Abbott	Clinical Investigation Plan Cover Page

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PIVSD PAS
The Amplatzer™ Post-infarct Muscular VSD Occluder Humanitarian Device Exemption (H070005) Post Approval Study
Study Document No: SJM-CIP-10191
Version E
Date: 11 December 2020

Sponsor

Abbott
5050 Nathan Lane
Plymouth, MN 55442
USA

PIVSD Occluder HDE PAS

The Amplatzer™ Post-infarct Muscular VSD Occluder
Humanitarian Device Exemption (H070005)
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[redacted]

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Clinical Investigation Plan (CIP)

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[redacted]

Table of Contents

1 Introduction

This document is a clinical investigational plan (CIP) for the Amplatzer™ Post-Infarct Muscular Ventricular Septal Defect (PIVSD) Occluder Humanitarian Device Exemption (HDE) Post Approval Study (H070005). This clinical study is intended to evaluate the safety and probable benefit of the Amplatzer™ PIVSD Occluder in transcatheter closure of muscular ventricular septal defects subsequent to acute myocardial infarction. This clinical study is sponsored by Abbott.

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

2 Background and Justification for Clinical Study

Muscular ventricular septal defect is an uncommon and life-threatening complication of myocardial infarction, which results in significant morbidity and mortality. Post-myocardial infarction muscular ventricular septal defect (post-MI VSD) occurs in <1% of patients who experience a myocardial infarction.[1] When left untreated it can result in rapid clinical deterioration characterized by cardiogenic shock and end-organ dysfunction with subsequent fatality. Standard practices and procedures used for the treatment of a post-infarct ventricular septal defect include one or more of the following:

1. Medical Therapy – Use of pharmacological therapy, such as vasodilators, to decrease left-to-right shunt associated with the defect, may increase cardiac output and stabilize the patient hemodynamically. However, vasodilators may be precluded in patients with severe cardiogenic shock. Inotropic agents and vasopressors, which may be used as alternatives to vasodilators, have the disadvantage of markedly increasing left ventricular work and myocardial oxygen consumption. The mortality rate of using medical therapy alone exceeds 90%.[2]
2. Mechanical Circulatory Support – Use of an intra-aortic balloon pump or a temporary ventricular assist device to support the circulatory system to recovery or as a bridge to additional therapy, such as a longer term mechanical circulatory support device or cardiac transplantation. Mortality rate using this approach is approximately 17%.[3]
3. Surgical Repair – Use of open cardiac surgery under cardiopulmonary bypass to repair the ventricular septal defect. Operative mortality rate ranges between 19% and 54%.[4]

Although open cardiac surgery may be used to repair a post-infarct VSD, many patients, particularly those in cardiogenic shock and with end-organ injury, may be poor candidates for surgery. Furthermore, patients who have significant residual shunting after open cardiac surgical repair may be at high risk for reoperation. The Amplatzer™ PIVSD Occluder is a minimally invasive alternative to achieving VSD closure in patients who are not satisfactory candidates for open surgical repair.

[redacted]

FDA issued a Humanitarian Device Exemption (HDE) approval order for the Amplatzer PIVSD Occluder (H070005) on January 10, 2017. The Conditions of Approval require that Abbott conduct a post approval study to evaluate the safety and probable benefit of the Amplatzer™ PIVSD Occluder.

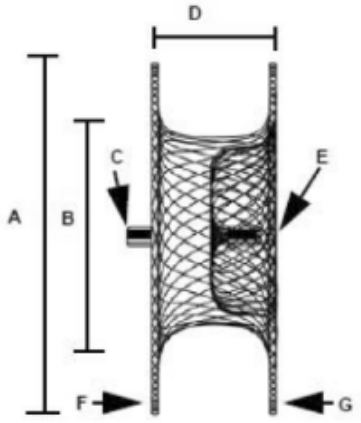
3 Device under Study

3.1 Identification and Description of the Devices under study

3.1.1 Identification

The Amplatzer™ Post-infarct Muscular VSD Occluder is illustrated in **Figure 1**, and a listing of the devices to be included in this PAS appears in **Table 1.**

Figure 1: Amplatzer™ Post Infarct Muscular VSD Occluder



A. Disc diameter
B. Device size (at waist)
C. Marker bands
D. Waist length
E. Delivery cable connector
F. Distal (left ventricular) disc
G. Proximal (right ventricular) disc

