instructions for Use

CAUTION - Investigational device. Limited by Federal (or United States) law to investigational use.

Exclusively for clinical investigation

conformal®
THE SHAPE OF STROKE PREVENTION

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THE SHAPE OF STROKE PREVENTION

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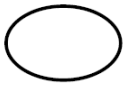
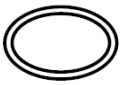
conformal®
THE SHAPE OF STROKE PREVENTION

1 Symbols Glossary

The symbols in this glossary appear in the labels, packaging, and/or manual for the CLAAS® System.

Table 1: Symbols for CLAAS® System and Accessories

SYMBOL	EXPLANATORY TEXT
	Catalogue number
	Batch code
	Use-by date
	Do not use if package is damaged and consult instructions for use
	Do not re-use
	Do not resterilize
	Keep away from sunlight
	Keep dry
	Consult instructions for use or consult electronic instructions for use
	Sterilized using ethylene oxide

SYMBOL	EXPLANATORY TEXT
	Medical device manufacturer
	Number of pieces per package
	MR Conditional
	Medical device
	Inner Diameter
	Outer Diameter
	Date of manufacture
	Single sterile barrier system
	Double sterile barrier system

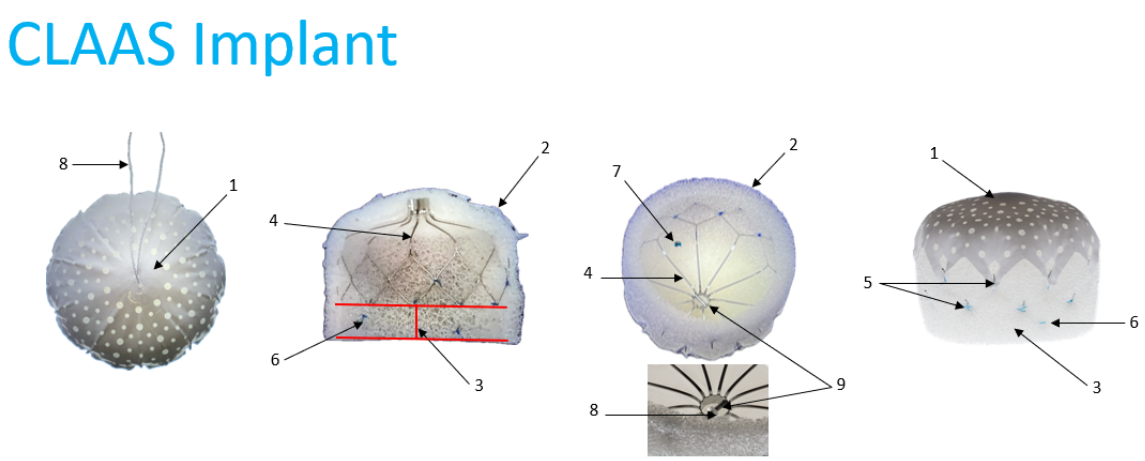
2 Indications for Use

The CLAAS® System is intended to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who:

- Are at increased risk for stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc scores and are recommended for oral anticoagulation (OAC) therapy; AND
- Are deemed by their physician to be suitable for OAC; AND
- Have an appropriate rationale to seek a non-pharmacological alternative to OAC, taking into account the safety and effectiveness of the device compared to OAC.

3 Device Description

The CLAAS Implant is a permanent implant designed to occlude the left atrial appendage (LAA) to eliminate blood flow into and clot passage from the LAA. It is a self-expanding occluder consisting of a cylindrical Nitinol endoskeleton (with low-profile anchor barbs around the midpoint) covered with a porous foam cup. The proximal face of the foam cup has an ePTFE cover to enhance re-sheathing, and the distal portion of the foam cup extends beyond the frame to serve as an atraumatic leading edge.



1. ePTFE Outer Cover – thromboresistant surface
2. Foam Body
3. Foam Bumper – 5mm height
4. Endoskeleton
5. Anchors – 2 rows; 10/row for Regular 27mm CLAAS or 12/row for Large 35mm CLAAS
6. Bumper Markers (x4 within the Bumper)
7. Shoulder Marker (for placement reference)
8. Tether
9. Tether Pin

Figure 1: CLAAS Implant components of construction.

The Implant is designed to conform to irregular LAA anatomies while maintaining secure fixation and is partially re-sheathable and re-deployable prior to final release from the Delivery System via a removable, flexible tether. The implant is available in two sizes: Regular (27 mm) and Large (35 mm).

In addition to the Implant, the CLAAS System includes a Delivery System (Access Sheath & Delivery Catheter) that allows percutaneous delivery of the Implant to the LAA via standard femoral venous access and transseptal puncture. The insertable length of the access sheath is 77.5cm. The insertable length of the delivery catheter is 73cm.

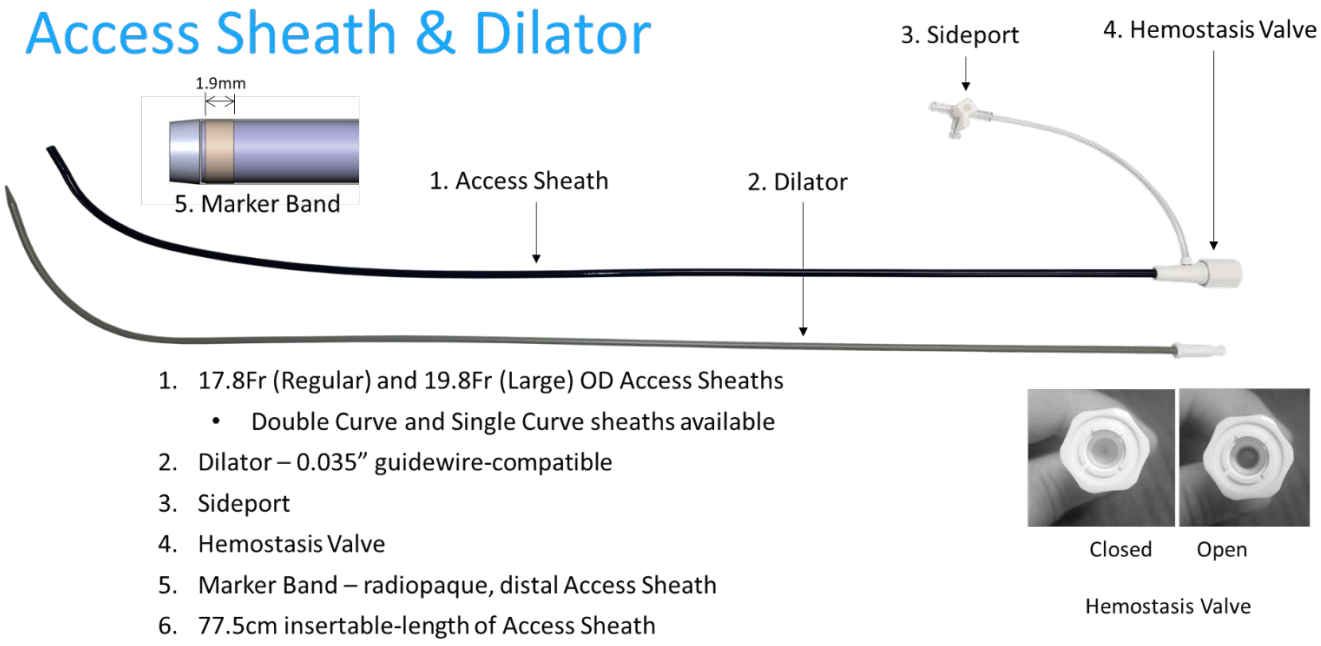


Figure 2: Single curve Access Sheath with Dilator components

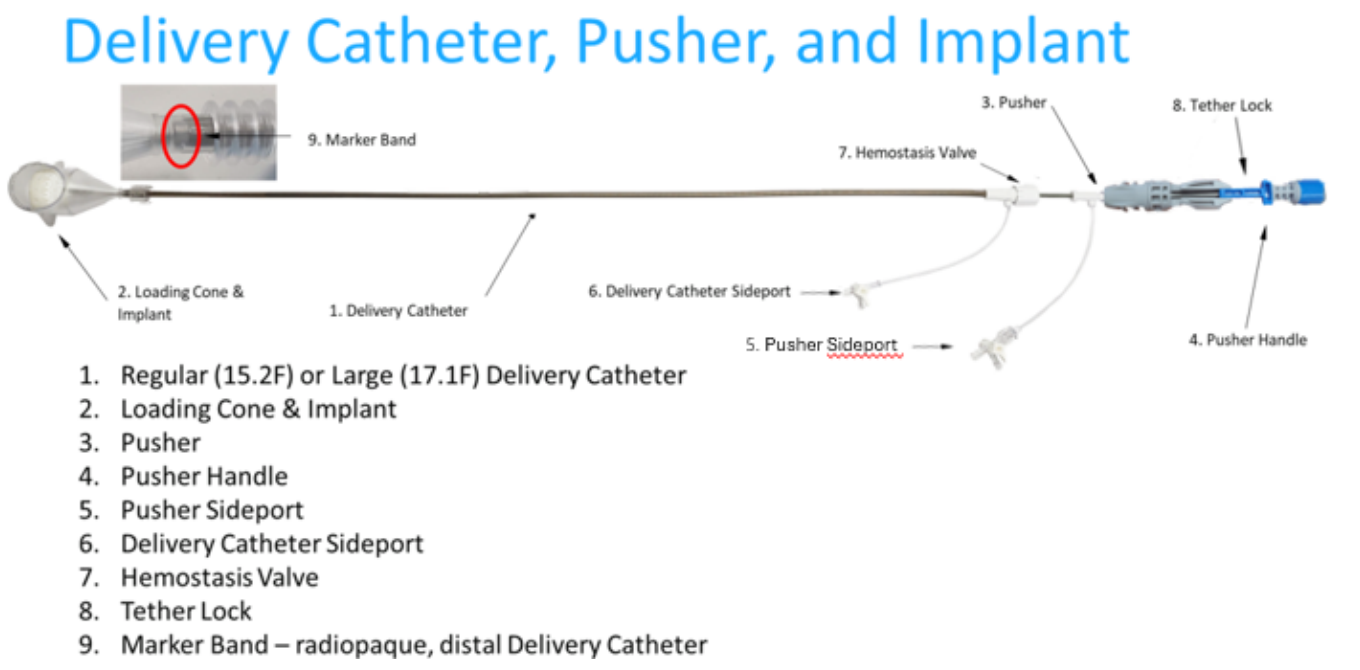


Figure 3: Delivery Catheter, Pusher, and Implant

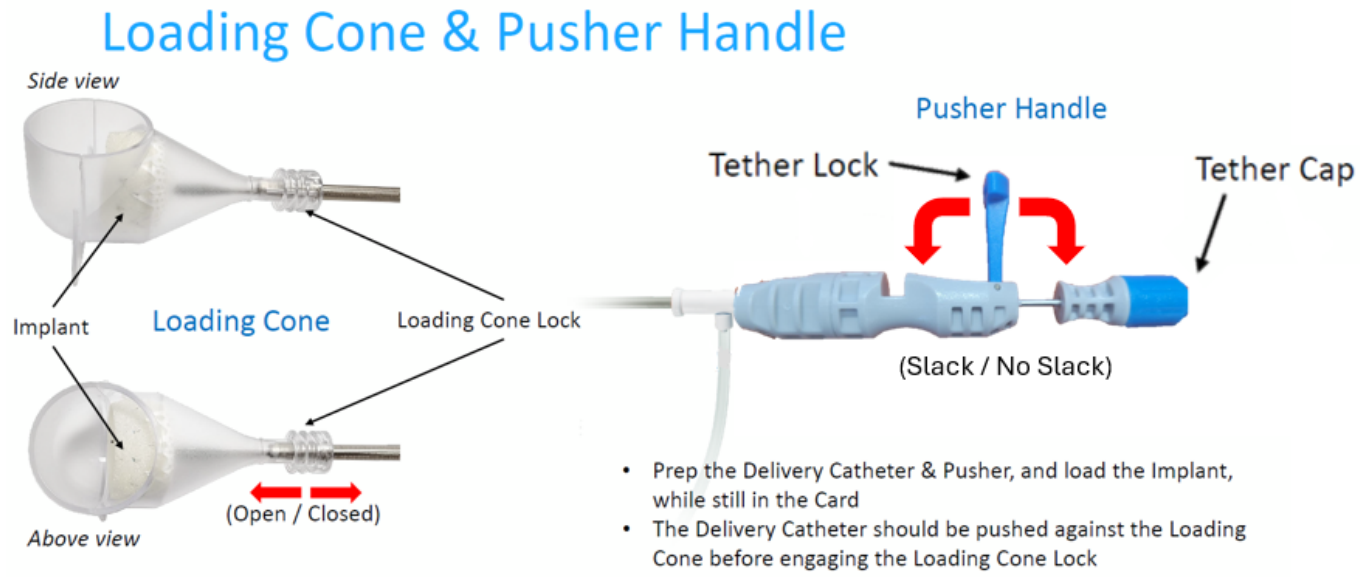


Figure 4: Loading Cone and Pusher Handle

4 Contraindications

Do not use the CLAAS System if:

