

Clinical Investigation Plan

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Trevisio Post-Approval Study
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Sponsor

Abbott
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Plymouth, MN 55442, USA
USA

Clinical Investigation Plan

Trevisio Post-Approval Study

A single-arm, non-randomized, multi-center clinical study of the Amplatzer™ Trevisio™ Intravascular Delivery System for facilitating percutaneous, transcatheter implantation of the Amplatzer™ Occluder Devices

Version Number	Version A
Date	03 June 2020
Planned Number of Sites and Region(s)	Up to 30 sites in Europe
Clinical Investigation Type	Single arm, non-randomized, multi-center, post-approval study
Abbott Medical Expert	[REDACTED]
Sponsor	Abbott 5050 Nathan Lane N Plymouth, MN 55442, USA
Electronic Data Capture Software	Oracle
CIP Author of Current Version	[REDACTED]

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SITE PRINCIPAL INVESTIGATOR SIGNATURE PAGE

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

Site Principal Investigator

Printed name:
Signature:
Date:

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COMPLIANCE STATEMENT:

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

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1.0 INTRODUCTION

This document is a clinical investigational plan (CIP) for a prospective, multi-center, single-arm, post-market study intended to support clinical follow-up of the CE-Marked Amplatzer Trevisio™ Intravascular Delivery System (Amplatzer Trevisio Delivery System). The device is intended for use with CE-Marked Amplatzer™ Occluder devices. This clinical study is sponsored by Abbott.

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

1.1 Background

The Amplatzer™ TorqVue™ Delivery System (ITV) has historically been used to facilitate the attachment, loading, delivery, and deployment of the Amplatzer Occluder devices. The Amplatzer Trevisio Delivery System is a new design iteration of the Amplatzer TorqVue delivery system with a redesigned delivery cable and a more flexible distal end, which is intended to impart less bias (i.e., tilt) on the occluder during the placement evaluation period before releasing the occluder from the delivery system. The delivery cable also has a proximal indicator to alert physicians when the occluder is approaching the end of the delivery sheath, which may reduce the use of fluoroscopy and patient exposure to radiation. All other components of the delivery system are identical to the currently marketed Amplatzer TorqVue Delivery System.

1.2 Rationale for Conducting this Clinical Study

The purpose of this study is to evaluate the safety and effectiveness of the design iteration of the Amplatzer™ TorqVue™ Delivery System—the Amplatzer Trevisio Delivery System—in a post-approval clinical setting. Data on the safety and effectiveness of the Amplatzer™ Trevisio Delivery System in patients undergoing closure of a patent foramen ovale (PFO), atrial septal defect (ASD), muscular ventricular septal defect (VSD), and post-infarct muscular VSD with Abbott's Amplatzer™ PFO Occluder, Amplatzer™ Septal Occluder (ASO), Amplatzer™ Multi-fenestrated Septal Occluder – “Cribiform” (ASD-MF), Amplatzer™ Muscular VSD Occluder, and Amplatzer™ Post-Infarct Muscular VSD Occluder will be collected. This study is intended to fulfill post-CE Mark requirements.

2.0 CLINICAL STUDY OVERVIEW

2.1 Clinical Study Objective

The primary objective of this clinical study is to characterize the safety and effectiveness of the Amplatzer Trevisio Delivery System for facilitating percutaneous, transcatheter implantation of the Amplatzer PFO Occluder, Amplatzer ASO, Amplatzer ASD-MF Occluder, Amplatzer Muscular VSD Occluder, and Amplatzer Post-Infarct Muscular VSD Occluder. The Amplatzer Trevisio Delivery System is CE-Marked and commercially available.

2.1.1 Name of the Device(s) Being Studied

The device being studied is the Amplatzer Trevisio Delivery System, which is used to facilitate implantation of Abbott's Amplatzer Occluder devices. Model numbers for the Amplatzer Trevisio Delivery System can be seen in Table 1. Refer to the Instructions for Use (IFU) for further detail about the delivery

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system and occlusion devices (see Amplatzer Trevisio Intravascular Delivery System IFU; Amplatzer PFO Occluder IFU; Amplatzer Septal Occluder IFU; Amplatzer Multi-fenestrated Septal Occluder – “Cribiform” IFU; and the combined Amplatzer Muscular VSD Occluder and Post-Infarct Muscular VSD Occluder IFU).

Table 1. Device Name and Model Numbers

Device name (market-released)	Model/Type	Manufacturer
Amplatzer™ Trevisio™ Intravascular Delivery System	9-ATV06F45/60 9-ATV07F45/60 9-ATV07F45/80 9-ATV08F45/60 9-ATV08F45/80 9-ATV09F45/80 9-ATV10F45/80 9-ATV12F45/80 9-ATV13F45/80	Abbott Medical

2.1.2 Indication for Use

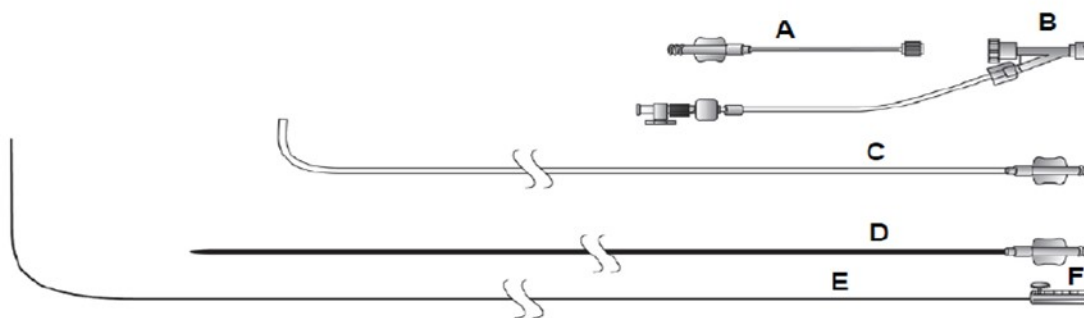
The Amplatzer Trevisio Intravascular Delivery System is intended to facilitate the attachment, loading, delivery and deployment of the Amplatzer Occluder devices.