Table 1: Identification of Devices under Study

DEVICE NAME	MODEL*	WAIST DIAMETER (DEVICE SIZE)	DISC DIAMETER	WAIST LENGTH	REGULATORY STATUS
Amplatzer™ PIVSD Occluder	9-VSDMPIHDE-016	16 mm	26 mm	10 mm	HDE Designation
Amplatzer™ PIVSD Occluder	9-VSDMPIHDE-018	18 mm	28 mm	10 mm	HDE Designation
Amplatzer™ PIVSD Occluder	9-VSDMPIHDE-020	20 mm	30 mm	10 mm	HDE Designation
Amplatzer™ PIVSD Occluder	9-VSDMPIHDE-022	22 mm	32 mm	10 mm	HDE Designation
Amplatzer™ PIVSD Occluder	9-VSDMPIHDE-024	24 mm	34 mm	10 mm	HDE Designation

*Model numbers for subjects may reflect the pre-HDE designation of 9-VSDMPIIDE-016, -018, -020, -022, and -024

3.1.2 Device Description and Intended Purpose

The Amplatzer™ PIVSD Occluder is intended for percutaneous transcatheter closure of post-myocardial infarct muscular VSDs in patients who are not satisfactory surgical candidates. The occluder is implanted percutaneously to close post-myocardial infarct muscular VSD.

The implant procedure is performed using a transcatheter approach under general anesthesia or conscious sedation, and can be performed in a catheterization laboratory setting under fluoroscopic and echocardiographic guidance.

The Amplatzer™ PIVSD Occluder is a self-expanding, double-disc device made from nitinol wire mesh (**Figure 1**) and designed to facilitate occlusion of muscular VSDs that occur post-myocardial infarction. The discs are linked together by a waist corresponding to the size of the VSD. To increase its closing ability, the discs and waist are filled with polyester fabric that is sewn securely to the device with polyester thread. Radiopaque marker bands at each end of the device provide visualization under fluoroscopy.

The Amplatzer™ PIVSD Occluder is designed to accommodate the damaged muscular tissue of the septal wall of myocardial infarction patients, and is available in five sizes: 16 mm, 18 mm, 20 mm, 22 mm, and 24 mm. All five device sizes have the same waist length of 10 mm.

The Amplatzer™ TorqVue™ system, which is 510(k) cleared, is used to deliver the Amplatzer™ PIVSD Occluder. The delivery system consists of a delivery sheath with Touhy-Borst hemostatic adapter, dilator, loader, plastic vise, and delivery cable. A 9 Fr sheath is recommended for the 16 mm and 18 mm PIVSD occluders, and a 10 Fr sheath is recommended for the 20 mm, 22 mm, and 24 mm PIVSD occluders.

3.1.3 Device Handling and Storage

Consult the User's Manual for instructions for use, storage and handling instructions, preparation for use and any precautions.

The sponsor requires all products to be stored according to the labeling and Instructions for Use in a secure area to prevent unauthorized access or use.

3.2 Device Accountability

Device accountability independent of the study is required for the Amplatzer™ PIVSD Occluder since it is designated as a Humanitarian Use Device (HUD). As defined in 21 CFR 814.3(n), an HUD is a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year. As part of post approval obligations, Abbott will annually report to FDA the number of devices shipped or sold since initial HDE marketing approval (21 CFR 814.126(b)(1)(iii)). If that number exceeds 8,000 then Abbott will provide an explanation.

4 Clinical Study Design

4.1 Clinical Study Design

This is a multi-center, observational study to evaluate the safety and probable benefit of the Amplatzer™ PIVSD Occluder for use in transcatheter closure of muscular ventricular septal defects following a myocardial infarction in the post approval setting.

As described in section 4.2, this study has five endpoints (safety: acute and chronic survival; effectiveness: technical success, acute and chronic closure). Two cohorts will be utilized to obtain study endpoint data. Cohort 1 will be comprised of all available Emergency and Compassionate PIVSD Occluder subject data from 2011 until the end of 2016 and these data will be used to determine technical success, acute survival, and chronic survival. [redacted]

[redacted]

[redacted] This cohort will be used to determine acute and chronic closure, and chronic survival. For living subjects, the index procedure must have occurred >6 months prior to enrollment. Subject identification will occur until data on a [redacted] with PIVSD Occluders for post myocardial infarct VSD and post-procedure echocardiogram available for evaluation of residual shunt by the echocardiography core laboratory have been enrolled.

