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SJM-CIP-10035

CardioMEMS™ HF System Post Approval Study

Version Number	C
Date	February 19, 2018
Steering Committee	Lynne Warner-Stevenson, MD (Chair) William Abraham, MD Robert Bourge, MD Maria Rosa Costanzo, MD Akshay Desai, MD James Heywood, MD Lisa Rathman, CRNP Nirav Raval, MD David Shavelle, MD Richard Shlofmitz, MD
Planned Number of Sites and Region(s)	Up to 150 clinical sites in the United States
Clinical Investigation Type	Prospective, multi-center, open-label clinical trial
Abbott Medical Expert	Philip B. Adamson, MD, MSc, FACC Divisional Vice President and Medical Director 6300 Bee Cave Rd, Bldg 2. #100 Austin, TX 78746 USA Tel: +1 512 286 4526 Email: philip.adamson@abbott.com
Sponsor	St. Jude Medical 23 Fourth Avenue Burlington, MA 01803 United States of America
Electronic Data Capture Software	Oracle Clinical
CIP Author of Current Version	Jason Berlin

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LIST OF ABBREVIATIONS

AE	Adverse Event
ADE	Adverse Device Effect
CEC	Clinical Events Committee
CRF	Case Report Form
CRT-D	Cardiac Resynchronization Therapy Defibrillator
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GFR	Glomerular Filtration Rate
HF	Heart Failure
ICH	International Committee on Harmonization
ICD	Implantable Cardioverter Defibrillator
INR	International Normalized Ratio
IRB	Institutional Review Board
IV	Intravenous
KCCQ	Kansas City Cardiomyopathy Questionnaire
LVEF	Left Ventricular Ejection Fraction
MedDRA	Medical Dictionary for Regulatory Activities
MDR	Medical Device Reporting
MEMS	Micro-electromechanical Systems
NYHA	New York Heart Association
OPC	Objective Performance Criterion
PA	Pulmonary Artery
PAS	Post Approval Study
PI	Principal Investigator
PMA	Post-Market Approval
PT	Prothrombin Time
PTT	Partial Thromboplastin Time
RHC	Right Heart Catheterization
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
VAD	Ventricular Assist Device

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PROTOCOL SYNOPSIS

Sponsor:	St. Jude Medical, Burlington, MA
Protocol Title:	CardioMEMS™ HF System Post Approval Study
Document Control Number:	SJM-CIP-10035
Device:	The CardioMEMS HF System consists of a wireless, battery-less pressure sensor implanted into the pulmonary artery and an external electronics that powers and communicates with the sensor and transmits pulmonary artery pressure waveforms and measurements to a secure website for Investigator review and patient management.
Purpose:	The purpose of this Post Approval Study (PAS) is to evaluate the use of the CardioMEMS HF System in patients with Class III Heart Failure (HF) in a commercial setting.
Objective:	The objective of this PAS is to confirm safety and effectiveness in a commercial setting.
Study Population:	Adults with New York Heart Association (NYHA) Class III Heart Failure who have experienced a heart failure hospitalization within the past 12 months. At least 35% of the enrolled patients will be women. The patients will serve as their own historical controls for effectiveness (1 year prior implantation). All subjects who sign the informed consent form and satisfy the inclusion/exclusion criteria. Ejection fraction data must be taken within the last 3 months to enroll in the study.
Study Design:	This is a prospective, multi-center, open-label trial conducted in the United States (US). All subjects who sign the informed consent form and satisfy the inclusion/exclusion criteria will be enrolled into the CardioMEMS HF System PAS and will be scheduled for follow-up visits at 1 month and every 6 months for 2 years. Following sensor implant and hospital discharge, subjects will take PA pressure measurements on a daily basis, or as directed by the investigator. These measurements will be automatically transmitted to the secure Patient database (CardioMEMS HF website).
Timeline:	Study visits will be scheduled at Month 1, Month 6, and every 6 months thereafter for 2 years or until study termination.