2.1.3 Description of the Delivery System

The Amplatzer Trevisio Delivery System is designed to deliver Amplatzer Occluder devices. The delivery system is shipped separately from the occluders. The body of the delivery system sheath is radiopaque for visibility under fluoroscopy. The Amplatzer Trevisio Delivery System was sterilized with ethylene oxide and is for single use only. The more flexible delivery cable included in the Amplatzer Trevisio Delivery System will impart less bias (i.e., tilting) on the occluder during the placement evaluation period before releasing the occluder from the delivery system.

The components of the Amplatzer Trevisio Delivery System are shown in Figure 1. The Trevisio cable is offered in both 60 cm and 80 cm sheath lengths with a 45° curve and has the same French sizes as the Amplatzer TorqVue™ 45° Delivery System. Please refer to the IFU for additional information regarding the delivery system used in this clinical study.

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- A. Loader – introduces the AMPLATZER™ Occluder into the sheath
- B. Hemostasis valve with extension tube and stopcock - Allows flushing of the delivery system and controls blood backflow.
- C. Sheath – Provides a pathway through which an AMPLATZER™ Occluder is delivered
- D. Dilator – Eases penetration of tissue and minimizes vessel trauma
- E. Delivery Cable – Attaches to the AMPLATZER™ Occluder to control its movement through the sheath, and releases the occluder upon deployment
- F. Cable Vise – Attaches to the delivery cable and serves as a handle for disconnecting (unscrewing) the delivery cable from an AMPLATZER™ Occluder.

Figure 1. Amplatzer Trevisio Intravascular Delivery System

2.1.4 Device Handling

Refer to the Amplatzer Trevisio Intravascular Delivery System IFU for more detail about proper handling, storage, and use requirements.

3.0 CLINICAL STUDY DESIGN

3.1 Purpose

The purpose of this prospective, multi-center, single-arm, post-approval study (PAS) is to characterize the safety and effectiveness of the Amplatzer Trevisio Delivery System.

3.2 Design overview

This PAS is a non-randomized, multi-center, single arm clinical study to evaluate the safety and effectiveness of the Amplatzer Trevisio Delivery System for facilitating percutaneous, transcatheter implantation of the Amplatzer PFO Occluder, Amplatzer ASO, Amplatzer ASD-MF Occluder, Amplatzer Muscular VSD Occluder, and Amplatzer Post-Infarct Muscular VSD Occluder.

A minimum of 215 subjects undergoing PFO or ASD closure will be enrolled from up to thirty (30) centers in Europe (at least 100 of these subjects must be undergoing PFO closure). In addition to the 215 subjects undergoing PFO or ASD closure, a minimum of

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44 subjects undergoing muscular VSD or post-infarct muscular VSD closure will be enrolled. Subjects will be evaluated at baseline (pre-procedure), implant procedure, and prior to discharge or 7 days after the procedure, whichever occurs first. [REDACTED]

3.3 Clinical Study Procedures and Follow-up Schedule

Each subject will be assessed at baseline (pre-procedure), implant procedure, and prior to discharge or at 7 days, whichever occurs first. The study assessment flow chart is shown in Figure 2.

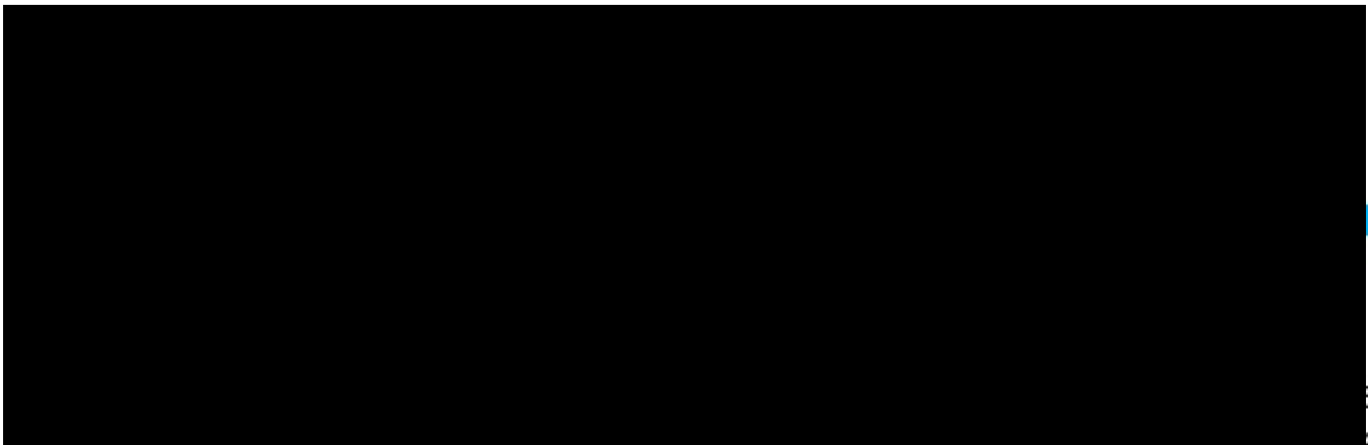


Figure 2. Clinical Study Flow Chart

3.4 Measures Taken to Avoid and Minimize Bias

This PAS is a non-randomized, multi-center, single arm clinical study. In order to minimize selection bias sites will make every effort to seek consent for participation from all eligible patients within their institution who are undergoing ASD, PFO, or VSD closure with the Amplatzer Trevisio Delivery System.

3.5 Suspension or Early Termination of the Clinical Study

No formal statistical rule for early termination of the clinical study for insufficient effectiveness of the device being studied is defined.

The Sponsor reserves the right to discontinue the clinical study at any stage with suitable written notice to the Principal Investigator. Possible reason(s) may include, but are not limited to:

- Sponsor oversight (e.g., Medical Director) decides to stop or terminate the clinical study due to a safety concern (such as higher frequency of anticipated adverse device effects)
- The study is no longer required by a regulatory authority, or the scope is reduced

Should the clinical study be discontinued by the Sponsor, subjects will be followed per routine hospital practice with device-related AEs reported to the Sponsor as per vigilance/commercial reporting requirements. Should this occur, the Principal Investigator shall return all clinical study materials to the Sponsor and provide a written statement to the EC (if applicable). All applicable clinical study documents shall be subject to the same retention policy as detailed in Section 10.5 of the CIP.