[redacted]

[redacted]

Table 1: Estimated Timeline of Milestone Events

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

4.2 Objective

The objective of this clinical study is to evaluate the safety and probable benefit of the PIVSD Occluder in patients undergoing implantation of the PIVSD Occluder following an acute myocardial infarction.

4.2.1 Effectiveness Endpoints

Technical Success: Technical success occurs when a subject is successfully implanted with a PIVSD device in the ventricular septal defect. An implant attempt occurs when the delivery system is inserted in the subject's vasculature.

Acute Closure: Acute closure is defined as the absence of a residual shunt ≥3 mm, and will be assessed based on an echocardiogram obtained immediately after the successful deployment of the device and up to 7 days post-procedure.

Chronic Closure: Chronic closure is defined as the absence of a residual shunt ≥3 mm at 6 months or later.

4.2.2 Safety Endpoints

Acute Survival: Acute survival is defined as survival for at least 24 hours following an attempted PIVSD device implant.

Chronic Survival: Chronic survival is defined as survival for at least 183 days post-procedure.

4.3 Implanter Training

The study is expected to enroll subjects who have been implanted with a PIVSD Occluder; therefore no implanter training is planned under this CIP.

4.4 Study Population

The intended population for the Amplatzer™ PIVSD Occluder is patients with post-myocardial infarct muscular VSD who are not satisfactory surgical candidates. The study will enroll subjects in two cohorts:

Cohort 1: All available Emergency and Compassionate PIVSD Occluder subject data from 2011 until the end of 2016 will be utilized to determine technical success, acute survival, and chronic survival. All subjects belonging to this cohort must have undergone an attempt to close a post-infarct VSD using the Amplatzer™ PIVSD Occluder.

Cohort 2: This cohort will consist of subjects over the age of 18 years who have previously been successfully implanted with the PIVSD Occluder and:

- for living subjects, the subject or subject's legally authorized representative has provided consent to participate in this study.
- the subject's post-procedure echocardiogram is evaluable and can be sent to the echocardiography core laboratory for residual shunt assessment.

Therefore, this cohort will be composed of retrospectively enrolled subjects. This cohort will be utilized to determine acute and chronic closure, and chronic survival.

5 Procedures

Approval from the Sponsor must be received prior to initiating study procedures. Baseline, procedure, post-procedure, and six month subject data will be collected retrospectively on each subject. The following sections provide a detailed description of procedures required by this CIP.

5.1 Informed Consent Process

Cohort 1

A fully executed informed consent form is required prior to each Emergency and Compassionate PIVSD procedure. These previously executed procedure consent forms contain language that allows for Sponsor data collection. The Sponsor will verify that an executed consent form is present and covers the access and use of stored data for research analysis prior to utilizing a subject's data for the analysis of the endpoints.

Cohort 2

For living subjects, the Principal Investigator or his/her authorized designee will conduct the Informed Consent process (this retrospective group may include re-consenting previously implanted Emergency and Compassionate Use patients or those implanted with the approved HUD), as required by applicable regulations and the center's IRB. This process will include a verbal discussion with the subject or legally authorized representative on all aspects of the clinical study that are

relevant to the subject's decision to participate (or the legally authorized representative's decision to consent), such as details of data to be collected, anticipated benefits, and potential risks of clinical study participation. During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect the subject's legal rights. The subject or legally authorized representative shall be provided with the informed consent form written in a language that is understandable to the subject or legally authorized representative and has been approved by the center's IRB. The subject or legally authorized representative shall have adequate time to review, ask questions, and consider participation.

If the subject or legally authorized representative agrees to participate, the Informed Consent form must be signed and dated by the subject or the subject's legally authorized representative and by the person obtaining the consent. The signed original will be filed in the subject's hospital or research charts, and a copy will be provided to the subject or the subject's legally authorized representative.

The Principal Investigator or his/her authorized designee will document the informed consent process in the subject's hospital and/or research charts. The date of signature will be entered on the applicable Case Report Form (CRF).