1. The LAA anatomy will not accommodate the CLAAS device (See Table 2).
2. There is presence of intracardiac thrombus or dense, spontaneous echo contrast consistent with thrombus, as visualized by TEE prior to implant
3. Left Ejection Fraction (LVEF) <30%
4. Moderate or large circumferential pericardial effusion >10 mm or symptomatic pericardial effusion, signs, or symptoms of acute or chronic pericarditis, or evidence of tamponade physiology
5. Atrial septal defect that warrants closure
6. High risk patent foramen ovale (PFO), defined as an atrial septal aneurysm (excursion >15 mm or length > 15 mm) or large shunt (early [within 3 beats] and/or substantial passage of bubbles, e.g., ≥20)
7. Moderate or severe mitral valve stenosis (mitral valve area <1.5 cm^2)
8. Complex atheroma with mobile plaque of the descending aorta and/or aortic arch
9. Evidence of cardiac tumor
10. There are contraindications to the use of OAC, aspirin or P2Y12 inhibitors.
11. The patient has a known hypersensitivity to any portion of the device material or the individual components (see Device Description).

5 Warnings and Precautions

Implantation of the CLAAS should only be performed by physicians trained in percutaneous and transseptal procedures who have completed Conformal Medical, Inc.'s CLAAS training.

NOTE: The LAA is a thin-walled structure. Use caution when accessing the LAA and deploying the Device.

- The CLAAS Access Sheath and Delivery Catheter with Implant are sterile and intended for single patient use only. Do not reuse or resterilize.
- If the sterile barrier has been compromised in any way or appears damaged DO NOT USE.

Precaution: If using a power injector, connect to the Pusher Side port. Maximum pressure setting is not to exceed 100 PSI.

6 Adverse Events

The device and procedure are both associated with risks. Below is a summary of the risks that may occur. Risks are delineated by events associated with the procedure and those associated with the CLAAS System. There may be additional risks that are unknown at this time.

Procedural Risks: The risks of delivery of the CLAAS Implant are similar to those of other procedures that require a transseptal puncture and transcatheter delivery of an implant through the venous system, across the interatrial septum, and into the left atrium using a large bore catheter (e.g., EP procedures and/or other LAA occlusive devices such as Watchman). These risks are well recognized,

and experienced clinicians that are well versed in the use of large bore catheters have mitigated these risks to the extent possible in their standard of care.

The recognized procedural risks observed in CLAAS clinical studies and observed with other LAAO products include, but are not limited to (in alphabetical order):

- Acute Kidney Injury/Renal Failure potentially requiring need for dialysis
- Air embolus
- Allergic reaction to contrast media necessary for imaging during procedure
- Altered Mental Status
- Anesthesia risks (e.g., nausea/vomiting, aspiration pneumonia)
- Anoxic encephalopathy
- Arrhythmia
- Bleeding/anemia requiring transfusion
- Cardiac perforation
- Chest pain/angina
- Contrast related nephropathy
- Damage to vasculature or cardiac structure (e.g., valve, chordae)
- Death
- Deep Vein Thrombosis or Pulmonary Embolism
- Dyspnea
- Edema
- Electrolyte imbalance
- Fever
- Heart Failure
- Hematuria
- Hemodynamic Instability (hypotension/hypertension)
- Hemoptysis
- Hemothorax

- Iatrogenic ASD requiring treatment
- Improper wound healing
- Interatrial septum thrombus
- MI including ST segment elevation
- Pericardial Effusion/tamponade
- Pleural Effusion
- Pulmonary Edema
- Pulmonary Vein/Pulmonary Artery perforation
- Radiation Injury
- Respiratory failure/Hypoxia
- Stroke/TIA related to embolic, thromboembolic, or hemorrhagic event
- Systemic Infection including pneumonia
- TEE/intubation risks including throat pain, trauma to airway or esophagus with or without bleeding
- Thrombocytopenia
- Vasovagal reactions
- Venous access site complications including pain, AV fistula, pseudoaneurysm, infection, hematoma, bleeding requiring transfusion and/or the need for surgical repair

Device Risks: In addition to the risks of undergoing an interventional procedure, there should be consideration to the risks which are specific to the CLAAS Implant and CLAAS Delivery System. Conformal Medical has identified a set of risks, the rates of which may be different due to the design of the CLAAS System as outlined below. A number of the risks have been determined to be present with other interventional (e.g., Watchman) as well as surgical implants designed to occlude the LAA. These risks include but are not limited to (in alphabetical order):

- Arrhythmias
- Cardiac perforation, puncture, tamponade, and/or effusion caused by device
- Chest pain/angina
- Death
- Deep Vein Thrombosis or Pulmonary Embolism

- Device embolization or thrombosis
- Device fracture
- Device malfunction/breakage resulting in the inability to reposition, resheath or retrieve requiring further intervention.
- Device manipulation resulting in the inability to reposition, resheath or retrieve requiring further intervention.
- Device migration requiring intervention
- Edema
- Heart Failure
- Infection
- Major bleed requiring transfusion
- Myocardial Erosion
- Prolonged procedure time risk/Radiation injury
- Pulmonary Vein/Pulmonary Artery perforation
- Re-intervention due to incomplete seal
- Re-intervention to remove device
- Residual leak in LAA
- Stroke/TIA or Systemic embolization
- Thrombus formation

7 Pre-Procedural Instructions

Oral anticoagulation (Warfarin or DOAC) should be discontinued prior to the procedure. DOAC's should be managed according to the drug specific Prescribing Information. Warfarin should be discontinued as per site protocol with confirmation of appropriate INR on the day of the procedure.

The following loading doses should be administered prior to the index procedure:

- ASA 81-100 mg (administered 1 day prior to procedure)

or

- ASA 325 mg (chewed 1 hour prior to procedure)

A baseline TEE or Cardiac CT should be performed to verify LAA anatomy meets CLAAS implant sizing criteria and the absence of contraindications 1-9.

- For ICE guided implant procedures, reference the current ICE Imaging Protocol
- For TEE guided implant procedures, reference the current TEE Imaging Protocol

1. Assess the following through multiple imaging planes (e.g., 0°, 45°, 90°, 135°).
    a. LAA size/shape, number of lobes in the LAA and location of lobes relative to ostium
    b. Confirm the absence of thrombus (use Color Doppler and echo contrast as necessary)
    c. Record the largest (D_{max}) and smallest (D_{min}) LAA ostium diameters and LAA depth (0°, 45°, 90° and 135° sweep).
2. Confirm LAA anatomy is appropriate for CLAAS Implant based on sizing criteria (Table 2).

Table 2: CLAAS Implant sizing

CLAAS Size	Mean LAA Ostium Diameter (D_{min} + D_{max}) / 2	LAA Ostium Diameter Ranges (D_{min} & D_{max} must be within range)	Minimum Landing Zone (Depth)
Regular	≤ 25 mm	10 – 33 mm	10 mm
Large	≤ 32 mm	20 – 40 mm	10 mm

7.1 Accessory / Optional Devices Needed for Implantation Procedure

- (Optional) 18F or 20F Venous Introducer
- Transseptal access system
- 0.035” guidewire (exchange length, e.g., extra support)
- Angiographic Pigtail Catheter
- 50cc syringe with luer connection
- (Optional) VizaraMed Multiflex Steerable Sheath (**15.5F only**) used in compliance with the product’s instructions for use for Regular CLAAS Implant

7.2 CLAAS Devices Needed for Implantation Procedure

- CLAAS Access Sheath (Single or Double Curve) with Dilator
- CLAAS Delivery Catheter with Implant

7.3 Implantation Procedure

NOTE: **DO NOT USE** if the sterile barrier, labeling, packaging, or any component of the Delivery System (Access Sheath, Dilator, Delivery Catheter, Pusher, and Implant) have been compromised or appear damaged.

8 Delivery System (Access Sheath & Delivery Catheter) Preparation

8.1 Access Sheath and Dilator

- Remove the CLAAS Access Sheath and Dilator from its sterile packaging, using sterile technique
    - Inspect both for any damage and check that the stopcock is securely connected to the Sideport
- Flush and de-air the CLAAS Access Sheath with Dilator. Advance the Dilator through the Access Sheath; secure this combination by snapping the Dilator Hub to the Access Sheath Hemostasis Valve.

8.2 Delivery Catheter with Implant

Prepare the CLAAS Implant and Delivery Catheter:

- Remove the Delivery Catheter with Implant from the sterile packaging using sterile technique
- Leave the Delivery Catheter Secured to the Backer Card in which it is packaged
- Inspect prior to use to ensure there is no damage to the handle, catheter, connections, and Implant
- Unfasten the Pusher Handle and Sideports
- Make sure all luer connections are secure; this includes stopcocks, the connection between the Pusher & Pusher Handle, and Tether Cap
- Ensure Tether Lock is snapped securely in the locked position
- Ensure Delivery Catheter Hemostasis Valve is closed
- Ensure the Delivery Catheter Marker Band can be seen in the distal neck of the Loading Cone and the Loading Cone Lock is closed
- Flush the Pusher, while gently tapping the length of the Pusher and Delivery Catheter, until de-aired
- Flush the Delivery Catheter, while gently tapping the length of the Delivery Catheter, until de-aired
    i. The Loading Cone should fill with flush and submerge the Implant
- Ensure the Loading Cone, Delivery Catheter, and Support Tube are secured together, before loading the Implant
    i. The Support Tube is pre-packaged around the Delivery Catheter to provide support during the loading of the Implant
- Pull the Pusher to load the Implant into Delivery Catheter, while ensuring the Loading Cone, Delivery Catheter, and Support Tube do NOT separate from each other during loading of the Implant
- Unlock and remove the Loading Cone from the Delivery Catheter
- Confirm the distal foam bumper of the loaded Implant is within the range of the radiopaque marker of the Delivery Catheter
- Inspect for air bubbles

i. If air bubbles are present, slightly elevate the Delivery Catheter while flushing the Delivery Catheter sideport

The system is ready for use and may be removed from the Support Tube and Card.

9 Intra-Procedure

Intraprocedural anticoagulation should be maintained according to physician standard practice in accordance with published guidelines and local standards of care, with a goal of maintaining an activated clotting time (ACT) of 250-350 sec (or equivalent) throughout the procedure.

1. Once the presence of intracardiac thrombus and exclusion criteria are ruled out and LAA anatomy is confirmed to meet CLAAS Implant sizing criteria (Table 2), prepare the patient for standard transcatheter procedure via femoral venous access
2. Use a standard, commercially available transseptal access system to cross the inter-atrial septum
3. Position an appropriate 0.035’ guidewire in the left upper pulmonary vein (LUPV) or loop it in the left atrium (LA). Remove the transseptal access sheath while maintaining wire position
4. Advance the prepared CLAAS Access Sheath and Dilator over the guidewire into the LA
    - Once sufficiently across the septum, separate the Dilator from the Access Sheath and remove the Dilator and guidewire, leaving the Access Sheath in the LA or LUPV
    - Aspirate from the side port to minimize the potential of introducing air into the system, then flush the Access Sheath

NOTE: Use caution when introducing the CLAAS Access Sheath to prevent damage to cardiac structures.