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If the Sponsor suspends or prematurely terminates the clinical study at an individual site the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, if appropriate.

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

4.0 **ENDPOINTS**

The study has a primary effectiveness endpoint, a primary safety endpoint, and a number of descriptive endpoints.

4.1 **Primary Endpoints**

Primary Effectiveness Endpoint: Technical success – successful deployment and release of at least one device

Primary Safety Endpoint: Device- or procedure-related serious adverse events through discharge or 7 days, whichever occurs first, including:

- Cardiac perforation
- Sustained atrial fibrillation requiring intervention
- Device thrombus
- Device erosion
- Device embolization
- Vascular complication requiring surgical intervention
- Device- or procedure related serious adverse event leading to death

4.2 **Descriptive Endpoints**

- The number of times the device is recaptured
- The number of times the device is repositioned
- Total fluoroscopy time
- Ease of use – investigators will be asked survey questions about their first experience with the Amplatzer Trevisio Delivery System.

5.0 **SUBJECT SELECTION AND WITHDRAWAL**

5.1 **Subject Population**

This clinical study will enroll male and female adults and children with a PFO (adults only), ASD or VSD who are indicated for transcatheter closure. Patients must meet all general eligibility criteria and provide written informed consent prior to sites conducting any study-specific procedures not considered standard of care.

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5.2 Subject Screening and Informed Consent

5.2.1 Subject Screening

Potential subjects and/or legal guardians of potential pediatric (minor) subjects presenting at the clinical sites will be fully informed about the clinical study, following the established Informed Consent process (described in Section 5.2.2). Once a duly dated and signed Information and Consent Form is obtained, the clinical study-specific screening procedures may begin. For potential subjects who are considered minors, an informed assent or consent process will be followed in accordance with EC requirements (described in Section 5.2.2.1) prior to commencement of study-specific screening procedures.

Subjects must be screened for clinical study eligibility by a member of the site's clinical study team previously trained to the CIP.

Patients being considered for PFO, ASD, or VSD closure with an Amplatzer occluder will be asked to sign an Informed Consent form if they wish to participate in the clinical study. Subject data will be collected following written, informed consent to participate in the clinical study. However, subjects will not be considered enrolled until they have met enrollment criteria as defined in Section 5.3.

In case the subject does not meet all study eligibility criteria after provision of Informed Consent, the subject will not be included in the study. The Principal Investigator or the delegated clinical study personnel will record the screening failure in the hospital records and on a screening log as required.

5.2.2 Informed Consent

The Principal Investigator or his/her authorized designee (only if the patient is considered a minor) will conduct the informed consent process, as required by applicable regulations and the center's EC. *Adults above the legal age of consent who choose to participate in the study must be able to provide their own written, informed consent (i.e., no authorized designee may sign on their behalf).* This process will include a verbal discussion with the patient or legally authorized representative (if the patient is a minor) on all aspects of the clinical study that are relevant to the patient's decision to participate, such as details of clinical study procedures, anticipated benefits, and potential risks of clinical study participation. The patient and the legally authorized representative must be informed about their right to withdraw from the clinical study at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled. Withdrawal from the clinical study will not jeopardize their future medical care or relationship with the Investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the patient and will respect the patient's legal rights. Financial incentives will not be given to the patient. The patient or patient's legally authorized representative shall be provided with the Informed Consent form written in a language that is understandable to the patient and has been approved by the center's EC. The patient or legally authorized representative shall have adequate time to review, ask questions, and consider participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the patient and/or subject's legal guardian understands the information provided. If the patient and/or legally authorized representative agree(s) to participate, the Informed Consent form and appropriate assent form must be signed and dated by the patient and legally authorized representative and thereafter by the person obtaining the consent prior to any clinical study-specific procedures. The signed originals will be filed in the subject's hospital or research charts, and a copy will be provided to the subject and his/her legally authorized representative. Failure to obtain informed consent from a subject prior to clinical study enrollment should be reported to Sponsor within 5 working days and to the reviewing center's EC according to the EC's reporting requirements.

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

5.2.2.1 Special Circumstances for Informed Consent

Individuals who are considered minors may be enrolled in this clinical study. Written informed assent or consent must be obtained using the EC-approved informed assent or consent process in accordance with EC requirements. The legally authorized representative, which will in most cases be the minor's parent(s), will represent the individual during the informed consent process, which will be performed according to the requirements in Section 5.2.2. The legally authorized representative(s) must sign an Informed Consent form in all cases. The minor will also be informed about the clinical study with respect to his/her ability to understand. The explicit wish of the minor who can form an opinion and assess information to decline participation or withdraw from the clinical study at any time will be respected.

All other aspects of the informed consent process will be conducted in compliance with Section 5.2.2.

5.3 Eligibility Criteria

5.3.1 General Eligibility Criteria

Assessment for general eligibility criteria is based on medical records of the site and interview with a candidate patient. Patients must meet ALL of the inclusion criteria to be considered for the clinical study. If ANY of the exclusion criteria are met, the patient is excluded from the clinical study and cannot be enrolled.

5.3.2 Inclusion Criteria

5.3.2.1 General Inclusion Criteria

1. Patient is indicated for implantation with the Amplatzer Septal Occluder for occlusion of a secundum atrial septal defect (Note: This does not include the indication for closure of a fenestration following a fenestrated Fontan procedure) OR subject is indicated for implantation with the Amplatzer PFO Occluder OR subject is indicated for implantation with the Amplatzer Muscular VSD Occluder OR subject is indicated for implantation with the Amplatzer Post-Infarct Muscular VSD Occluder
2. Patient is of legal age and has provided his/her own written, informed consent

OR

Patient is a minor and has provided verbal and/or written informed consent or assent per local EC requirements, and his/her legally authorized representative, or representatives, have provided written informed consent on behalf of the minor according to local EC requirements