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 IRB according to the IRB's reporting requirements.

5.1.1 Special circumstances for informed consent

A legally authorized representative may represent the subject during the informed consent process, which will be performed according to the requirements in section 5.1. The subject, if living, will also be informed about the clinical study within his/her ability to understand.

When obtaining informed consent from the subject is not possible because of the subject's medical condition, the Informed Consent of the subject's legally authorized representative will be requested.

In the event the subject has died, informed consent is not applicable. HIPAA compliance and other applicable federal, state and local laws will be reviewed by the center's IRB to determine the application of the Privacy Rule to a deceased subject's protected health information.

All other aspects of the informed consent process will be in compliance with section 5.1.

5.2 Point of Enrollment

Cohort 1
The presence of a fully executed informed consent form is required prior to each Emergency and Compassionate PIVSD procedure. These previously executed procedure informed consent forms contain language that allows for Sponsor data collection. All Emergency and Compassionate use patients will be included in Cohort 1, therefore, the point of enrollment is not defined for this cohort.

Cohort 2
A subject is considered enrolled in this study if the subject has been successfully implanted with the PIVSD Occluder; a post-procedure echocardiogram is able to be evaluated for residual shunt by the

echocardiography core laboratory; and, for living subjects, the subject or the subject's legally authorized representative (LAR) has provided consent to participate in this study.

Potential subjects with PIVSD Occluder implants at study sites will be selected for screening of medical records followed by enrollment. For living subjects, upon obtaining consent, the Principal Investigator or delegated study personnel will record enrollment information (name of the clinical study and date of consent) in the hospital records and complete and submit an applicable CRF in a timely manner. For deceased subjects, the applicable CRF will be completed prior to sending the post-procedure echocardiogram for evaluation. Notification of subject consent (for living subjects only) to the Sponsor is considered to have occurred when the Sponsor has received the applicable CRF. However, the subject is not considered enrolled until a post-procedure echocardiogram is able to be evaluated for residual shunt by the echocardiography core laboratory.

5.3 Procedures

For Cohort 1, all available Emergency and Compassionate PIVSD Occluder subject data from 2011 until the end of 2016 will be utilized to determine technical success, acute survival, and chronic survival. Any available demographic/medical history information implant success and survival within 24 hours of the procedure and through 183 days post-procedure will be documented. No additional information will be collected in this cohort.

[redacted] The Principal Investigator is responsible for ensuring all clinical study data is collected as required per CIP scheduled procedures.

5.3.1 Baseline

The following information will be collected retrospectively via subject's medical records:

- Date of myocardial infarct
- Demographics
- Cardiovascular history and previous cardiac procedures
- Risk factors and relevant comorbidities

5.3.2 Implant/Procedure and Post-Procedure

The following procedure information will be collected retrospectively via each subject's medical records:

- Date of procedure (if multiple procedures occurred, date of each procedure)
- Procedure success in a subject
- Implanted device(s) model number(s)
- Post-procedure echocardiogram obtained immediately after the successful deployment of the device and up to 7 days post-procedure is evaluable and can be sent to the echocardiography core laboratory for residual shunt evaluation.

5.3.3 Follow-up

The following data from at least 6-months post-procedure will be retrospectively collected:

- Survival assessment
- Implant status of PIVSD Occluder
- Echocardiogram (the echocardiography core laboratory will assess the residual shunt on this echocardiogram)

5.4 Study Flow Chart

The **Figure 2** and the **Table 3** below summarize subject flow and requirements of the study.