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Number of Subjects	Twelve hundred subjects will be enrolled with at least 35% of the enrolled patients being women (420 women out of 1200). Enrollment will be limited to 15% of the total study population at any one site.
Number of Sites:	This is a prospective, multi-center, open-label clinical trial to be conducted at up to 150 sites.
Safety Measures:	Primary safety endpoints will be evaluated at 2 years: 1) freedom from device/system related complications and 2) freedom from pressure sensor failure. Safety will also be assessed throughout the study by the frequency of Adverse Device Effects (ADEs), Serious Adverse Events (SAEs) and Serious Adverse Device Effects (SADEs). A Clinical Events Committee (CEC) will evaluate all SAEs to determine whether or not the SAE is device / system-related complication or pressure sensor failure.
Effectiveness Measures:	The primary effectiveness endpoint is the annualized HF hospitalization rate at 1 year . Supplemental analyses include mortality at 1 year, HF hospitalization or death at 1 year, patient compliance over the trial, training evaluation, Quality of Life evaluations, and subgroup analyses. Information regarding all hospitalizations and deaths will be collected throughout the study and will be adjudicated by the CEC.
PAS Sub-study:	Sub-study within the main PAS cohort with an effectiveness endpoint of comparison of the HF hospitalization rate over 1 year in study to the 1 year HF hospitalization rate in Part 1 of the CHAMPION trial Control Cohort. The safety endpoints will be the same as the main PAS cohort.
Statistical Considerations:	Primary Safety Endpoints The primary safety hypotheses are that the device / system-related complication-free proportion of subjects will be at least 80% at 24 months (OPC used in the CHAMPION trial) and that the pressure sensor failure-free proportion of subjects will be at least 90% at 24 months (OPC used in the CHAMPION trial). Plotting and analysis of safety endpoints will also be displayed using Kaplan-Meier methods. All safety analyses will be performed on the safety population. Primary Effectiveness Endpoint The primary effectiveness evaluation will compare the annualized HF hospitalization rate at 1 year compared to the HF hospitalization rate in the year prior to enrollment.

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	The effectiveness population consists of all subjects who received a sensor implant regardless of study completion status. Supplemental Analyses Mortality at 1 year will be analyzed. Plotting and analysis of mortality will be displayed using Kaplan-Meier methods. The annualized HF hospitalization or death rate at 1 year in study will be compared to the HF hospitalization rate in the year prior to enrollment. Patient compliance over the trial will be examined. The total number of pulmonary artery (PA) pressure readings taken will be reported as a percentage of patient days at home. To assess the effectiveness of the training program, the safety and effectiveness results will be reported for Academic Hospitals and Community Hospitals. Effectiveness analyses will be performed by the following subgroups: Women, Men, Reduced Ejection Fraction (< 40%), Preserved Ejection Fraction (≥ 40%), Ischemic Etiology, Non-ischemic Etiology, With ICD/CRT-D, and Without ICD/CRT-D.
Reporting of Interim and Primary Analyses	In addition to the primary safety and effectiveness analyses, updates from the PAS will be submitted to FDA as a PMA supplement every 6 months for the first two years of the study (annually thereafter) and updated in the device labeling. This information will include the following: study enrollment and follow-up status; demographic information; safety and effectiveness results; mortality; serious adverse events; days alive outside of the hospital for heart failure; patient compliance; sensor performance; and medication changes in response to PA pressure. The primary safety analyses will be reported after all patients complete 24 months post enrollment or discontinue early. The primary effectiveness analyses will be reported after all patients complete 12 months post enrollment or discontinue early.
Version:	C
Date:	19 February 2018

SUB-STUDY PROTOCOL SYNOPSIS

Sub-Study Purpose:	The purpose of this sub-study is to evaluate the use of the CardioMEMS™ HF System in a commercial setting in patients with NYHA Class III heart failure who are optimally managed and are clinically similar to the Control group in the CHAMPION study based on pre-enrollment data.

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Sub-Study Objective:	The objective of this sub-study is to confirm the post-market safety and effectiveness of the CardioMEMS™ HF System to premarket.
Sub-Study Population:	The sub-study patient population will consist of patients selected by an independent committee from the PAS (Main Cohort) who are optimally managed and are clinically similar to the Control group in the CHAMPION study based on pre-enrollment data. The independent committee will identify these patients from the main cohort with NYHA Class III HF who have experienced a HF hospitalization within the past 12 months.
Sub-Study Design:	This is a prospective, multi-center, open-label trial conducted in the United States (US). All subjects who sign the informed consent form, satisfy the inclusion/exclusion criteria, and are selected by the independent committee from the PAS (Main Cohort) will be included in the sub-study. Patients will be scheduled for follow-up visits at 1 month and every 6 months for 2 years. Following sensor implant and hospital discharge, subjects will take PA pressure measurements on a daily basis, or as directed by the investigator. These measurements will be automatically transmitted to the secure Patient database (CardioMEMS HF website).
Timeline:	Study visits will be scheduled at Month 1, Month 6, and every 6 months thereafter for 2 years or until study termination.
Sub-Study Number of Subjects	A minimum of 256 patients will be selected by the independent committee for inclusion in the sub-study. However, the independent committee will identify all patients that are optimally managed and are clinically similar to the Control group in the CHAMPION study (Part 1). Therefore, the eligible patients for this sub-study cohort and the resultant sample size may be greater.
Number of Sites:	This is a prospective, multi-center, open-label clinical trial to be conducted at up to 150 sites.
Sub-Study Safety Measures:	Primary safety endpoints will be evaluated at 2 years: 1) freedom from device/system related complications and 2) freedom from pressure sensor failure. Safety will also be assessed throughout the study by the frequency of Adverse Device Effects (ADEs), Serious Adverse Events (SAEs), and Serious Adverse Device Effects (SADEs). A Clinical Events Committee (CEC) will evaluate all SAEs to determine whether or not the SAE is a device / system-related complication or pressure sensor failure.
Sub-Study	The primary effectiveness objective is to demonstrate that there is