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5.3.3 Exclusion Criteria

5.3.3.1 General Exclusion Criteria

1. Presence of anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the Principal Investigator's opinion, could limit the subject's ability to participate in the clinical study or to comply with follow-up requirements.
2. Exclusion Criteria for Patients Undergoing ASD Closure with the Amplatzer ASO or Amplatzer ASD-MF Occluder
 - Patients known to have extensive congenital cardiac anomaly that can only be adequately repaired by cardiac surgery
 - Patients known to have sepsis within 1 month prior to implantation, or any systemic infection that cannot be successfully treated prior to device placement
 - Patients known to have demonstrated intracardiac thrombus on echocardiography (especially left atrial or left atrial appendage thrombi)
 - Patients whose size or condition (e.g., too small for transesophageal echocardiography [TEE] probe, catheter size, vasculature size, active infection) would cause the patient to be a poor candidate for cardiac catheterization
 - Patients with defect margins less than 5 mm to the coronary sinus, inferior vena cava rim, an atrioventricular valve, or the right upper lobe pulmonary vein
3. Exclusion Criteria for Patients Undergoing PFO Closure
 - Presence of thrombus at the intended site of implant, or documented evidence of venous thrombus in the vessels through which access to the defect is gained. Thrombus must be ruled out prior to introducing the delivery system.
 - Active endocarditis or other infections producing bacteremia
 - Patients whose vasculature, through which access to the defect is gained, is inadequate to accommodate the appropriate sheath size
 - Anatomy in which the Amplatzer™ PFO device size required would interfere with other intra-cardiac or intravascular structures, such as valves or pulmonary veins
 - Patients with known hypercoagulable states
 - Patients with intra-cardiac mass or vegetation, thrombus, or tumor
4. Exclusion Criteria for Patients Undergoing VSD Closure with the Amplatzer Muscular VSD Occluder or Amplatzer Post-Infarct Muscular VSD Occluder
 - Body weight <8 kg
 - Tetralogy of Fallot
 - Intracardiac thrombi on echocardiography

5.4 Subject Enrollment

A subject is considered enrolled in the clinical study when the subject and the subject's legal representative (if applicable) provides written informed consent, has been confirmed to meet all inclusion criteria and none of the exclusion criteria, and implantation of an Amplatzer PFO Occluder, Amplatzer ASO, Amplatzer ASD-MF Occluder, Amplatzer Muscular VSD Occluder, or Amplatzer Post-Infarct Muscular VSD Occluder has been attempted with the Amplatzer Trevisio Delivery System, with implant attempt defined as the delivery system entering the subject's anatomy.

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5.5 Subject Withdrawal

Each subject meeting all general screening and eligibility criteria shall remain in the clinical study until completion of the required follow-up period; however, a subject's participation in any clinical study is voluntary and the subject has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but not be limited to, the following:

- Subject death
- Subject voluntary withdrawal

No additional follow-up will be required and no data will be recorded from subjects once withdrawn from the clinical study, except for survival status (deceased/alive).

However, if a subject withdraws from the study due to problems related to the safety or performance of the device under study, the Principal Investigator shall ask for the subject's permission to follow his/her status/condition outside of the clinical study.

5.6 Number of Subjects

5.6.1 Subjects undergoing PFO or ASD closure

A minimum of 215 subjects with PFO or ASD will be enrolled in the clinical study, with a predefined minimum of 100 subjects undergoing PFO closure. Enrollment will be closely monitored to ensure this minimum number of subjects is met early in the first half of the enrollment period. No site may enroll more than 20% of the maximum number of PFO and ASD subjects (n=43).

5.6.2 Subjects undergoing muscular VSD or post-infarct muscular VSD closure

A minimum of 44 subjects with muscular or post-infarct muscular VSD will be enrolled in the clinical study.

5.7 Total Expected Duration of the Clinical Study

[REDACTED]

6.0 TREATMENT AND EVALUATION OF ENDPOINTS

6.1 Baseline

The baseline visit will occur prior to the procedure.

6.1.1 Baseline Clinical Assessments

Data collected during prior examinations may be used for the study if the data were collected no more than 90 days prior to the baseline study assessment. The following assessments and information will be collected at the baseline visit:

- Demographics- includes subject's age and gender

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- Physical examination- includes subject's height, weight, blood pressure (measurements taken during visit)
- Medical history- indicates subject's risk factors, relevant co-morbidities, previous cardiac procedures, and medication use
- Electrocardiogram (ECG), if performed
- Previous echocardiography report indicating PFO, ASD or VSD morphology and pre-closure shunt status. If previous imaging reports are unavailable, intraprocedural echocardiography may be performed prior to the implant attempt (see section 6.2.1)

6.2 Index Procedure

6.2.1 Assessments at the Time of Procedure

The following assessments and information will be collected at the time of the procedure (PFO, ASD, or VSD closure) through prospective tests and evaluations per the local standard of care. If it is determined at the time of the procedure that the subject does not meet the definition of enrollment, the subject will not be considered enrolled.

- Total fluoroscopy time
- Time first catheter in, time last catheter out
- PFO, ASD, or VSD morphology (if not obtained prior to the procedure)
- Pre-closure shunt status as assessed by intraprocedural echocardiography (if not obtained prior to the procedure)
- Procedure details (e.g., PFO, ASD, or VSD morphology; type of sedation; ancillary product use)
- Procedure outcome (implant success or failure)
- The number of times the device is recaptured
- The number of times the device is repositioned
- Post-closure (intra-procedural) shunt status as assessed by echocardiography
- Adverse events, if applicable

6.3 Post-procedure (pre-hospital discharge or 7 days, whichever occurs first)

6.3.1 Subjects will undergo the following evaluations prior to hospital discharge:

- Physical exam
- ECG
- Adverse events, if applicable

6.4 Schedule of Events

The following schedule applies to all subjects enrolled in the study.

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Table 2. Schedule of Events

Study Activity	Enrollment & Baseline	Procedure	Discharge or 7 days
Informed Consent	X		
Demographics, Clinical History	X		
Physical Examination	X		X
Electrocardiography	(X)		X
Echocardiography	(X)	X ¹	
Adverse Event Assessment		X	X

¹For subjects who do not have echocardiography images available prior to the procedure, two sets of imaging assessments will be performed during the procedure (i.e., pre-closure and post-closure).

X = Required follow up; (X) = Optional measurement

7.0 Adverse Events

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

7.1 Definitions

7.1.1 Adverse Event

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

Note 1: This definition includes events related to the medical device being studied.

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

Note 3: For users or other persons, this definition is restricted to events related to medical devices being studied.