NOTE: The Access Sheath’s Hemostasis Valve can be opened/loosened or closed/tightened. After introduction or removal of equipment, ensure the Access Sheath’s Hemostasis Valve is sufficiently closed/tightened to prevent unnecessary bleeding from the hub.

5. Advance an angiographic pigtail catheter through the Access Sheath, into the distal portion of the LAA, under fluoroscopic guidance. Obtain an angiogram of the left atrial appendage in the optimal projection
6. Slowly remove the pigtail catheter while maintaining Access Sheath position
7. Advance the prepared Delivery Catheter into the Access Sheath
    - Advance the Delivery Catheter until the hubs meet, and snap together
    - Fluoroscopy may be used to visualize the movement of the Delivery Catheter, but the Delivery Catheter should not extend beyond the Access Sheath
8. Using fluoroscopy and/or ultrasound imaging, confirm the position of the Access Sheath tip (distal to the ostium) before initiating deployment of the Implant
9. While using fluoroscopy, hold the Access Sheath / Delivery Catheter assembly in one hand and the Pusher in the other hand, slowly advance the Pusher until 3-5 mm of the Implant is exposed beyond the Access Sheath Marker Band

- Under fluoroscopy, the 4 distal Bumper Markers will be slightly separated and need to be at least 2.5 millimeters beyond the Access Sheath Marker Band
- Do not advance the Pusher any farther

10. Position the Delivery System (Access Sheath and Delivery Catheter) so the Implant Shoulder Marker is at the LAA ostium
11. Prior to full deployment, ensure the Implant Shoulder Marker is correctly positioned
    - Adjust placement as necessary and desheath the Implant until the Implant is fully deployed
    - Desheathing/Unsheathing: Fix the Pusher in place with slight forward pressure, then slowly pull back on the Access Sheath/Delivery Catheter Assembly to expose and deploy the Implant
12. Upon deployment, provide Tether slack
    - Unsnap the Tether Lock and secure in the unlocked position
        i. Advance the Tether Cap until it abuts the Pusher Handle
        ii. Slowly retract the Delivery System from the Implant to ensure there is no contact

9.1 Device Deployment Optimization

1. Evaluate the Implant position with fluoroscopy /angiography and/or ultrasound, and adjust as needed to align the CLAAS device with the LAA ostium (See Release Criteria Guidelines below).
2. NOTE: The Pusher should be close to, but not touching, the Implant for contrast injections through the Pusher Sideport

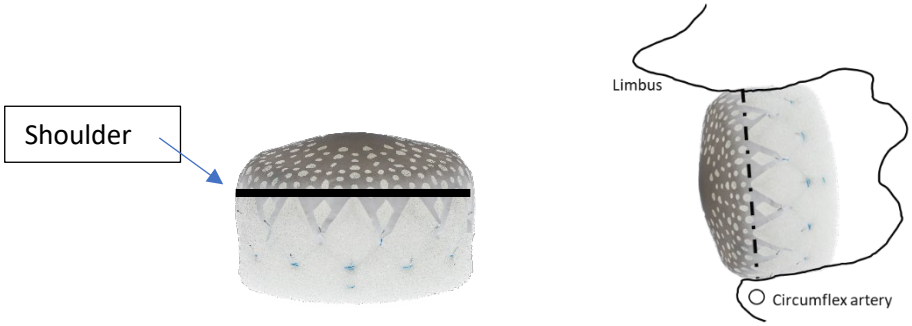


Figure 5: CLAAS Implant (left) with Shoulder delineated which is coincident with internal fluoroscopic marker and CLAAS Implant in optimal position (right), shoulder aligned with LAA ostium.

3. Evaluate Implant Anchoring with a Tug Test
    - Retract the Pusher approximately 2 cm from the surface of the Implant
        i. Unscrew the Tether Cap and gently pull Tether while observing motion of the Implant and LAA tissue
    - Evaluate the seal with angiography and ultrasound

9.2 Release Criteria Guideline: Anchoring, Seal, Position

Verify **ASP Guideline Criteria** before releasing the Implant:

1. **A**nchoring – With the Tug Test
    a. Observe tissue movement with the Implant, with ultrasound imaging
    b. Repeat if it is observed that the Implant moved from its original position
2. **S**eal – Using ultrasound imaging
    a. Target ≤ 3mm leak in all ultrasound views (0°, 45°, 90°, 135°)
        i. For ICE guided procedures, reference the current ICE Imaging Protocol
        ii. For TEE guided procedures, reference the current TEE Imaging Protocol
3. **P**osition – The plane of the Shoulder Line of the CLAAS device should be at or just proximal to the LAA ostium. CLAAS Implant position in relation to the LAA ostium may vary based on individual patient anatomy and the imaging views.
    a. CLAAS position should be evaluated in all FOUR ultrasound views (0°, 45°, 90°, 135°)
    b. Target deployment is for the Shoulder Line to be <5mm proximal to the LAA ostium and not to exceed 8mm.

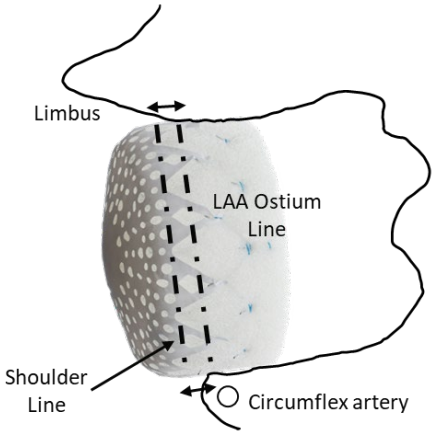


Figure 6: Example of Shoulder-to-ostium engagement.

If the Implant Anchoring, Seal, or Position are not acceptable, the Implant should be repositioned. The Implant will need to be partially resheathed before repositioning and may be partially resheathed into the Access Sheath, up to three times.

9.3 Device Repositioning

1. Remove Tether slack by retracting the Tether Cap and securing the Tether Lock in the closed position cradle
    - Resheath under fluoroscopy
    - Hold the Access Sheath/Delivery Catheter assembly in one hand and the Pusher in the other, then advance the Sheath/Catheter assembly over the Implant until the Implant Shoulder Marker is at the proximal edge of the Access Sheath Marker Band
    - The distal Bumper Markers should still be several millimeters beyond the Access Sheath Marker Band

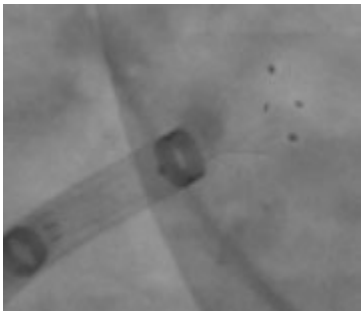


Figure 7: Access Sheath Marker Band (A) and distal Bumper Markers (B) positioned during partial resheath

2. Reposition the Implant, by adjusting the position of the Delivery System, using the Shoulder Marker as a guide
    - With light forward pressure on the Pusher, retract the Access Sheath/Delivery catheter assembly (desheath) to redeploy

NOTE: The Implant can be removed from the patient by fully resheathing the implant into the Access Sheath and then into the Delivery Catheter, which can then be removed from the Access Sheath. Do not reuse a device that has been fully resheathed.

9.4 Implant Release – Continued from Intra-Procedure

Note: the Implant has been deployed and tether slack has been provided

1. Remove the Tether Cap and apply slight tension
2. Advance the Pusher near the face of the Implant, while keeping the Tether Cap & Delivery Catheter/Access Sheath assembly stationary
3. Cut **one** of the exposed strands of the Tether
4. Slowly withdraw the Tether until it is fully removed from the Delivery Catheter
5. Retract the Pusher so its entirety is within the Access Sheath and slowly disconnect and remove the Delivery Catheter with Pusher from the Access Sheath
6. Re-confirm Implant Position and Seal with imaging
7. Slowly remove the Access Sheath
8. Confirm absence of pericardial effusions
9. Remove the femoral access sheath and close as per routine

Note: It is important to cut only one strand of the Tether when releasing the implant.

9.5 Post-Procedure / Follow-Up - Antiplatelet and oral anticoagulant therapy requirements

- Details of the post-procedure follow-up requirements are detailed in the CONFORM trial protocol.

10 Magnetic Resonance Imaging

Non-clinical testing demonstrated that the CLAAS Implant is MR Conditional. A patient with this implant can be scanned safely in an MR system under the following conditions:

MRI Safety Information

The Conformal Left Atrial Appendage Seal (CLAAS) Implant is MR Conditional. A patient with the Conformal Left Atrial Appendage Seal (CLAAS) Implant may be safely scanned under the following conditions. Failure to follow these conditions may result in injury to the patient.

MR Conditional

Parameter	*Condition*
Nominal Values of Static Magnetic Field (T)	1.5-T and 3.0-T
Maximum Spatial Field Gradient (T/m and gauss/cm)	40-T/m (4,000-gauss/cm)
Type of RF Excitation	Circularly Polarized (CP) (i.e., quadrature-driven)
Transmit RF Coil Information	There are no transmit RF coil restrictions. Accordingly, the following may be used: body transmit RF coil and all other RF coil combinations (i.e., body RF coil combined with any receive-only RF coil, transmit/receive head RF coil, transmit/receive knee RF coil, etc.)
Operating Mode of MR System	Normal Operating Mode
Maximum Whole Body Averaged SAR	2-W/kg (Normal Operating Mode)
Limits on Scan Duration	Whole body averaged SAR of 2-W/kg for 60 minutes of continuous RF exposure (i.e., per pulse sequence or back to back sequences/series without breaks)
MR Image Artifact	The presence of this implant produces an imaging artifact. Therefore, carefully select pulse sequence parameters if the implant is located in the area of interest.

11 How Supplied

The CLAAS Implant is provided with the Delivery Catheter.
The CLAAS products are supplied STERILE using an ethylene oxide (EO) process.
Do not use if package is opened or damaged.
Do not use if labeling is incomplete or illegible.

NOTE: Contents of inner package are STERILE.