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Effectiveness Measures:	not a worsening in HF hospitalization rate at 1 year in the sub-study compared to the 1 year HF hospitalization rate in the CHAMPION study Control group (Part 1).
Sub-Study Statistical Considerations:	Primary Safety Endpoints The primary safety hypotheses are that the device / system-related complication-free proportion of subjects will be at least 80% at 24 months (OPC used in the CHAMPION trial) and that the pressure sensor failure-free proportion of subjects will be at least 90% at 24 months (OPC used in the CHAMPION trial). Plotting and analysis of safety endpoints will also be displayed using Kaplan-Meier methods. All safety analyses will be performed on the safety population. Primary Effectiveness Endpoint The primary effectiveness evaluation will compare the HF hospitalization rate over 1 year in the sub-study to the 1 year HF hospitalization rate in the Control group (Part 1) of the CHAMPION trial. The effectiveness population consists of all subjects who received a sensor implant regardless of study completion status. Supplemental Analyses To assess the effectiveness of the training program, the safety and effectiveness results will be reported for Academic Hospitals and Community Hospitals. Effectiveness analyses will be performed by the following subgroups: Women, Men, Reduced Ejection Fraction (< 40%), Preserved Ejection Fraction (≥ 40%), Ischemic Etiology, Non-ischemic Etiology, With ICD/CRT-D, and Without ICD/CRT-D.
Reporting of Interim and Primary Analyses	In addition to the primary safety and effectiveness analyses, updates from the PAS will be submitted to FDA as a PMA supplement every 6 months for the first two years of the study (annually thereafter) and updated in the device labeling. This information will include the following: study enrollment and follow-up status; demographic information; safety and effectiveness results; mortality; serious adverse events; days alive outside of the hospital for heart failure; patient compliance; sensor performance; and medication changes in response to PA pressure. The primary safety analyses will be reported after all patients complete 24 months post enrollment or discontinue early. The primary effectiveness analyses will be reported after all patients complete 12 months post enrollment or discontinue early.

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BACKGROUND AND RATIONALE

4.1. Introduction

Heart failure (HF) is a clinical syndrome characterized by frequent hospitalization, poor quality of life, multiple comorbidities, high mortality and a complex therapeutic regimen. Affected individuals have a variety of symptoms such as dyspnea, fatigue, limited exercise tolerance, fluid retention, pulmonary congestion and peripheral edema. Patients suffer impairment in functional capacity and quality of life.

The incidence of HF is on the rise, affecting more than 5 million people in the US alone. Despite current guideline recommended therapies, rates of heart failure hospitalization remain high. Heart failure is the primary diagnosis in >1 million hospitalizations annually. Patients hospitalized for HF are at high risk for all-cause rehospitalization, with a 1-month readmission rate of 25% (Go, et al., 2013).

4.2. CHAMPION Trial Results

The CHAMPION trial demonstrated that management of heart failure using pulmonary artery pressure information obtained with the CardioMEMS HF System, in addition to traditional signs and symptoms, reduced HF hospitalizations.

The CHAMPION trial was conducted at 64 U.S. centers and enrolled 550 patients with NYHA Class III heart failure who had been hospitalized for heart failure in the previous year. All patients were implanted with a sensor and then randomized to Treatment (heart failure management on the basis of pulmonary artery pressure and standard of care) or Control (heart failure management on the basis of standard of care). CHAMPION met its primary endpoint of reduction in the rate of heart failure hospitalizations at 6 months with Treatment patients having 28% fewer heart failure hospitalizations compared to Control patients; benefit was sustained with a 37% reduction in heart failure hospitalizations over the full randomized study duration (Abraham, et al., 2011). All secondary endpoints were met with reduction in pulmonary artery pressures, reduction in proportion of patients hospitalized for heart failure, increase in days alive outside the hospital and improved quality of life.