Figure 2: Cohort 2 Flow Chart

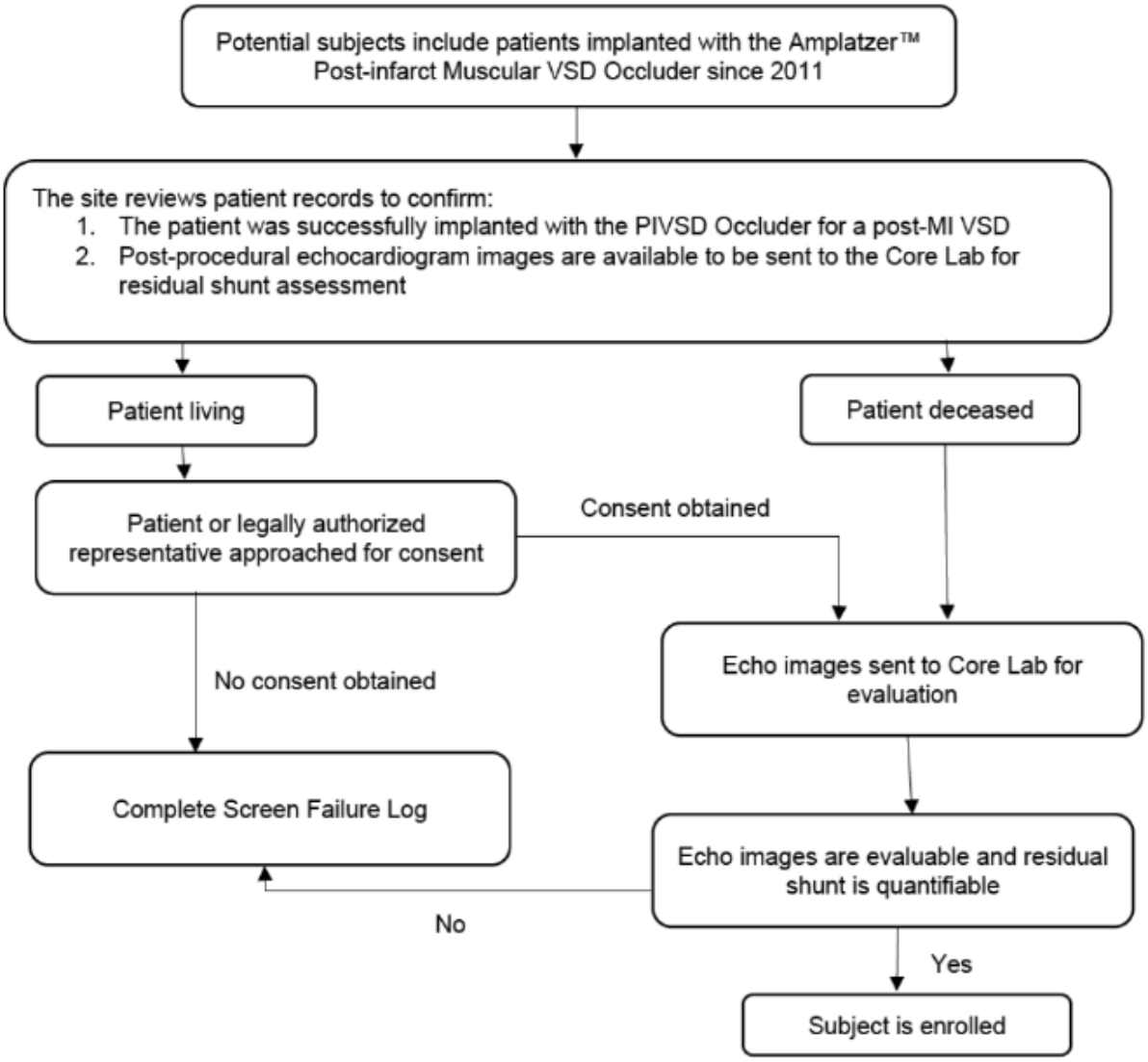


Table 2: Cohort 2 Data Collection tests and procedures

VISIT STUDY ACTIVITY	BASELINE	POST-PROCEDURE (UP TO 7 DAYS)	6 MONTHS* (>150 DAYS)	>6 MONTHS** (> 183 DAYS)
Informed Consent Process				X
Demographics/Medical History	X			
Echocardiogram		X	X*	

*If subject was alive during the visit window
**Since all data are retrospectively collected, informed consent occurs at 6 month or beyond the PIVSD occluder implant procedure

5.5 Requirements for Clinical Laboratories

An echocardiography core laboratory will assess echocardiograms for residual shunt and quantification of shunts.

5.6 Study Committee

5.6.1 Publication Committee (PC)

A Publication Committee may be established to oversee study publications. Publication Committee membership may include Principal Investigators, a representative of the Sponsor and a statistician. The Publication Committee will be responsible for identifying, selecting and approving publication proposals and determining authorship according to a Publication Plan. A Publication Committee charter will define membership of the committee and outline the roles and responsibilities of the committee, as well as rules to define authorship.