11.1 Handling and Storage

Store in a cool, dry, dark place

Conformal Medical, Inc.
15 Trafalgar Square, Suite 101
Nashua, NH 03063
603-864-0419

Tab Name: 11 Device Accountability

conformal™ The Shape of Stroke Prevention	Title:	Document No.
	Device Accountability Log	**F-042**
	Page 1 of 1	**Revision F**

Study	Site Number	Site Name	Principal Investigator

(FOR SPONSOR PRODUCT ONLY. PLEASE RECORD EACH UNIT INDIVIDUALLY)

#	DEVICE RECEIPT				DEVICE DISPOSITION				DEVICE RETURN	Site Initials/Date	Monitor/ Status Date
	Date of Site Receipt DD-MMM-YYYY	**Ref #** *On the product packaging or label*	**Lot #** *On the product packaging or label*	**Exp. Date** *On the product packaging or label*	**Disposition** *This refers to the outcome of the device*	**Subject ID (If applicable)**	**Date of Disposition** *This is the date the product was used, disposed or returned*	**Device Deficiency**	**RGA Number** *If shipping product back, Sponsor will give Number e.g. RGA-###*	*Complete this column once device outcome is complete*	*Date product was confirmed/monitored by CRA*
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			

At site or study closure:

Investigator Sign: ______________________________ Date: _______________ Log Page ____ of ____

conformal™ The Shape of Stroke Prevention	Title:	Document No.
	Device Accountability Log	**F-042**
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					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			

At site or study closure:

Investigator Sign: ___________________________________ Date: _________________ Log Page ____ of ____

conformal™ The Shape of Stroke Prevention	Title:	Document No.
	Device Accountability Log	**F-042**
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					☐ Used ☐ Disposed ☐ Returned ☐ Not Used			☐ Yes ☐ No			
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Investigator Sign: ______________________________ Date: ______________ Log Page ____ of ____

Tab Name: 12 Lab Documents

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Tab Name: 13 Mediata EDC

Study Information	
Client	Conformal Medical
Study Name	CONFORM Pivotal
Database System	Medidata Rave

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Date	
Role	Sponsor – Manager of Clinical Operations

CONFORM Pivotal Trial

eCRF Completion Guidelines

Contents

CONFORM Pivotal Trial

eCRF Completion Guidelines

1 General Instructions

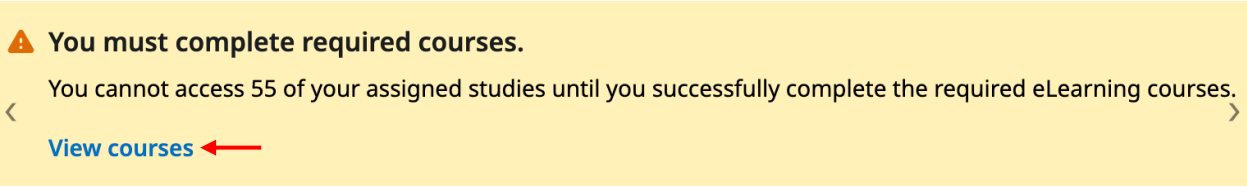
Note: These instructions are specific to the database as applies to patients consented under Protocol Revision K. If you need instructions for patients consented under an earlier Protocol Revision, please ask your site manager for the eCRF Completion Guidelines Version 1.0.

1.1 Database Access and Security

Rave Database Link:

https://login.imedidata.com/login

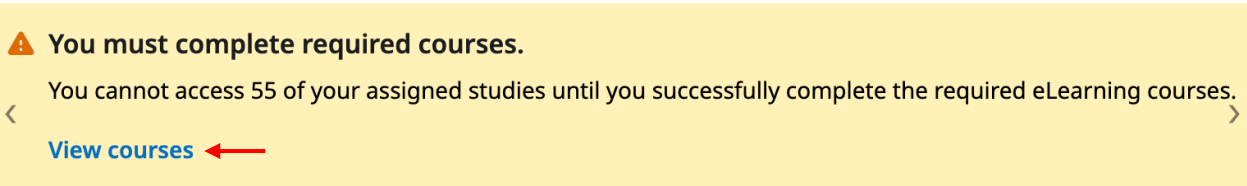
Existing users: You will receive an email from Medidata, informing you of access to the study. Depending on the user's role for the study, additional eLearning may be required prior to gaining access to the study EDC. Pending eLearning will be displayed on the home screen and can be accessed via the "View courses" link.



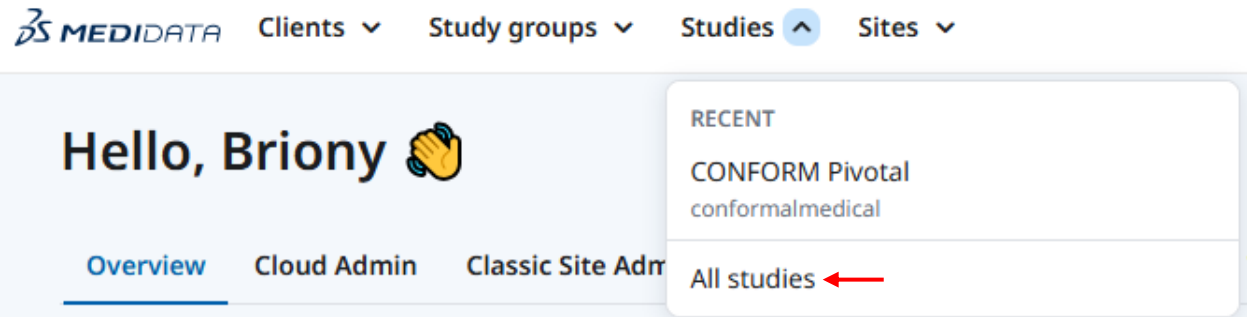
New users:

Request access through your assigned Conformal Site Manager, who will work with you to ensure appropriate training and documentation is in place prior to providing access.

A User Authorization Form will then be sent to you for signature via DocuSign. Once the form is completed and processed by the study team, an email invitation is sent to the end user for account activation. Required training (eLearning) videos in Medidata must be completed to gain access to the study database. The eLearning trainings can be accessed via the "View courses" link in the message displayed on the homepage.

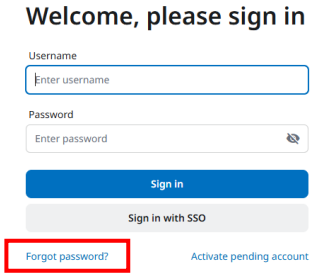


Upon logging into Medidata Rave, the study can be accessed via "Studies" then "All studies."



Once accessed, the study will then appear in your Recent Activity menu on the homepage and can also be accessed via “All studies” in that menu.

1.2 Forgotten Password



1. **Open** iMedidata
2. **Click** the link “I forgot my username or password"
3. **Enter** your email address and **click** “send”
4. In a few minutes, **check your email inbox** for an email invite to iMedidata

   - **IMPORTANT: The reset link in this email will only be valid for 4 hours.** After 4 hours the link will expire and you will need to repeat the process.

5. **Open** the email and **click** on “reset password”
6. **Answer** your security question (ie: your birthday date) and **click** “reset”
7. **Type** in your new password and confirm.
8. **Login** to iMedidata with your username and *new* password

https://login.imedidata.com/login

1.3 System Timeout

The system will time out after 15 minutes of inactivity. Make sure to save your data often.

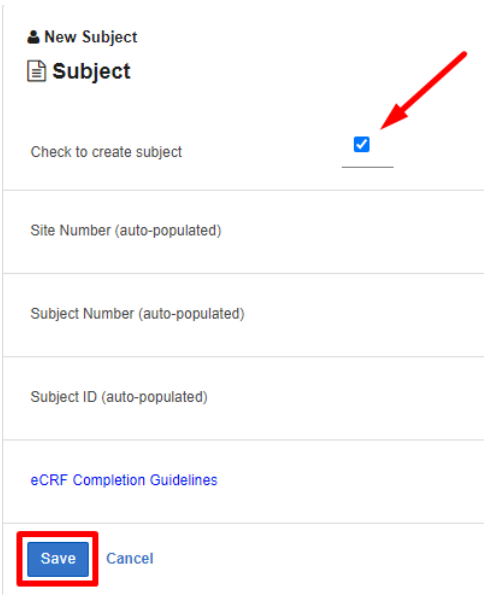
If data is not saved and the system times out, the data will need to be re-entered. Click the Save button at the bottom of the form.

2 Adding and Viewing Subjects

2.1 Add Subject

To add a subject, click the + Add Subject  icon in the upper right corner of the screen, which will take you to the New Subject record.

Check the box next to "Check to create subject." The subject is added into the system when the record is saved.



After the subject has been added, the subject will be enrolled in one of the following two categories:

ROLL-IN: Up to 3 subjects per site may be implanted with the CLAAS device as part of the roll-in phase of the trial. Sites that implanted 3 subjects with the Initial CLAAS system will be permitted to implant one additional roll-in subject with the Next Generation CLAAS System.

RANDOMIZED: When the subject has met all inclusion criteria and no exclusion criteria (including echocardiographic exclusion criteria), the subject will be randomized to either the CLAAS or Control device.

The category will be entered on the Informed Consent form (see 3.1.1 Informed Consent).

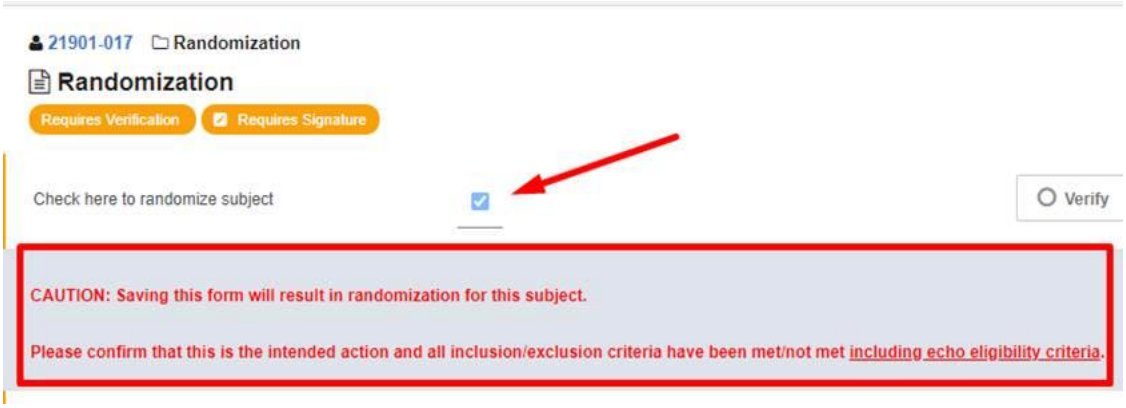
It is important to only add a subject in EDC after the subject has signed the informed consent form, as this action cannot be undone. If a new subject is entered into the database in error, contact your Site Manager immediately.

2.2 Randomization

When the subject has met all inclusion criteria and no exclusion criteria (including echocardiographic exclusion criteria), the subject will be randomized to either the CLAAS or Control device.

The LAA occlusion procedure shall take place no later than 14 days from the date of randomization.

Please ensure that more than one Study Personnel listed on your DOA has the ability to randomize subjects within the iMedidata system.

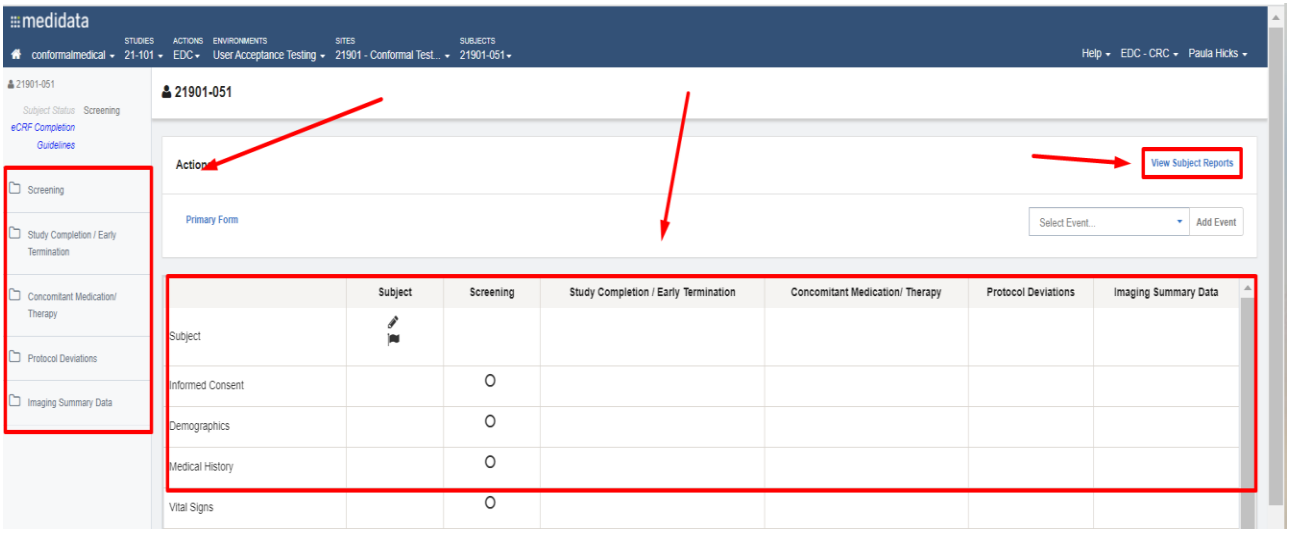


A Protocol Deviation is required if:

- Randomization occurs **greater than 90 days** from Original Informed Consent.
- Implant Procedure date is **greater than 14 days** from Randomization date.