4.3. Indication for Use

The CardioMEMS HF System is indicated for wirelessly measuring and monitoring pulmonary artery (PA) pressure and heart rate in New York Heart Association (NYHA) Class III heart failure patients who have been hospitalized for heart failure in the previous year. The hemodynamic data are used by physicians for heart failure management and with the goal of reducing heart failure hospitalizations.

4.4. CardioMEMS HF System

The CardioMEMS™ HF System provides PA hemodynamic data used for the monitoring and management of HF patients. The system measures changes in PA pressure which physicians use to initiate or modify heart failure treatment.

The system includes the following components:

- Implantable wireless sensor with delivery catheter
- Patient or hospital electronics system
- Patient database (CardioMEMS HF Website)

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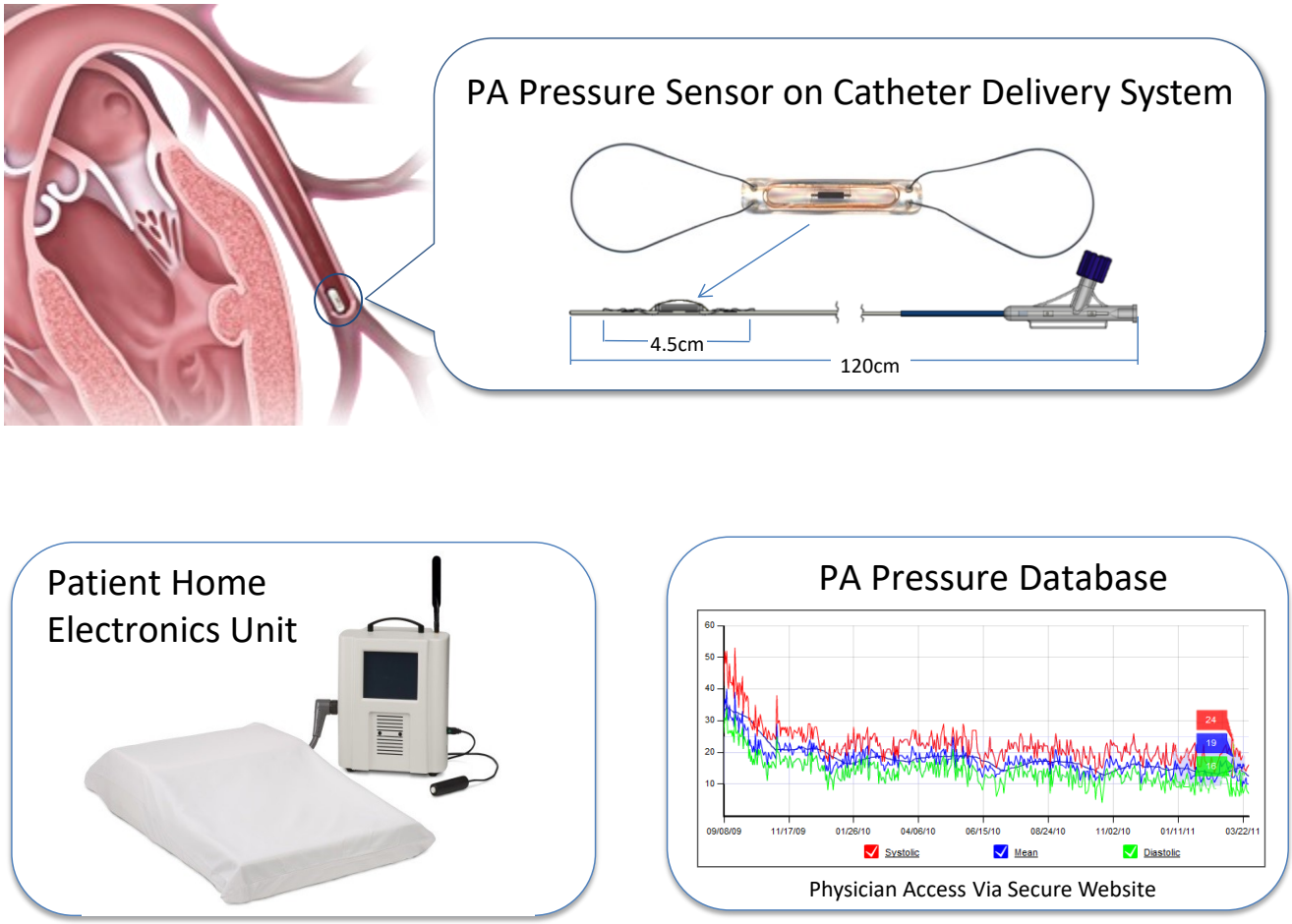
Figure 1. CardioMEMS HF System