6 Statistical Considerations

The following section describes the statistical methods for the clinical study and justification of the design.

6.1 Endpoints

There are five endpoints, three effectiveness endpoints and two safety endpoints. There are no hypotheses to be tested.

6.1.1 Effectiveness Endpoint 1: Technical Success

Technical success occurs when a subject is successfully implanted with a PIVSD device in the ventricular septal defect. An implant attempt occurs when the delivery system is inserted in the subject's vasculature.

6.1.1.1 Analysis Methods per Subject (Subject-Level Technical Success)

The proportion of subjects who experience technical success will be estimated. [redacted]

[redacted]

[redacted] The 95% confidence interval for the rate of technical success will be calculated using the exact binomial method.

[redacted]

[redacted]

6.1.2 Effectiveness Endpoint 2: Acute Closure

Acute closure is defined as the absence of a residual shunt ≥3 mm, and will be assessed based on an echocardiogram obtained immediately after successful deployment and up to 7 days post-procedure.

6.1.2.1 Analysis Methods

The proportion of subjects who have acute closure post-procedure, as determined by the echocardiography core laboratory, will be estimated. [redacted] he 95% confidence interval for the rate of acute closure will be calculated using the exact binomial method.

[redacted]

[redacted]

6.1.3 Effectiveness Endpoint 3: Chronic Closure

Chronic closure is defined as the absence of a residual shunt ≥3 mm at 6 months or later.

6.1.3.1 Analysis Methods

The proportion of subjects who have chronic closure at a follow-up visit 6 months or later (from the time of first successful implant), as determined by the echocardiography core laboratory, will be estimated. [redacted] The 95% confidence interval for the rate of chronic closure will be calculated using the exact binomial method.

[redacted]

[redacted]

6.1.4 Safety Endpoint 1: Acute Survival

Acute survival is defined as survival for at least 24 hours following an attempted PIVSD device implant.

[redacted]

6.1.4.1 Analysis Methods

The proportion of subjects who survive for at least 24 hours following an attempted PIVSD device implant will be estimated. [redacted] The 95% confidence interval for the rate of acute survival will be calculated using the exact binomial method.

[redacted]

[redacted]

6.1.5 Safety Endpoint 2: Chronic Survival

Chronic survival is defined as survival for at least 183 days from the time of first successful implant.

6.1.5.1 Analysis Methods

The probability of a subject who is alive for at least 183 days will be estimated by the Kaplan-Meier method. Subjects whose survival status is not known for at least 183 days post-procedure (first successful implant) will be censored on the date at which survival status was known. The day of procedure will be considered Day 0 when referring to a specific number of days for the Kaplan-Meier analysis. The 95% confidence interval for the rate of chronic survival will be calculated using Greenwood's formula for the variance of the Kaplan-Meier estimator.

[redacted]

[redacted]

6.2 [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

6.3 [redacted]

[redacted]

6.4 Subgroup Analysis

Subgroup analysis will be performed to examine the consistency of endpoints (technical success, acute closure, chronic closure, acute survival, and chronic survival) across males and females.

6.5 Timing of Analysis

Analysis will be performed when all sites have completed the required data entry for all enrolled subjects.

6.6 Additional Data

6.6.1 Baseline and Demographic Characteristics

Descriptive statistics of continuous variables will be summarized by sample size, mean, median, standard deviation, minimum and maximum. For categorical variables, the number and percentage of subjects in each category will be presented.

6.6.2 Adverse Events

Data in this study are being collected retrospectively; therefore, no adverse event information will be collected. Additionally, these data do not apply towards any of the study endpoints. Mortality data will be collected to estimate survival.

6.6.3 Deviations from the Statistical Plan

If any deviations from the analysis plan occur, such deviations will be documented in the clinical study report or statistical report containing the analysis results.

7 Risks and Benefits

The risks associated with the Amplatzer™ PIVSD Occluder can be found in the Instructions for Use. The study does not require any additional procedures or assessments over the standard of care. There are no additional risks introduced to study subjects.

7.1 Risks Associated with the Device under Study

A complete list of anticipated adverse events can be found in the Instructions for Use (IFU).

7.2 Risk-to-Benefit Rationale

Risks associated with participating in this clinical study are not expected to have any impact on the patient as data are collected retrospectively.