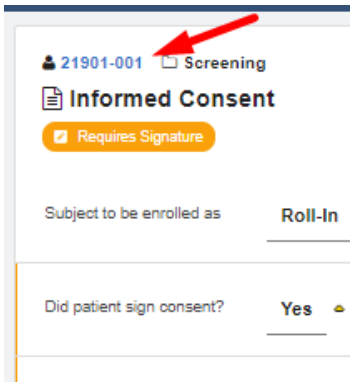
2.3 Subject Record Grid

Subject case report forms can be accessed one of two ways – either from the folders on the far-left side of the screen as indicated by the left arrow or from the subject grid as indicated by the middle arrow.



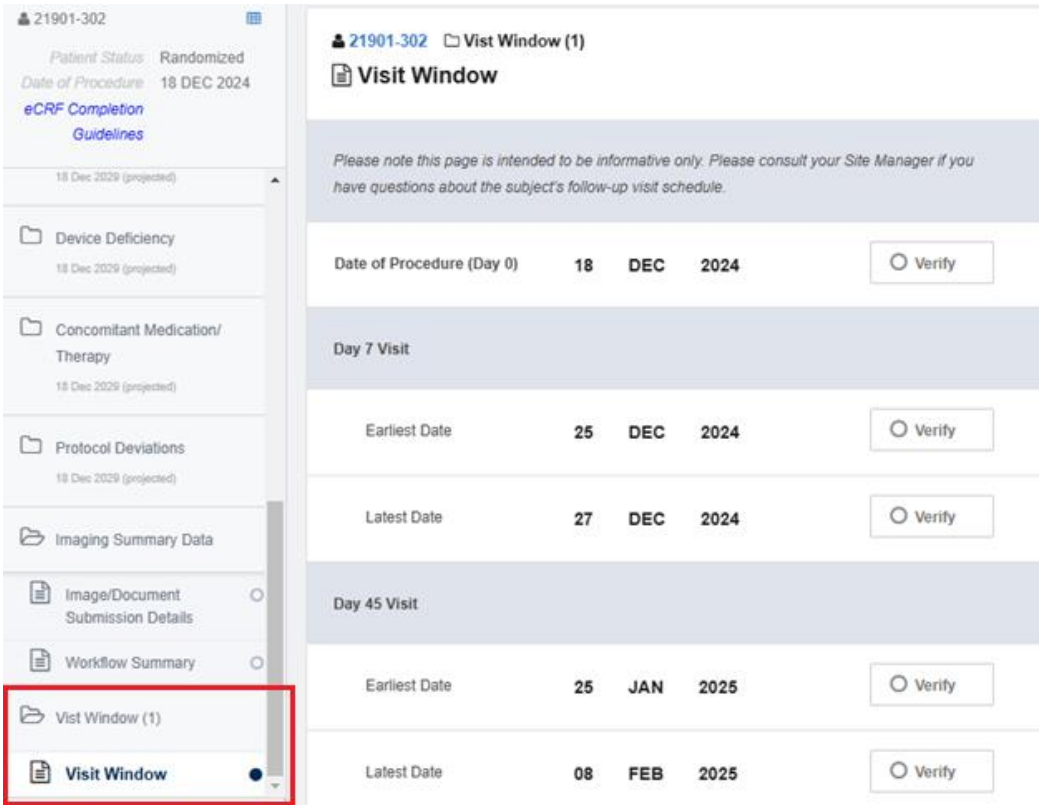
Note: Subject specific reports are also available for use and can be accessed using the link as indicated by the right arrow.

To return to the subject grid while in an individual case report form, click on the **Subject Record ID** link as indicated below, and it will return you to the subject grid. The image below is on the Informed Consent form.



2.4 Visit Window List

Once the date of procedure has been entered into the Procedure form, the Visit Window list will populate within the Visit Window folder on the left side of the screen. The earliest date and latest date for each study visit are listed on this form, calculated by the system using the protocol-specified visit windows.



3 Individual CRF Instructions

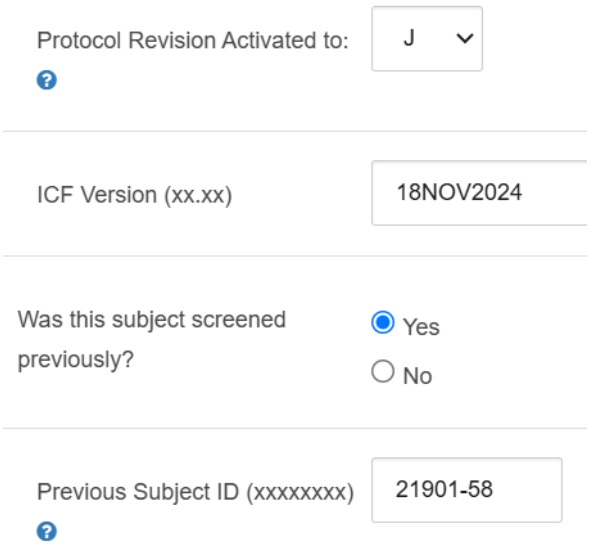
3.1 Screening and Randomization

3.1.1 Informed Consent

Please confirm the subject you are randomizing is in the roll-in or randomized category. If subject Randomization occurs **greater than 90 days** from the date of informed consent, a PD must be entered.

ICF Version (xx.xx): Enter the Version of the ICF as recognized by the site and will be recognized for monitoring purposes. Even though the format is listed as (xx.xx), both text and number values can be entered. It is suggested that date of ICF IRB approval be entered here, e.g., 18NOV2024.

If a subject was screen failed previously and is being reconsidered for the study, please enter information regarding prior subject ID on this page.

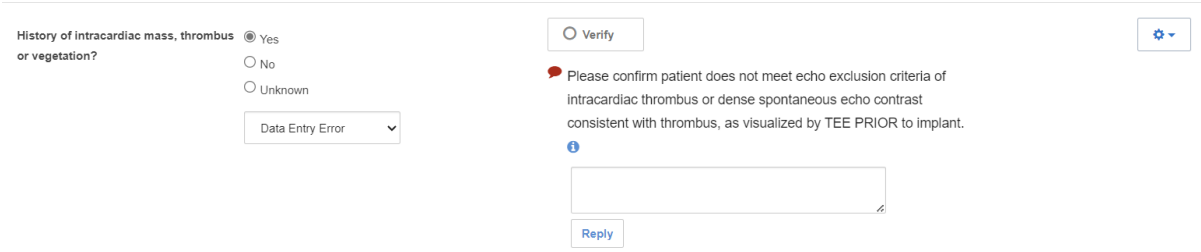


3.1.2 Medical History

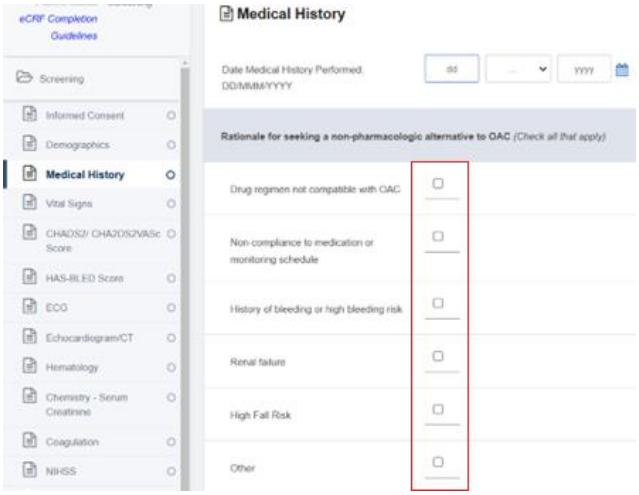
Medical history may be completed up to 30 days prior to consent as part of site standard of care. If it is completed greater than 30 days prior to the date of informed consent, a protocol deviation must be entered.

Medical history must be completed prior to index procedure for roll-in subjects and prior to randomization for randomized subjects.

Auto queries will populate for ”Yes” responses as related to Inclusion/Exclusion Criteria (e.g., History of CVA, History of Intracardiac Thrombus, etc.).



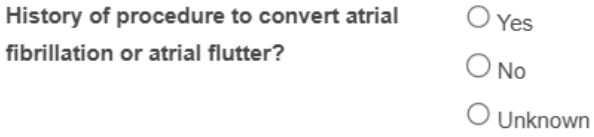
Rationale for seeking a non-pharmacologic alternative to OAC *(Check all that apply)*



To meet study inclusion, at least one of the boxes must be checked or "other" should be selected with information entered (i.e., occupational hazard risks, financial issues, etc.).

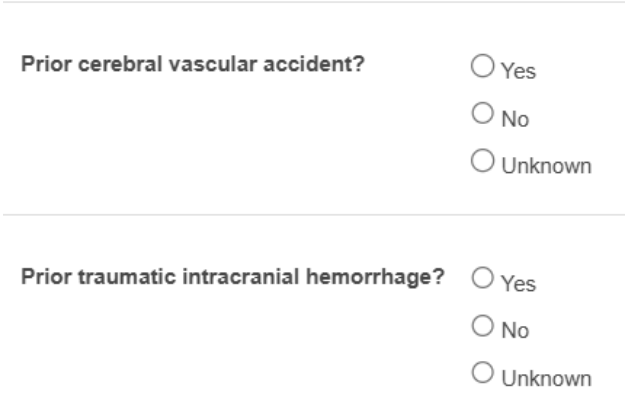
Every effort should be made to collect definitive yes/no responses from the Subject Medical Record. Your response may prompt queries to assess if any inclusion/exclusion criteria has not/has been met in relation to your response.

History of procedure to convert atrial fibrillation or atrial flutter? If both ablation and cardioversion have been performed for the subject, choose the procedure performed closest to screening data collection.



Prior cerebral vascular accident?

- If subject had a spontaneous brain hemorrhage, please only select "Yes"
- If subject had a brain hemorrhage as a result of a fall or trauma, please select "No" (if no other stroke) and response "Yes" to **Prior traumatic intracranial hemorrhage?**



Protocol Deviations are required to be reported for the following:

- Physical Exam and NYHA **greater than 30 days** prior to informed consent
- Lab collection at screening **greater than 60 days** prior to informed consent

3.1.3 Vital Signs

Vital signs are required to be collected and entered in EDC for Screening. Vital signs are not required at any other study visit and do not need to be entered into EDC for other visits.

Screening vital signs may be collected per site standard of care up to 60 days prior to informed consent.

3.1.4 Inclusion/Exclusion Criteria

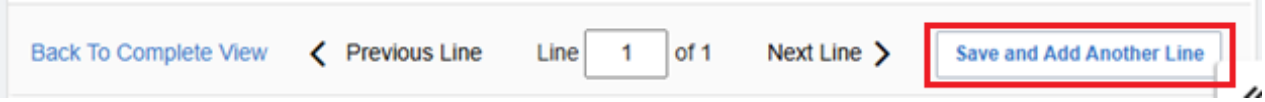
All patients must have CT or TEE Imaging prior to randomization. Conformal can support same day randomization (using the Procedural TEE) only if you have 3+ cases on any given day.

If "*Have all the inclusion criteria and none of the exclusion criteria, as specified by the protocol, been met for this subject?*" is answered "No," each individual Inclusion/Exclusion criteria will become visible.