7.1.2 Serious Adverse Event

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

- a) Led to a death,
- b) Led to a serious deterioration in health of the subject, that either resulted in
 1. a life-threatening illness or injury, or
 2. a permanent impairment of a body structure or a body function, or
 3. in-patient hospitalization or prolongation of existing hospitalization, or
 4. medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function, or

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5. chronic disease.

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

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

7.2 Device Relationship

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

7.3 Adverse Event and Complaint Reporting

7.3.1 Adverse Event Reporting

Safety surveillance and reporting starts as soon as the patient has provided written, informed consent (per section 5.2) to participate in the clinical study. Safety surveillance and reporting will continue until the last follow-up visit has been performed, the subject is deceased, the subject concludes participation in the clinical study or the subject withdraws from the clinical study. All AE data, including deaths, will be collected throughout the time period defined above and will be reported to the Sponsor on a CRF. Additional information with regard to an adverse event should be updated within the appropriate CRF, including determination of whether COVID-19 (SARS-CoV-2 virus) caused or contributed to an AE. Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported.

For the purposes of this clinical study, the following events will be reported:

- Serious adverse events
- Device- and/or procedure-related adverse events

SAE Reporting

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

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

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

7.3.2 Device Deficiency/Device Malfunction Reporting

A device malfunction is the failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the IFU or CIP. This includes any malfunction of the [REDACTED]

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Amplatzer Trevisio Delivery System. All device or delivery system deficiencies/malfunctions should be reported on the appropriate CRF (i.e., the Device Deficiency Form). Device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling. This includes the failure of the device or delivery system to meet its performance specifications or otherwise perform as intended. Note: Performance specifications include all claims made in the labeling of the device.

The Principal Investigator should report all device or delivery system deficiencies to the Sponsor as soon as possible but no later than outlined below.

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

Device deficiencies/malfunctions should be reported to the EC per the investigative site's local requirements.

7.3.3 Adverse Event Reporting to Country Regulatory Authorities by the Sponsor

The Sponsor will report SAEs and reportable device deficiencies/malfunctions to the country regulatory authority, per local requirements.

7.3.4. Complaints

The investigator is responsible for reporting all complaints to the Post Market Surveillance Department as they become aware of the complaint. A complaint is defined as any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a device or delivery system after it is released for distribution.

For events not reportable for this study (per section 7.3.1) and are considered as complaints, the investigator must notify [REDACTED] as soon as possible after becoming aware of the complaint. This information is not collected on a CRF for the study.

8.0 STATISTICAL CONSIDERATIONS

8.1 Analysis Populations

[REDACTED]

[REDACTED]

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8.2 Statistical Analyses

8.2.1 Primary Effectiveness Endpoint Analysis

The primary effectiveness endpoint is technical success – successful deployment and release of at least one device.

8.2.1.1 PFO and ASD Closure Groups

The performance goal for the primary effectiveness endpoint for the PFO and ASD closure groups is set at 95% [REDACTED]

Let π_1 be the proportion of subjects who experience successful deployment and release of at least one device.

The following hypothesis will be tested:

$$H_0: \pi_1 \leq 95\%$$

$$H_a: \pi_1 > 95\%$$

[REDACTED]

The hypothesis will be tested at a one-sided significance level of 2.5% [REDACTED]

8.2.1.2 Muscular and Post-Infarct Muscular VSD Closure Groups

The performance goal for the primary effectiveness endpoint for the muscular VSD and post-infarct muscular VSD closure groups is set at 80% [REDACTED]

Let π_2 be the proportion of subjects who experience successful deployment and release of at least one device.

The following hypothesis will be tested:

$$H_0: \pi_2 \leq 80\%$$

$$H_a: \pi_2 > 80\%$$

[REDACTED]

The hypothesis will be tested at a one-sided significance level of 5% [REDACTED]

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8.2.2 Primary Safety Endpoint Analysis

The primary safety endpoint is device- or procedure-related serious adverse events through discharge or 7 days, whichever is earlier, including:

- Cardiac perforation
- Sustained atrial fibrillation requiring intervention
- Device thrombus
- Device erosion
- Device embolization
- Vascular complication requiring surgical intervention
- Device- or procedure-related serious adverse event leading to death

8.2.2.1 PFO and ASD Closure Groups

A performance goal of 6% was chosen [REDACTED]

Let π_3 be the proportion of subjects who experience device- or procedure-related serious adverse events through discharge or 7 days.

The following hypothesis will be tested:

$$H_0: \pi_3 \geq 6\%$$

$$H_a: \pi_3 < 6\%$$

The hypothesis will be tested at a one-sided significance level of 2.5% [REDACTED]

8.2.2.2 Muscular and Post-Infarct Muscular VSD Closure Groups

There is no formal statistical hypothesis for the primary safety endpoint for the VSD closure groups. The primary safety endpoint will be reported descriptively in the VSD closure groups.

8.2.3 Descriptive Endpoint Analyses

Descriptive endpoints include:

- The number of times the device is recaptured
- The number of times the device is repositioned
- Ease of use – physicians will be asked survey questions about their experience with the Amplatzer Trevisio Delivery System compared to other device delivery systems

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- Total fluoroscopy time

For each descriptive endpoint, data will be presented using appropriate summary statistics. Continuous data will be summarized using descriptive statistics including mean, standard deviation, median and range. Categorical data will be summarized by the frequencies and percentages. Percentages will be based on the number of subjects in the analysis population as described in Section 8.1.

8.3 Sample Size Calculation and Assumptions

[REDACTED]

8.3.1 PFO and ASD Closure Groups

[REDACTED]

[REDACTED]

The sample size of 215 PFO and ASD closure subjects is therefore based on the primary safety endpoint.

8.3.2 Muscular and Post-Infarct Muscular VSD Closure Groups

[REDACTED]

The sample size of 44 VSD closure subjects is based on the technical success endpoint.

8.4 Timing of Analysis

[REDACTED]

The analyses will be completed for each cohort as the data for each cohort become available.

8.5 Subgroup Analysis

Sub-group analyses (e.g., sex) are planned for the study. Details about subgroup analysis will be described in the Statistical Analysis Plan.

[REDACTED]

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Baseline characteristics, demographics, primary endpoints and clinical outcomes will be analyzed separately for each of the defect closure groups (i.e., PFO and ASD closure; muscular VSD and post-infarct muscular VSD closure).