7.3 History of Device Modifications or Recall

There have been no modifications or recall in relation to safety and clinical performance of the Amplatzer™ PIVSD Occluder.

8 Requirements for Investigator Records and Reports

8.1 Deviations from the CIP

A deviation is defined as an instance of failure to follow, intentionally or unintentionally, the requirements of the CIP. The investigator should not deviate from the CIP.

The PI must maintain accurate, complete, and current records, including documents showing the date of and reason for each deviation from the CIP. Relevant information for each deviation will be documented as soon as possible on the applicable CRF.

The PI is required to adhere to local regulatory requirements for reporting deviations to IRB.

8.2 Safety Reporting

No adverse event information will be collected as adverse event data do not apply toward any of the study endpoints.

8.3 Complaints

The investigator will be responsible for reporting complaints involving the Amplatzer™ PIVSD Occluder for implant procedures that occur following HDE approval on January 10, 2017.

The investigator must notify the Abbott Postmarket Surveillance Department by emailing the information on the device to complaints_amplatzer@abbott.com or calling 651-756-5400 as soon as possible after becoming aware of the complaint.

8.4 Source records

Cohort 2 source documents will be maintained by the study site. The data reported on the CRFs will be derived from and be consistent with the source documents and any discrepancies will be explained in writing.

8.5 Records Retention

The Sponsor and the Principal Investigators will maintain the clinical study documents as required. Measures will be taken to prevent accidental or premature destruction of these documents. The Principal Investigator or the Sponsor may transfer custody of records to another person/party and document the transfer at the study site or the Sponsor's facility, as appropriate.
These documents must be retained by the study site for a period of 2 years after the conclusion of the clinical study and made available for monitoring or auditing by the Sponsor's representative or representatives of the applicable regulatory agencies.

All original source documents must be stored for the maximum time required by the regulations at the hospital, research institute, or practice in question. If original source documents can no longer be maintained at the site, the investigator will notify the Sponsor.

9 Clinical Data Handling

The Sponsor will be responsible for the data handling. The Sponsor and/or its affiliates will be responsible for compiling and submitting all required reports to governmental agencies. Data will be analyzed by the Sponsor and may be transferred to the Sponsor's locations worldwide and/or any other worldwide regulatory authority in support of a market-approval application.

9.1 Protection of Personally Identifiable Information

Abbott respects and protects personally identifiable information collected or maintained for this clinical study. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data. Confidentiality of data will be observed by all parties involved at all times throughout the clinical study. All data will be secured against unauthorized access.

9.2 Data Management Plan

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

Subject data will be captured in a validated electronic data capture (EDC) system hosted by the Sponsor.

Only authorized site personnel will be permitted to enter the CRF data through the EDC system deployed by Abbott. An electronic audit trail will be used to track any subsequent changes of the entered data.

9.3 Document and Data Control

9.3.1 Traceability of Documents and Data

The investigator will ensure accuracy, completeness legibility and timeliness of the data reported to the Sponsor on the CRFs and in all required reports.

9.3.2 Recording Data

The CRF will be reviewed by the authorized site personnel. An appropriate comment will be provided to explain changes to data reported on the CRF.

10 Monitoring

It is the responsibility of the Sponsor to ensure the clinical study is conducted, recorded, and reported according to the approved CIP, subsequent amendment(s), applicable regulations, and guidance documents.

Centralized monitoring will occur through routine internal data review. This monitoring is designed to identify missing and inconsistent data, data outliers, and potential CIP deviations that may be indicative of site non-compliance. On-site monitoring may occur at the discretion of the Sponsor.

11 Reporting

Progress reports submitted to FDA will include the number of study sites activated, the number of subjects enrolled, and a summary of the effectiveness and safety endpoint data.

The analysis for the final report will be performed after sites have completed the required data entry for all enrolled subjects.

12 Compliance Statement

12.1 Statement of Compliance

This clinical study will be conducted in compliance with the most current regional and local laws and regulations. Principles of Good Clinical Practice will be followed as based on the most current version of the World Medical Association (WMA) Declaration of Helsinki.