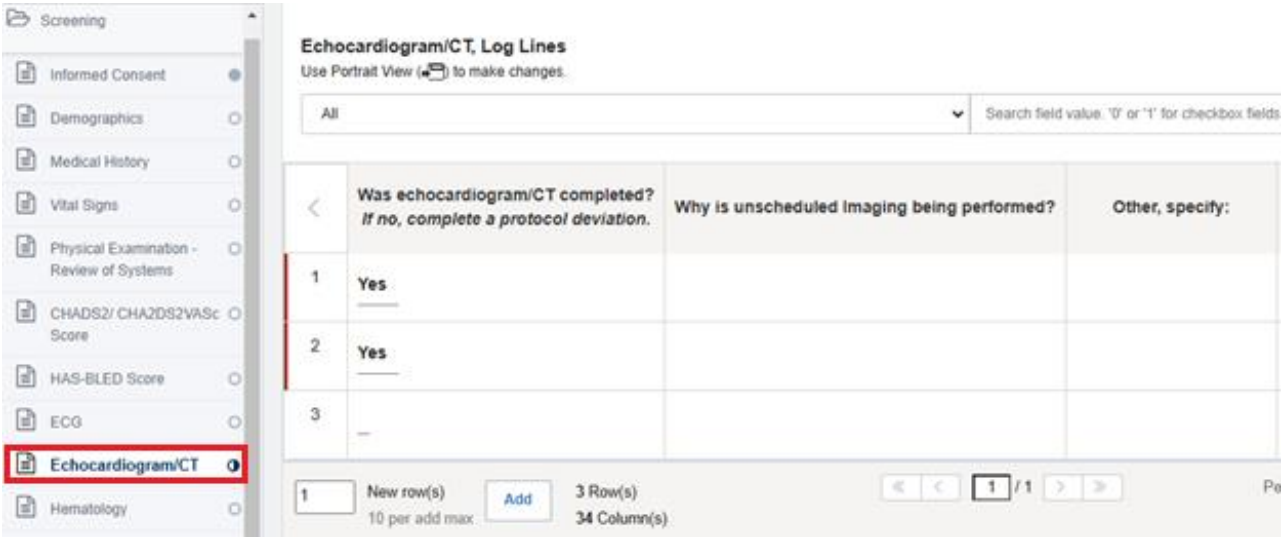
For Screen Failed subjects, "N/A – Not assessed" may be selected for any criteria not assessed prior to the subject screen failure.

3.1.5 Echocardiogram/CT

Screening imaging (TEE or CT) must be performed prior to randomization. If more than one Imaging was performed, select "Save and Add Another Line" to create a new Echocardiogram/CT Form within the EDC.



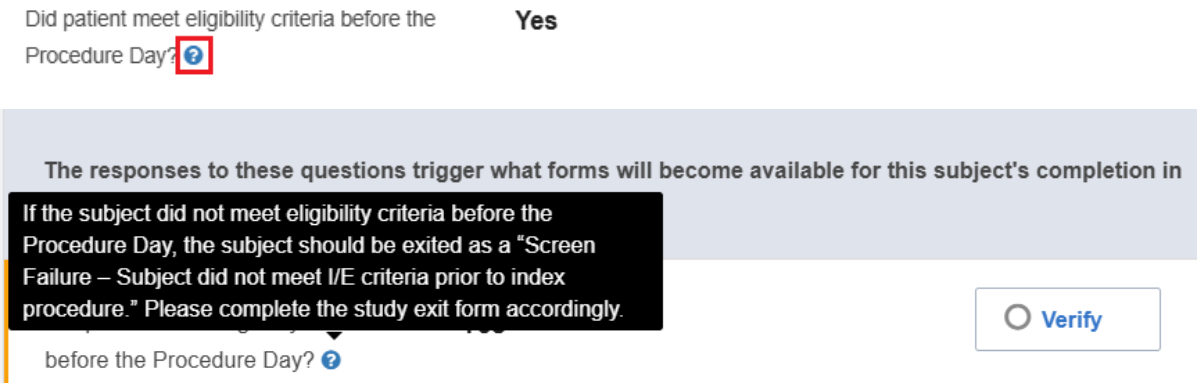
All Imaging Log Lines can be visualized by selecting "Echocardiogram/CT". Please upload all images into the Imaging Module.



A protocol deviation is required for screening imaging performed **greater than 6 months** prior to informed consent.

3.1.6 Patient Population

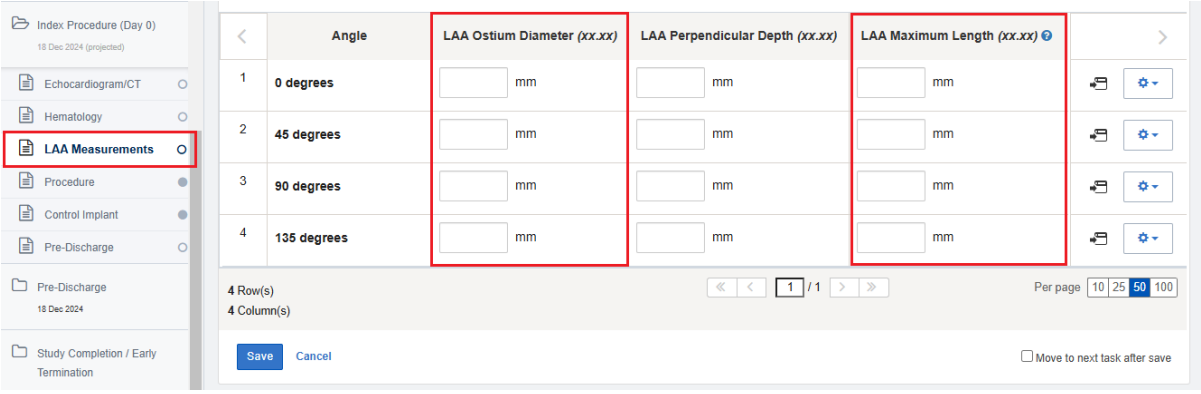
The responses to the questions in the *Patient Population* Form trigger what forms will become available for this subject's completion in EDC. Please hover over the question mark for guidance on the subject's required follow-up visits and patient exit classification.



3.2 Index Procedure and Pre-Discharge

3.2.1 LAA Measurements

The *LAA Measurements* form is located in the Index Procedure folder. If the subject was implanted with the control device, LAA measurements should be collected per the control device's IFU. Only the **LAA Ostium Diameter** and **LAA Maximum length** are required for a control device. A Protocol deviation is *not* required if the LAA Perpendicular Depth was not obtained for a control device.



3.2.2 CLAAS Implant/Control Implant

Either the *CLAAS Implant* form or *Control Implant* form will populate in the Index Procedure folder, depending on the device assigned to the subject in EDC. These forms are log line style forms, allowing for more than one device to be entered. All devices that are used or opened for this subject should be entered, including any that are opened but not used.

If needed, additional log lines can be added by clicking “Save and Add Another Line.”

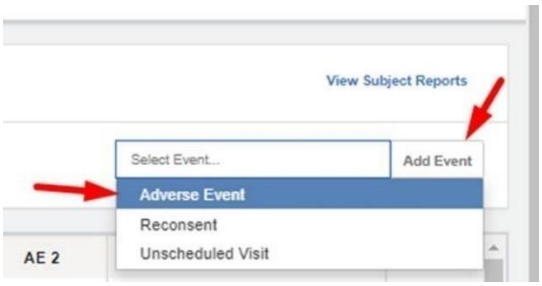
3.2.3 Pre-Discharge

On the *Visit Information* form, the duration between the Pre-discharge TTE and the time of access sheath removal will be automatically calculated by EDC using the time of the pre-discharge TTE entered in this form and the time of access sheath removal in the *Procedure* form.

A protocol deviation must be entered if the time between access sheath removal and pre-discharge TTE is **less than four hours**.

3.3 Adverse Events

To enter Adverse Events, select “Adverse Event” in the dropdown on the upper right-hand corner of the EDC page. Click on Add Event. Then, the Adverse Event CRF will populate in the grid.



The adverse events will populate towards the far right of the grid as individual events. They can be accessed by clicking on the radio button associated with the event.

Responses marked “Yes” under “Adverse Events with special interest?” may generate additional forms. For example, if Bleeding Event is marked “Yes,” a Bleeding Event form will populate for completion.

The CONFORM Pivotal Trial does not collect ALL AEs. Site Personnel should refer to the most current version of the CONFORM Pivotal Trial Protocol with attention to Section 12 Safety Reporting: Reportable Events by Investigational Sites and Safety Event Definitions.

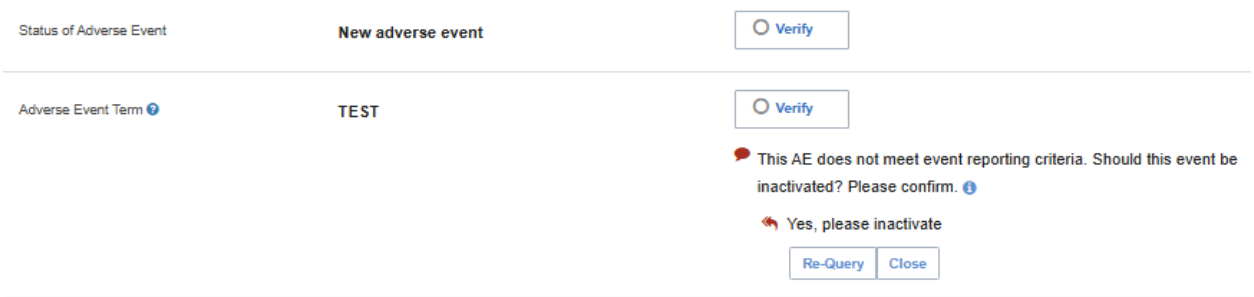
AE entry into the Database is considered the Date Sponsor Notified of AE. If RC does not have access to the database or is not yet sure if a discovered/reported event meets protocol specified reporting criteria, the RC should notify their Site Manager via email or phone call and file a printed copy of this notification in the Subject Binder. Alternatively, the site may notify the Sponsor via email at:

Safety@conformalmedical.com

Event Reporting emails should include the following: Subject ID, date of awareness, start date, and suspected AE Term.

3.3.1 Inactivating Adverse Event Forms

If an AE has been entered in error, has been reviewed to be not reportable per protocol, or can be combined with another AE, it may be necessary to inactivate the AE Form. AE form inactivation requests will be documented via query, which will be added by the Site Manager, Safety or Clinical Data Manager to confirm the site agrees with the inactivation. The Research Coordinator (RC) should respond to the query with clear confirmation that the form is to be inactivated.



If the **site** identifies an AE form that needs to be inactivated, an email should be sent to the site CRA confirming the following information:

Subject Line of email: CONFORM [Site #] AE Inactivation Request

Body of email:

Please inactivate the following Adverse Event(s) from the EDC:

Subject #:

AE # / AE Term

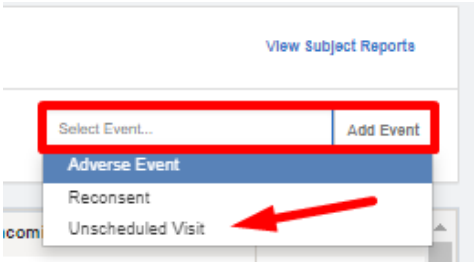
Reason for inactivation (e.g., duplicate of AE X, does not meet reporting requirements per protocol)

Once the email is received, the CRA will open a query to the DM (so no response is required from the site) confirming the form is to be inactivated.

Please contact your assigned Site Manager if you have any questions regarding AE data entry.

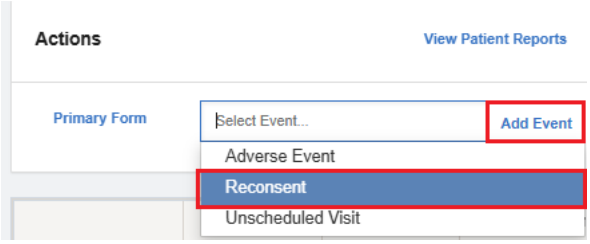
3.4 Unscheduled Visit

To enter an unscheduled visit, select "Unscheduled Visit" in the dropdown on the upper right-hand corner of the EDC page. Click on Add Event. The Unscheduled Visit CRF will populate in the grid. For example, per protocol, subjects with a suspected stroke shall be documented as an Unscheduled Visit in the Electronic Database System.



3.5 Reconsent

To enter a reconsent, select "Reconsent" in the dropdown on the upper right-hand corner of the EDC page. Click on Add Event. The Reconsent CRF will populate in the grid.