8.6 Procedures for Accounting for Missing Data

All analyses will be based on available data with missing data excluded. Any unused or spurious data will be noted as appropriate. Since the primary effectiveness endpoint is evaluated during the procedure, and the primary safety endpoint is an acute outcome evaluated prior to discharge or 7 days after the procedure, whichever occurs first (i.e., while the subject is still at the medical facility), missing data for the primary endpoints is anticipated to be minimal.

8.7 Statistical Criteria for Termination

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

8.8 Success Criteria

[REDACTED]

8.9 Deviations from Statistical Plan

Any major changes to the statistical plan will be documented in an amendment to the statistical plan. Less significant changes to the planned analyses will be documented in the final report.

9.0 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The Principal Investigator/institution will permit direct access to source data/documents for the purpose of performing audits, EC review and regulatory inspections.

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

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

10.1 Selection of Clinical Sites and Investigators

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

10.2 Clinical Study Finances and Agreements

The clinical study will be financed by Abbott. Investigational sites will be compensated by Abbott for participation in the clinical study per the conditions of agreement between the Sponsor and the investigational site.

[REDACTED]

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10.3 CIP Amendments

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

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

10.4 Training

10.4.1 Site Training

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

10.5 Monitoring

Sponsor and/or designee will monitor the clinical study over its duration according to the CIP-specific monitoring plan which will include the planned extent of source data verification. Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

- The Investigator understands and accepts the obligation to conduct the clinical study according to the CIP and applicable regulations and has signed the Clinical Trial Agreement.
- The Investigator and his/her staff should have sufficient time and facilities to conduct the clinical study and should have access to an adequate number of appropriate subjects to conduct the clinical study.
- Source documentation (including original medical records) must be available to substantiate proper informed consent procedures, adherence to CIP procedures, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.

10.6 Deviations from CIP

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

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

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

- Visiting the Principal Investigator and/or delegate
- Telephoning the Principal Investigator and/or delegate
- Corresponding with the Principal Investigator and/or delegate

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

10.7 Quality Assurance Audit

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

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

10.8 Sponsor Auditing

The following auditing requirements must be met:

1. The Sponsor shall prepare an audit plan as well as the operating procedures for the related duties and conduct audits in accordance with the audit plan and the operating procedures.
2. Individuals engaged in auditing (hereinafter referred to as "auditor") shall be different than those in charge of medical device development or monitoring.
3. The auditor shall prepare an audit report documenting the matters confirmed in the audit to certify and verify that the audit has been conducted and submit them to the Sponsor.

11.0 DATA HANDLING AND RECORD KEEPING

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

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CRF data collection will be performed through a secure web portal and only authorized personnel will access the Electronic Data Capture (EDC) system using a unique username and password to enter, review or correct data. Passwords and electronic signatures will be strictly confidential.

The data will be subjected to consistency and validation checks within the EDC system and supplemental review by the Sponsor.

At the conclusion of the clinical study, completed CRF images with the date-and-time stamped electronic audit trail indicating the user, the data entered, and any reason for change (if applicable) will be provided to the study sites.

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

11.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical study.

The Sponsor implements technical and physical access controls to ensure that Personal Information is accessible only to and processed only on a 'need to know' basis, including periodic review of access rights, and revocation of access when an individual's employment is terminated or the individual transitions to a role that does not require access to Personal Information, and appropriate restrictions on physical access to premises, facilities, equipment, and records containing Personal Information.

The Sponsor requires the study sites to transfer into Sponsor's data management systems only pseudonymous Personal Information (key-coded) necessary to conduct the Clinical study, such as the patient's medical condition, treatment, dates of treatment, etc. The Sponsor discloses as part of the clinical study informed consent process that some Sponsor representatives still may see Personal Information at the participating sites for technical support of the participating physicians on the device implant or procedures, monitoring and quality control purposes. Confidentiality of Personal Information will be observed by all parties involved at all times throughout the clinical study. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data.

The Sponsor data management systems and processes were designed, developed, and tested according to industry standards to appropriately safeguard Confidential Information (including any Personal Information) against unauthorized access and/or interference by third parties, intrusion, theft, destruction, loss or alteration. Clinical study data are encrypted in transit and at rest.

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

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11.2 Data Management Plan

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

11.3 Source Documentation

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

- Medical history/physical condition of the subject before involvement in the clinical study sufficient to verify CIP entry criteria
- Dated and signed notes on the day of entry into the clinical study referencing the Sponsor, CIP number, subject ID number and a statement that informed consent was obtained
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Adverse events reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of SAEs and of Investigator assessment of device relationship for SAEs.
- CIP-required laboratory reports and 12-lead ECGs, reviewed and annotated for clinical significance of out of range results (if applicable).
- Notes regarding CIP-required and prescription medications taken during the clinical study (including start and stop dates)
- Subject's condition upon completion of or withdrawal from the clinical study
- Any other data required to substantiate data entered into the CRF
- Patient reported outcome measures may be completed using CRF worksheets. These serve as the source documentation.

11.4 Case Report Form Completion

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the CIP and CRF completion. The Principal Investigator will ensure accuracy, completeness, legibility and timeliness of the data reported to the Sponsor on the CRFs and in all required reports. Data on CRFs will be collected for all subjects that are enrolled into the clinical study. Only authorized site personnel will be permitted to enter the CRF data through the EDC system deployed by the Sponsor. An electronic audit trail will be used to track any subsequent changes of the entered data.

11.5 Record Retention

The Sponsor and Principal Investigator/Site will archive and retain all documents pertaining to the clinical study as per the applicable regulatory record retention requirements. The Principal Investigator must

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obtain permission from Sponsor in writing before destroying or transferring control of any clinical study records.

12.0 ETHICAL CONSIDERATION

12.1 Institutional Review Board/Medical Ethics Committee Review and Approval

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

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

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

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

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

13.0 CLINICAL STUDY CONCLUSION

The end of the clinical study will coincide with the last subject's pre-discharge assessment, or assessment at 7 days following the procedure, whichever occurs first. The clinical study report will be submitted within one year of the end of the study.