The investigator will sign a Clinical Trial Agreement and agree to be compliant with it. The investigator will not start enrolling subjects or requesting informed consent from any subject prior to obtaining IRB approval and relevant Regulatory Authority approval, if applicable, and authorization from the Sponsor in writing for the clinical study. If additional requirements are imposed by the IRB or relevant Regulatory Authority, those requirements will be followed. If any action is taken by an IRB or a relevant Regulatory Authority with respect to the clinical study, that information will be forwarded to the Sponsor.

12.2 Quality Assurance Audits and Regulatory Inspections

The investigator and/or delegate should contact the Sponsor immediately upon notification of a regulatory authority inspection at the site. A monitor or designee will assist the investigator and/or delegate in preparing for the audit. The Sponsor may perform quality assurance audits, as required.

The Principal Investigator or institution will provide direct access to source data during and after the clinical study for monitoring, audits, IRB review and regulatory authority inspections, as required. The Principal Investigator or institution will obtain permission for direct access to source documents from the subject, hospital administration and national regulatory authorities before starting the clinical study.

12.3 Repeated and Serious Non-Compliance

Since data in this study are being collected retrospectively, this section is not applicable.

13 Suspension or Premature Termination of the Clinical Study

Since data in this study are being collected retrospectively, this section is not applicable.

14 Clinical Study Conclusion

The clinical study will be concluded when:

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

15 Publication Policy

Publications or presentations of clinical study methods or results will adhere to Abbott's publication policy, which is based on Good Publication Practices and International Committee of Medical Journal Editors (ICMJE) guidelines.

Publication planning and authorship determinations will be overseen by the Abbott's Publications Committee (see section 5.10.1), and investigators will be notified via email about the dissemination of study data and opportunities for involvement as authors on publications/presentations.

16 Reporting Results on ClincalTrials.gov Website

Upon receiving approval from the FDA, this clinical study will be registered on ClinicalTrials.gov. A full report of the pre-specified outcomes, regardless of the results, will be made public through the ClinicalTrials.gov website no later than 12 months after clinical study completion, as required by section 801 of the FDA Amendments Act. If this clinical study is terminated early, the Sponsor will make every effort to hasten the release of the pre-specified outcomes through the ClinicalTrials.gov website.

Appendix A: CIP Revisions

Procedure for CIP Amendments

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.

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

Revision History

AMENDMENT NUMBER	VERSION	DATE	RATIONALE	DETAILS
Not	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

AMENDMENT NUMBER	VERSION	DATE	RATIONALE	DETAILS
[redacted]				

Appendix B: Study Specific Definitions

Acute Closure
Acute closure is defined as the absence of a residual shunt ≥3 mm, and will be assessed based on a echocardiogram obtained immediately after successful deployment of the device up to 7 days post-procedure.

Acute Survival
Acute survival is defined as survival for at least 24 hours following an attempted PIVSD device implant.

Chronic Closure
Chronic closure is defined as the absence of a residual shunt ≥3 mm at 6 months or later.

Chronic Survival
Chronic survival is defined as survival for at least 183 days from the time of first successful implant.

Complaint
A complaint means any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.

Hemodynamically Significant
Hemodynamically significant in relation to VSDs is defined as a VSD(s) that requires closure to establish hemodynamic stability.

Procedure End Time
Procedure end time is defined as the time in which the vascular access site is closed.

Technical Success
Technical success occurs when a subject is successfully implanted with a PIVSD device in the ventricular septal defect. An implant attempt occurs when the delivery system is inserted in the subject's vasculature.

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Appendix D: References

[1, 3, 4] Cinq-Mars A, Voisine P, Dagenais F, Charbonneau E, Jacques F, Kalavrouziotis D, Perron J, Mohammadi S, Dubois M, Le Ven F, Poirier P, O'Connor K, Bernier M, Bergeron S, Sénéchal M, Ris factors of mortality after surgical correction of ventricular defect following myocardial infarction: retrospective analysis and review of literature. *International Journal of Cardiology* 2016; 206: 27-36.

[2] Crenshaw BW, Granger CB, Birnbaum Y, Pieper KS, Morris DC, Kleiman NS, Vahanian A, Califf RM, Topol EJ. Risk factors, angiographic patterns, and outcomes in patients with ventricular septal defect complication acute myocardial infarction. GUSTO-I (Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries) Trial Investigators. *Circulation* 2000; 101:27-32.

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