3.6 Study Exit

The CONFORM Pivotal Trial has provided a Study Exit Flowchart in MOP-13. Refer to this Flowchart in determining Study Exit timepoints for your subject. Note that responses entered on the Patient Population form directly impact the Study Exit form.

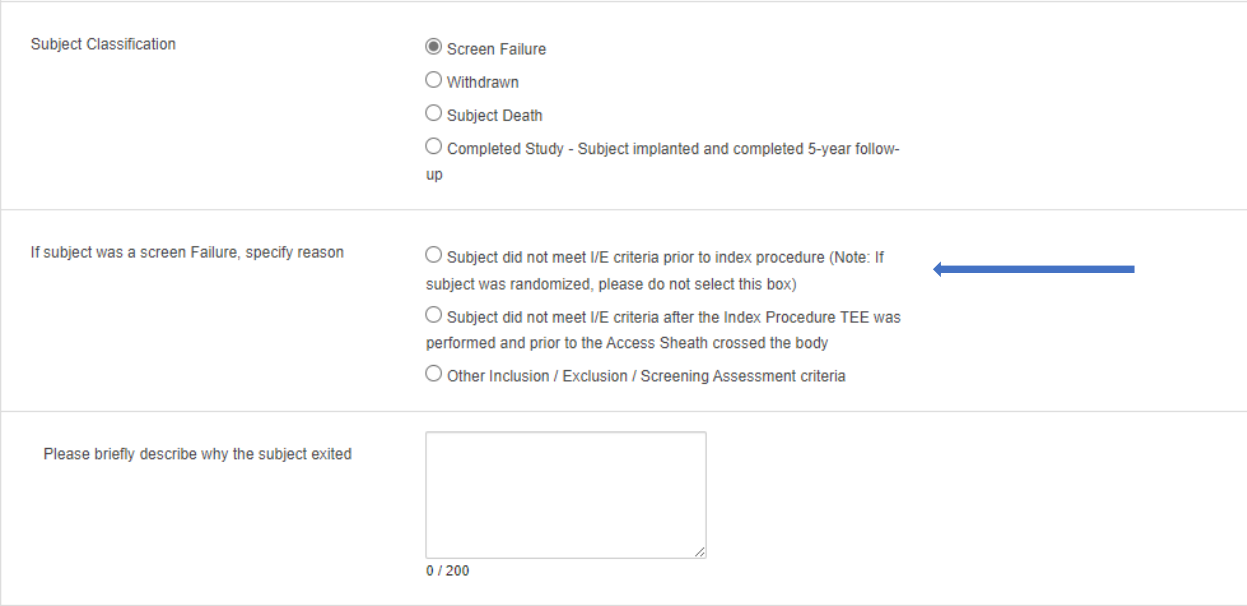
The following four categories of Subject Classification will be tracked as documented in EDC on the Study Exit Form.

- **Screen Failure**
- **Withdrawn**
- **Subject Death**
- **Completed Study**

3.6.1 Screen Failure

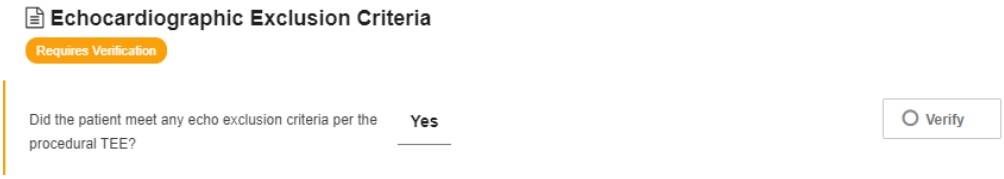
The following three categories of Screen Failure will be tracked on the Study Exit form. Specific reasons for the screen failure must also be documented.

1. Subject did not meet I/E criteria prior to index procedure (Note: if subject was randomized, please do not select this box)
2. Subject did not meet I/E criteria after the Index Procedure TEE was performed and prior to the Access Sheath crossing the body
3. Other Inclusion/Exclusion / Screening Assessment criteria (Note: This should only be chosen if a patient was randomized, but never had the Procedural TEE, and did not meet I/E criteria).



In Brief Description: enter which I/E criteria has not been met.

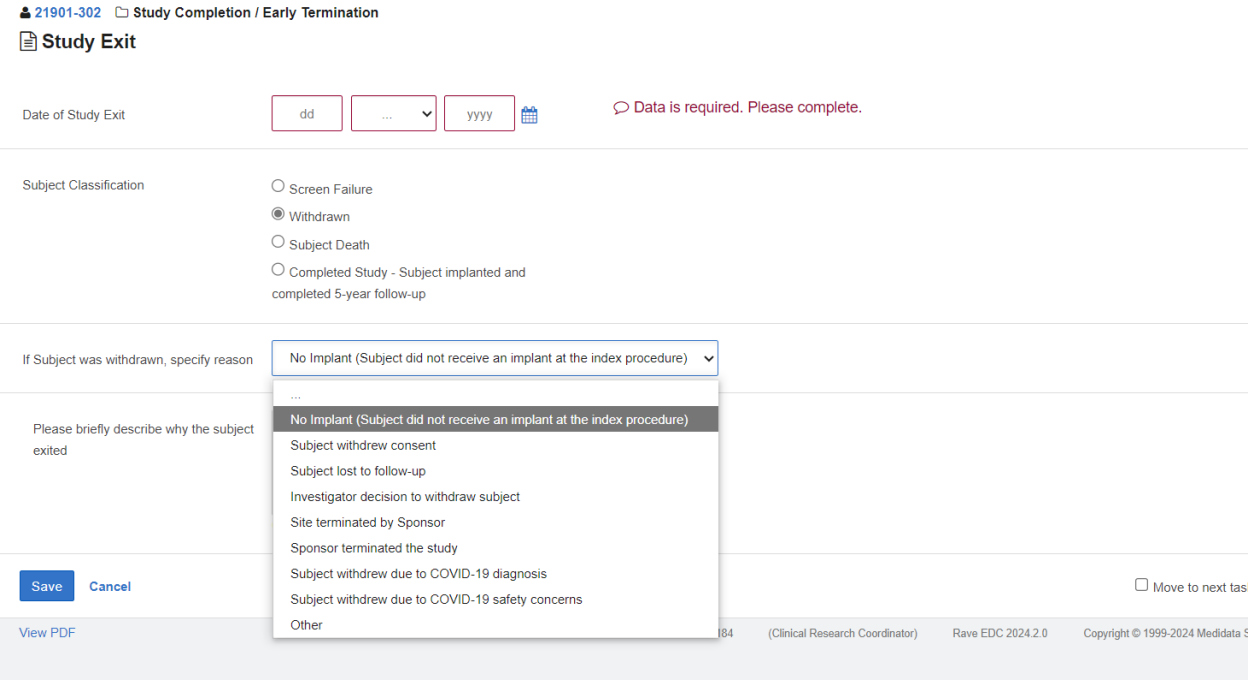
For Screen Failures after Procedure TEE performed but prior to Access Sheath (2): it would be expected that the subject has met an Echo Exclusion Criteria, in the Randomization Folder Echocardiographic Exclusion Criteria eCRF: ***Did the subject meet any echo exclusion Criteria per the procedural TEE***? would be expected to be "Yes."



3.6.2 Withdrawn

If a subject has been randomized and Study Exit is not related to Death or Completed Study, *Withdrawn* should be selected for data entry.

At any time point of the study, whether a subject has been randomized or not, if a subject decides to withdraw consent or the Investigator decides to withdraw the subject, *Withdrawn* should also be selected for data entry.



If a randomized subject meets all I/E Criteria at Screening and at Procedure TEE, but does not receive an implant, enter the subject classification as *Withdrawn* and the reason as *No Implant* (as pictured above).

If subject is **lost to follow-up** (subject is unreachable, missed visit has occurred, and site personnel made all reasonable efforts to locate and communicate with subject per protocol requirements), enter the subject classification as *Withdrawn* and the reason as *Subject Lost to Follow-up*.

3.6.3 Subject Death

If Subject Death is chosen the following query will populate: ***Please complete the Adverse Event and Death Form.*** Ensure only one AE has an outcome of Death.

Date of Study Exit and Date of Death should be the same.

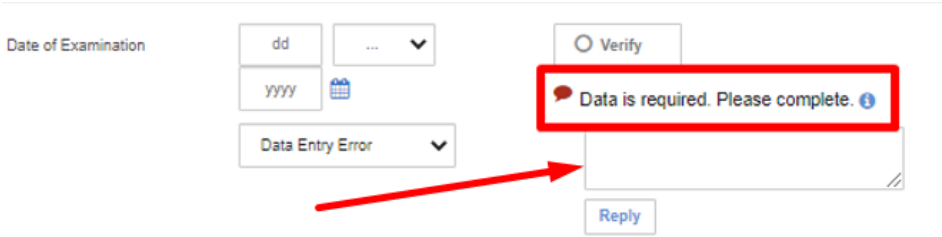
Conform Study Appendix A: Definitions: ***Mortality*** should be referenced for determination of Primary cause of death for data entry**.** Source documentation should be available to monitoring for determination of Cardiovascular/Non-Cardiovascular death. AE Event Term may be updated per Certificate of Death or Autopsy as assessed. Every effort should be made by site research staff to obtain any source related to subject's death and provided to Safety as required.

4 Data Management

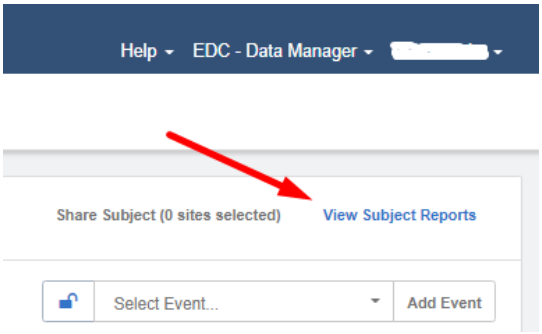
4.1 Data Queries

Queries refer to questions or flags raised by the system or study personnel when inconsistencies, missing information, or potential errors are detected within the clinical trial data entered by sites. Queries can be auto generated or created manually by data managers, the safety team, or CRAs.

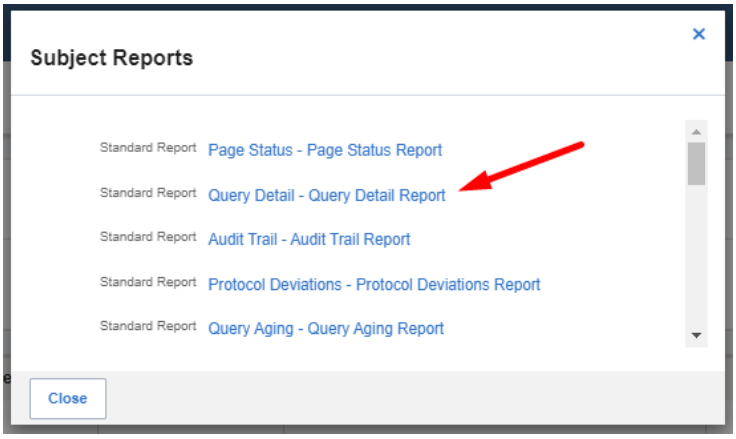
To reply to a query, enter a response in the field below the query and click “Reply”. If query resolution requires data to be added/updated, please complete/update the field first as you may find the query closes automatically without requiring a response.



A list of each subject’s queries can be accessed through View Subject Reports on the subject page.