The clinical study will be concluded when:

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

14.0 PUBLICATION POLICY

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

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

15.0 RISK ANALYSIS

The risks associated with the Amplatzer Trevisio Delivery System can be found in the IFU. The study does not require any additional procedures or assessments over standard of care. There are no additional risks introduced to study subjects.

15.1 Anticipated Clinical Benefits

The Amplatzer PFO Occluder is indicated for percutaneous, transcatheter closure of a PFO to reduce the risk of recurrent ischemic stroke in patients who have had a cryptogenic stroke due to presumed paradoxical embolism. The Amplatzer Septal Occluder is a percutaneous, transcatheter, atrial septal defect closure device intended for the occlusion of ASDs in secundum position or patients who have undergone a fenestrated Fontan procedure and who now require closure of the fenestration. The Amplatzer Cribriform Occluder is a percutaneous, transcatheter, ASD closure device intended for the closure of multi-fenestrated (cribriform) atrial septal defects. Patients indicated for ASD closure have echocardiographic evidence of fenestrated ostium secundum atrial septal defect and clinical evidence of right ventricular volume overload. The Amplatzer Muscular VSD Occluder is a percutaneous, transcatheter, VSD closure device indicated for use in patients with complex ventricular septal defects (VSD) of significant size to warrant closure (large volume left to right shunt, pulmonary hypertension, or clinical symptoms of congestive heart failure who are considered to be at high risk for standard transatrial or transarterial surgical closure based on anatomical conditions and/or based on overall medical condition. The Amplatzer Post-Infarct Muscular VSD Occluder is a minimally invasive alternative to achieving post-infarct muscular VSD closure in patients who are not satisfactory candidates for open surgical repair. The Amplatzer Trevisio Delivery System is an important accessory for delivery of Amplatzer occlusion devices and therefore shares the life-saving benefits of these occlusion devices. There are no additional benefits of being in the PAS beyond standard of care.

15.2 Foreseeable Adverse Events and Anticipated Adverse Device Effects

Risks associated with the specified device and procedure, together with their likely incidence, are described Appendix I. There may be risks related to the device under study that are unknown at present. Likewise, the exact frequency of those risks may be unknown.

15.3 Residual Risks Associated with the Device Under Study, as Identified in the Risk Analysis Report

Risk analysis of the Amplatzer Trevisio Delivery System has been performed in accordance with the Risk Analysis Plan and Use Failure Mode Effect Analysis (UFMECA) to systemically identify potential hazards associated with the design and use of this device. Based upon bench testing, published literature and post market data from previous device, all risks have been identified and determined to be within acceptable levels (see Appendix I). Information of residual risks and safety is disclosed in the IFU in the form of clear instructions of what actions to take or to avoid in order to avoid a hazardous situation of harm from occurring (contra-indications, warnings, and precautions). The anticipated AEs disclosed in the

[REDACTED]

[REDACTED]

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IFU provide further information to enable the user, and potentially the patient, to make an informed decision that weights the residual risk against the benefit of using the device.

15.4 Risks Associated with Participation in this Clinical Study

Use of the Amplatzer Trevisio Delivery System in this study is identical to the use outside of this study. Thus, the possible risks and discomforts are similar to any routine commercial use of the Amplatzer Trevisio Delivery System. These risks have been identified in the IFU. All pre-protocol required procedures are considered standard of care and do not constitute as additional risk for the clinical study participants.

15.5 Steps Taken to Control or Mitigate Risks

In-depth recommendations, special precautions and instructions regarding device handling and placement are included in the IFU. It is also stated in the IFU that the devices can only be used by physicians who are trained in standard transcatheter techniques. This statement is interpreted to mean that the physician users are expected to be aware of the known and foreseeable safety risks associated with the use of the devices including the surgical and/or non-surgical treatment of these conditions.

All Investigators involved in the conduct of the clinical study will be qualified by education, training, or experience to perform their tasks. All adverse events and device deficiencies will be reported to the Sponsor and will be monitored internally for safety surveillance purposes.

15.6 Risk to Benefit Rationale

The benefit of using the Amplatzer PFO, ASD, and VSD devices is stated in section 15.1. The Amplatzer Trevisio Delivery System allows use of these devices as intended and thus shares the life-saving benefits of these occlusion devices. The residual risk evaluated in the risk analysis/evaluation documents has been judged to be acceptable based on the criteria defined in the risk management report. Based on this analysis and the benefit that these devices provide, it has been determined that the benefits of the devices outweigh the risks associated with use, design, and process.

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APPENDIX I. RATES OF FORESEEABLE ADVERSE EVENTS

[REDACTED]

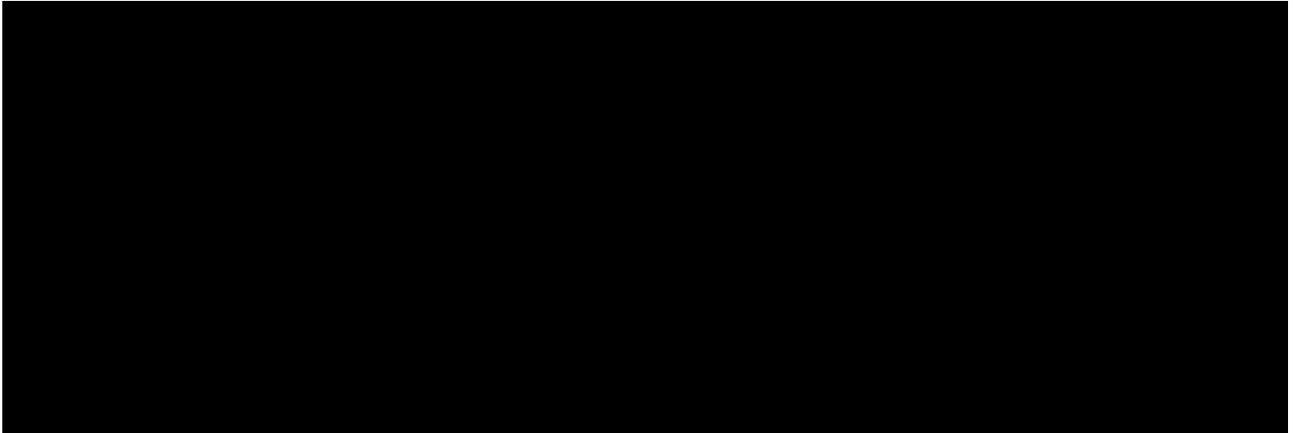
[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