The system provides the physician with the patient's PA pressure waveform including systolic, diastolic, and mean pressures as well as heart rate. The Sensor is permanently implanted into the distal PA using transcatheter techniques in the catheterization laboratory; the sensor baseline is set to the mean PA pressure using a pulmonary artery catheter. Daily PA hemodynamic measurements are taken by the patient in a supine position at home. The patient measurement system consists of an antenna and electronics unit that guides the patient through the short reading process. The data can be recorded from the home, hospital, physician's office, or clinic. The hemodynamic data is transmitted to the website which is accessible via a secure website to the patient's physician or nurse.

Implantable Sensor

The sensor measures pulmonary artery pressure using MEMS (micro-electromechanical systems) technology and requires neither batteries nor leads. It is silicon wafer fabricated and measures 15 mm in length, 3.4 mm in width and 2 mm in thickness. The sensor is permanently implanted in a branch of the left or right pulmonary artery via a catheter. The Patient Electronics Unit provides both wireless communication and power to the sensor.

Implantable Sensor Delivery System

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The sensor is tethered to an over-the-wire delivery catheter. A right heart catheterization is performed, and a hand injected selective pulmonary angiogram is performed via the pulmonary artery catheter to define the distal pulmonary artery branch anatomy. An 0.018" guidewire is then advanced through the pulmonary artery catheter into the distal pulmonary artery. The pulmonary artery catheter is removed, and the delivery system is advanced over the guidewire. Once it is optimally positioned, the sensor is separated from the delivery system by releasing the tether wires and delivery system is then removed.

Patient Electronics System

The electronics unit uses an antenna to transmit low power pulses of radiofrequency energy to power and communicate with the sensor. The electronics unit transmits the PA pressure information to the CardioMEMS HF Website.

CardioMEMS HF Website

The CardioMEMS HF Website provides a secure user interface through a website for the clinician to review the PA pressure data from the CardioMEMS HF System.

STUDY OBJECTIVE

The objective of this Post Approval Study is to provide safety and effectiveness data regarding the use of the CardioMEMS HF System in a commercial setting.

STUDY DESIGN

This is a prospective, multi-center, open-label clinical trial to be conducted up to 150 sites in the US.

Subjects who sign the informed consent form and meet the eligibility criteria at the Baseline visit will be eligible for the trial. Subjects will undergo the study-related procedures, including clinical laboratory measurements and body mass index (BMI) calculation. Note that for study related procedures/visits Investigator refers to the Principal Investigator or designee.

Eligible subjects will be scheduled for the Implant procedure (PA sensor implant in conjunction with a RHC procedure).

Subjects must also have an appropriately sized (≥7mm diameter) pulmonary artery branch identified by a selective pulmonary angiogram prior to Sensor implant. Subjects who do not meet this inclusion criteria will be documented as consented not implanted and will be followed for 30 days for safety.

Prior to hospital discharge, subjects will be trained on the home monitoring system and instructed to take pulmonary artery pressure measurements daily or as directed by their physician. Subjects will be supplied with a patient implant identification card, a Patient System Manual, and a Helpline phone number.

After discharge, the subject will take PA pressure measurements at home, as directed by the investigator, utilizing the CardioMEMS HF System. These measurements will be transmitted via modem to a secure data base. Patient compliance will be monitored by the sponsor and reported to the Investigator.

The Investigator or designee will review the PA pressure measurements transmitted from the home monitoring unit. Pressure thresholds are automatically set as described in Appendix D. These threshold notifications are intended to guide the Investigator to review the CardioMEMS HF Website. If the PA pressures are elevated or low, the Investigator or designee should make medication changes according to the guidelines in Appendix D. The Investigator or designee will review the PA pressure measurements on a weekly basis at a minimum and appropriately utilize the information obtained to assist in the clinical management of subjects. Weekly logins to the database will be monitored by the sponsor. Reminders

will be sent to the clinical sites if there are no logins noted during the course of a 7 day window. Clinical and technical support will be available to the Investigator as needed.