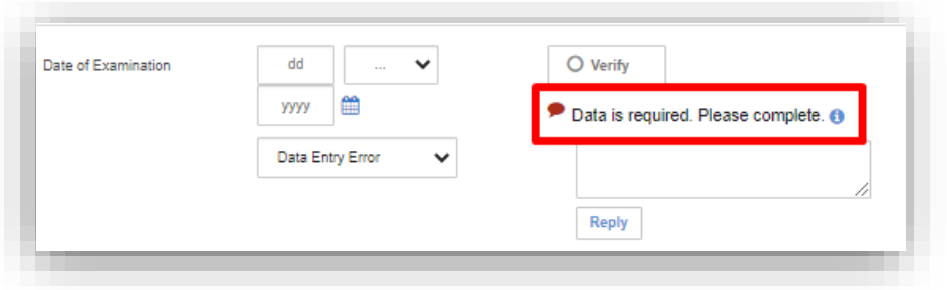


Select the Query Detail - Query Detail Report which shows all the queries for the subject.

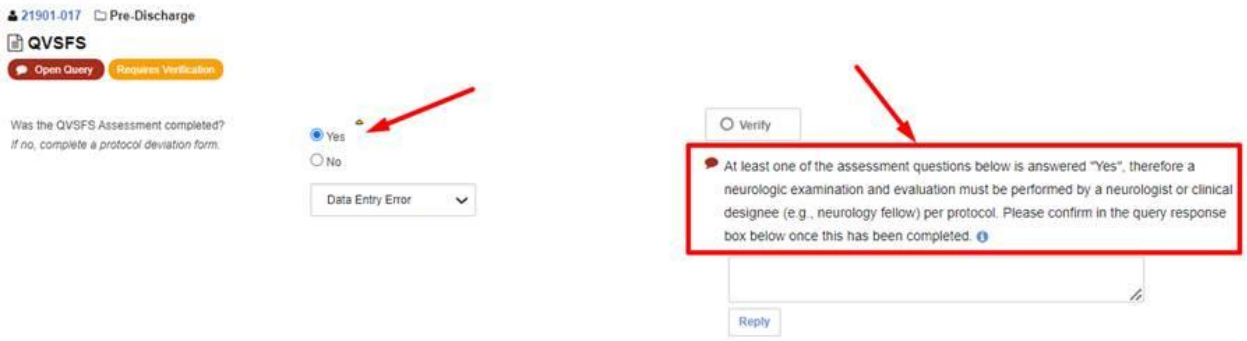


4.2 Mandatory Fields and Edit Checks

If a required question is not answered, a query will generate stating "Data is required. Please complete." The query will automatically close when data is entered.



Depending on the response to each field, additional fields may display as needed. Queries may generate based on the data entered such as values or dates or values out of range. Another query example is below:

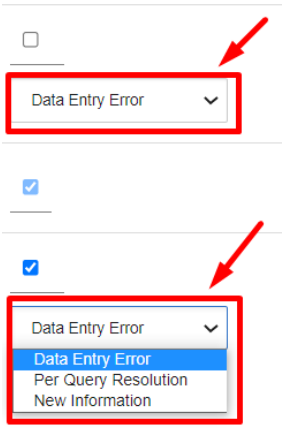


Reminder: Update the data in fields as needed prior to responding to queries. Most queries will automatically close once data is entered and saved. If the query remains open once data is entered, respond to the query.

4.3 Changing Previously Entered Data

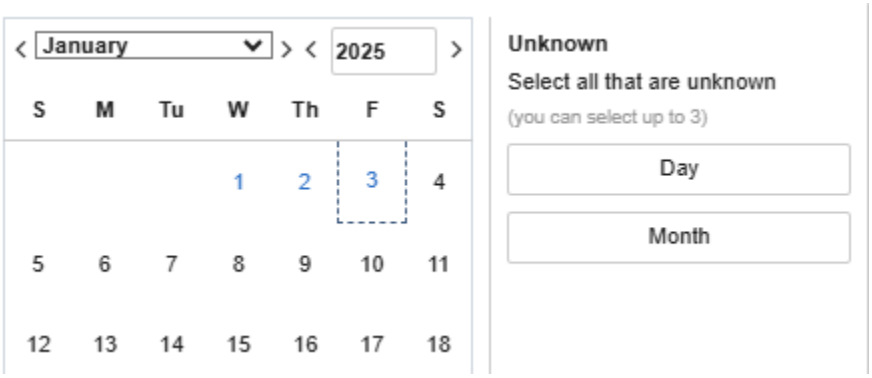
If data is changed for an existing record, the system will require a reason for change.

When a saved response is changed, a box will display below the field with a reason for change. The default reason is "Data Entry Error." There are three options to choose from on the dropdown list (see image to the right). Select the response that applies. Do this for each field that is changed. Click SAVE at the bottom of the screen when done to save the changes.



4.4 Unknown Date Entry

Date fields occur throughout the forms in the EDC. Some fields will allow a partial date to be entered (but the year will always be required). Date fields that allow a partial date will display the "unknown" options when you click on the calendar next to the date field:



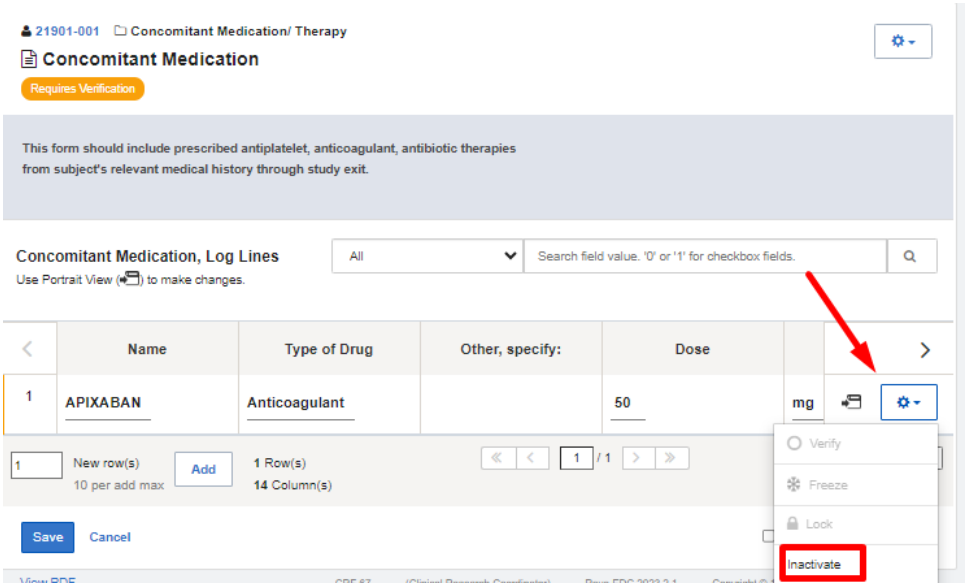
For fields that require a full date where you are unable to determine the day, please record as 01MonYYYY in EDC. If unable to determine day **and** month, please record as 01JanYYYY. Every effort should be made to at least obtain an approximate year. Do not enter "UNK" for unknown fields. If the year definitely cannot be determined, this should be recorded as 1901.

4.5 Inactivating Log Lines

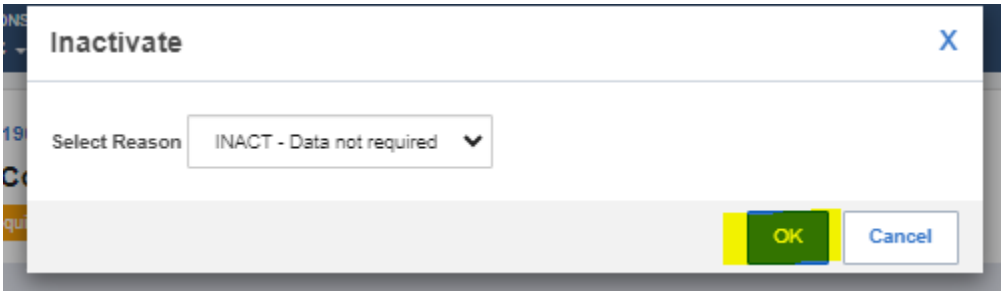
In the event that data has been entered in error (i.e., data entered into the wrong subject, study does not require data, entry error, etc.) sites have the ability to inactivate Con Meds, Imaging, and PDs on their own. Adverse Event inactivation process is detailed in the Adverse Event section of this document.

Reminder: Medication assessment data collection includes the use of antiplatelet, anticoagulation and endocarditis prophylactic antibiotic medication only.

Log lines can be inactivated by the site. Click the gear icon at the end of the log line and select "Inactivate."

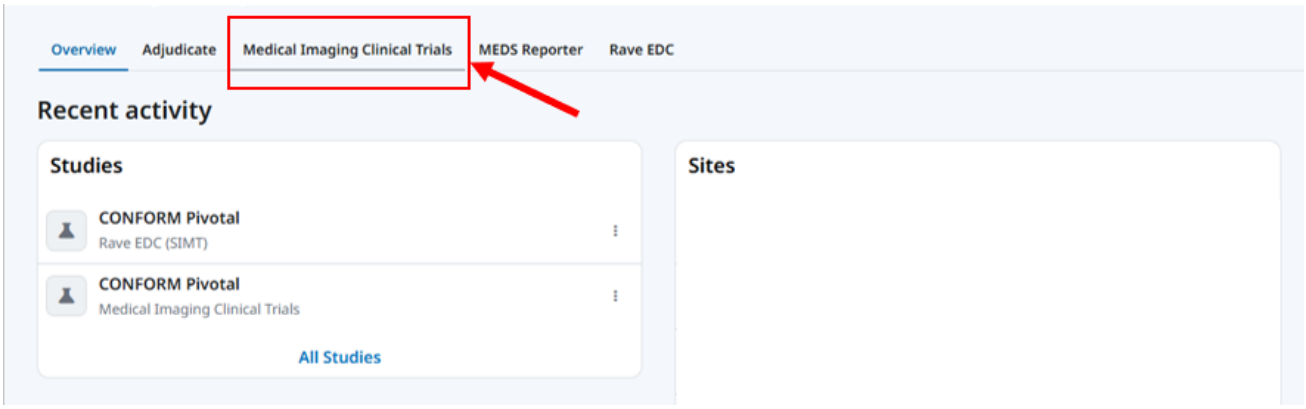


A popup will display, select “OK” and the change is complete. It is not necessary to save the form.

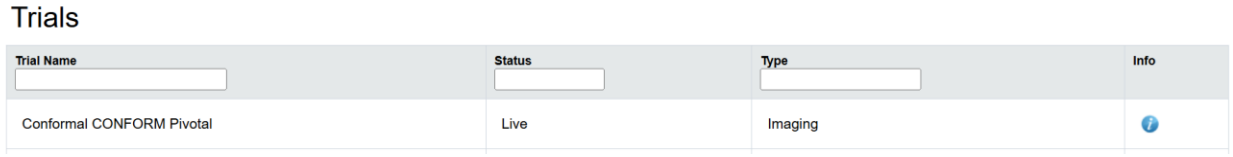


5 Imaging Uploads

Imaging is uploaded in a separate app within Medidata. To access the app, click “Medical Imaging Clinical Trials” along the top of the Medidata home page.



Clicking the **conformalmedical** link will take you to the next page shown below. Next, click on "Conformal CONFORM Pivotal."



You will be directed to the imaging home page, where you can see all patients who are currently in the trial at your site.

Note: there is a folder in EDC called "Imaging Summary Data." Information will automatically be pulled from the Medidata imaging app into a form in this folder, called "Image/Document Submission Details." The information in this form cannot be edited in EDC and must be edited within the separate imaging app.

For detailed instructions on navigating the imaging app and uploading images, see the Imaging Upload section of the Manual of Procedures, section 7.

6 Conclusion

If you need additional support with eCRF Completion Guidelines, or if you encounter issues, please reach out to your assigned Site Manager. Further contact information is available on the next page.

CONFORM Pivotal Trial

eCRF Completion Guidelines

Contact Information	
Organization	Name
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Revision History			
Version	Description	Name	Date
1.0	New Document	Paula Hicks	22JUN2022
2.0	Updated all sections to clarify general guidance and form-specific guidance	Briony Macdonald-McMillan	14JAN2025

Tab Name: 14 Correspondence

No documents behind this tab

Tab Name: 15 Miscellaneous

No documents behind this tab