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APPENDIX II: ABBREVIATIONS AND ACRONYMS

AE = adverse event

ASD = atrial septal defect

ASD PMS II = Atrial Septal Defect Post-Market Surveillance Study II

ASO = Amplatzer Septal Occluder

CIP = clinical investigation plan

CRF = case report form

DMP = data management plan

EC = ethics committee

ECG/EKG = electrocardiogram

EDC = electronic data capture

FDA = Food and Drug Administration

ICE = intracardiac echocardiogram

IFU = instructions for use

ITV = TorqVue Intravascular Delivery System

M-F ASD = multi-fenestrated atrial septal defect

PFO = patent foramen ovale

RESPECT = Randomized Evaluation of Recurrent Stroke comparing PF₀ Closure to
Established Current Standard of Care Treatment (a randomized trial to assess
safety and effectiveness of PFO closure with the Amplatzer PFO Occluder in
cryptogenic stroke patients)

SAE = serious adverse event

TEE = transesophageal electrocardiogram

UCB = upper confidence bound

UFMECA = Use Failure Mode Effect Analysis

VSD = ventricular septal defect

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APPENDIX III: SITE CONTACT INFORMATION

Contact information for each participating clinical site is available under separate cover.

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APPENDIX IV: LABELS

Product labels will be provided under a separate cover. A copy of the Labels can be obtained upon request from the Sponsor Clinical Project Manager.

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APPENDIX V: CASE REPORT FORMS

Case Report Forms will be provided under a separate cover. A copy of the Case Report Forms can be obtained upon request from the Sponsor Clinical Project Manager.

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APPENDIX VI: INFORMED CONSENT FORM

Informed Consent Forms will be provided under a separate cover. A copy of the Informed Consent Forms can be obtained upon request from the Sponsor Clinical Project Manager.

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APPENDIX VII: MONITORING PLAN

A copy of the Monitoring Plan can be obtained upon request from the Sponsor Clinical Project Manager for the clinical study.

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APPENDIX VIII: REVISION HISTORY

This CIP may be amended as appropriate by the Sponsor. Rationale will be included with each amended version in the revision history table below. The version number and date of amendments will be documented.

EC and relevant Regulatory Authorities, if applicable, will be notified of amendments to the CIP.

[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

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APPENDIX IX: CIP SUMMARY

Clinical Study Name and Number	ABT-CIP_10319 Ver. A [REDACTED] Trevisio PAS
Title	A single-arm, non-randomized, multi-center clinical study of the Amplatzer™ Trevisio™ Intravascular Delivery System for facilitating percutaneous, transcatheter implantation of the Amplatzer™ Occluder Devices
Objective(s)	The primary objective of this clinical study is to characterize the safety and effectiveness of the Amplatzer Trevisio Delivery System for facilitating percutaneous, transcatheter implantation of the Amplatzer PFO Occluder, Amplatzer ASO, Amplatzer Cribiform Occluder, Amplatzer Muscular VSD Occluder IFU, and Amplatzer Post-Infarct Muscular VSD Occluder IFU).
Device Under Investigation	Amplatzer™ Trevisio™ Intravascular Delivery System
Number of Subjects Required for Inclusion in Clinical Study	A minimum of 215 subjects with a PFO or ASD, and a minimum of 44 subjects with a VSD, will be enrolled in the clinical study.
Clinical Study Design	Prospective, multi-center, single-arm, post-approval study
Primary Endpoint(s)	<p>Primary Effectiveness Endpoint: Technical success – successful deployment and release of at least one device</p> <p>Primary Safety Endpoint: Device- or procedure-related serious adverse events through discharge or 7 days, whichever occurs first</p>
Subject Follow-up	Subjects will be followed through hospital discharge or 7 days, whichever occurs first. Post-implant follow-up data will include: shunt closure status (TEE/TTE imaging), adverse events, EKG results, and physical exam results.
Inclusion Criteria	Subject is indicated for implantation with the Amplatzer Septal Occluder, Amplatzer Multi-fenestrated Septal Occluder (“Cribiform”), Amplatzer PFO Occluder, Amplatzer Muscular VSD Occluder, or Amplatzer Post-Infarct Muscular VSD Occluder. For further detail see CIP section 5.3.2, p. 15.
Exclusion Criteria	<p>Exclusion criteria for subjects undergoing ASD closure include:</p> <ul style="list-style-type: none"> • Patients known to have extensive congenital cardiac anomaly that can only be adequately repaired by cardiac surgery • Patients known to have sepsis within 1 month prior to implantation, or any systemic infection that cannot be successfully treated prior to device placement • Patients known to have demonstrated intracardiac thrombus on

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	<p>echocardiography (especially left atrial or left atrial appendage thrombi)</p> <ul style="list-style-type: none"> • Patients whose size or condition (e.g., too small for transesophageal echocardiography [TEE] probe, catheter size, vasculature size, active infection) would cause the patient to be a poor candidate for cardiac catheterization • Patients with defect margins less than 5 mm to the coronary sinus, inferior vena cava rim, an atrioventricular valve, or the right upper lobe pulmonary vein <p>Exclusion Criteria for Subjects Undergoing PFO Closure</p> <ul style="list-style-type: none"> • Presence of thrombus at the intended site of implant, or documented evidence of venous thrombus in the vessels through which access to the defect is gained • Active endocarditis or other infections producing bacteremia • Patients whose vasculature, through which access to the defect is gained, is inadequate to accommodate the appropriate sheath size • Anatomy in which the AMPLATZER™ PFO device size required would interfere with other intra-cardiac or intravascular structures, such as valves or pulmonary veins • Patients with known hypercoagulable states • Patient with intra-cardiac mass or vegetation, thrombus, or tumor <p>Exclusion Criteria for Patients Undergoing VSD Closure with the Amplatzer Muscular VSD Occluder or Amplatzer Post-Infarct Muscular VSD Occluder</p> <ul style="list-style-type: none"> • Body weight <8 kg • Tetralogy of Fallot • Intracardiac thrombi on echocardiography <p>For further detail see CIP section 5.3.3, p. 16.</p>
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