Follow-up study visits will be scheduled at Month 1, Month 6, and every 6 months thereafter for 2 years. Follow-up visits will include a physical exam, evaluation of NYHA Class (Appendix C), AE assessment, HF medications review, and assessment of any hospitalizations that may have occurred between visits.

STUDY POPULATION

Study subjects must meet the following inclusion and none of the exclusion criteria to be eligible for the study:

7.1. Inclusion Criteria

1. Written informed consent obtained from subject or legal representative
2. ≥ 18 years of age
3. Diagnosis of NYHA Class III Heart Failure *Note: Subjects who are on continuous inotrope therapy should be considered in Stage D refractory heart failure and are not eligible for enrollment in the study.*
4. At least 1 HF hospitalization within 12 months of Baseline visit
5. Subjects with reduced LVEF heart failure should be receiving a beta blocker for 3 months and an ACE-I or ARB for one month unless in the investigator's opinion, the subject is intolerant to beta blockers, ACE-I or ARB.
6. Subjects with a BMI ≤ 35. Subjects with BMI >35 will require their chest circumference to be measured at the axillary level, if > 65 inches the patient will not be eligible for the study.
7. Subjects with pulmonary artery branch diameter ≥ 7mm - (implant target artery - assessed during the RHC)
8. Subjects willing and able to comply with the follow-up requirements of the study

7.2. Exclusion Criteria

1. Subjects with an active infection
2. Subjects with history of recurrent (> 1) pulmonary embolism or deep vein thrombosis
3. Subjects who, in the Investigator's opinion, are unable to tolerate a right heart catheterization
4. Subjects who have had a major cardiovascular event (e.g., myocardial infarction, open heart surgery, stroke, etc.) within 2 months of Baseline Visit
5. Subjects with Cardiac Resynchronization Device (CRT) implanted < 3 months prior to enrollment
6. Subjects with a Glomerular Filtration Rate (GFR) < 25 ml/min (obtained within 2 weeks of the baseline visit) who are non-responsive to diuretic therapy or who are on chronic renal dialysis
7. Subjects with congenital heart disease or mechanical right heart valve(s)
8. Subjects who have received a Ventricular assist device (VAD) or are likely to undergo heart transplantation or VAD within 6 months of baseline visit.
9. Subjects with known coagulation disorders
10. Subjects with a hypersensitivity or allergy to aspirin, and/or clopidogrel

7.3. Study or Site Termination

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The Sponsor or the Investigator has the right to discontinue the study at any time. As much as possible, this should occur after mutual consultation. The Investigator (or sponsor, where appropriate) is responsible for informing the Institutional Review Board (IRB) of trial closure.

Conditions may arise during the study that could prompt termination of the study or the study sites. Conditions that may prompt such considerations include, but are not limited to, the following:

- The discovery of unexpected serious, or unacceptable risk to the subjects enrolled in the study
- A decision on the part of Sponsor to suspend, discontinue, or shorten the study
- Study conduct at the study site may warrant termination under conditions that include the following:
  - Failure of Investigator(s) to enroll eligible subjects into the study
  - Failure of Investigator(s) to comply with the Food and Drug Administration (FDA) regulations
  - Submission of false information from the research facility to Sponsor, the Clinical Monitor, or a regulatory authority
  - Insufficient adherence to protocol requirements
  - A conflict of interest of the Investigator, his/her institution, or site personnel that would negatively impact the integrity of the clinical trial
  - Institution or IRB under investigation for cause by a federal agency

STUDY PROCEDURES

All subjects will be followed for 2 years. A subject is considered to have successfully completed the study upon completion of the 2 year visit (see Appendix B for the Schedule of Events).

8.1. Screening Visit

During the screening visit, the following procedures/assessments will be performed to determine subject eligibility:

- Informed Consent prior to the conduct of any study-related procedures
- Physical examination including vital signs (temperature, heart rate, respiratory rate, blood pressure), weight, height, BMI calculation (refer to Appendix H)
- Medical and surgical history including ejection fraction data must be taken within the last 3 months to enroll in the study.
- Patient history of heart failure hospitalizations in the 12 months previous to the baseline visit as documented in information provided by the patient's cardiologist, internist, or referring physicians and review of all source documents of any heart failure hospitalization(s) reported in the previous year.
- Demographics

- NYHA Functional Classification
- Calculation of GFR (requires creatinine - refer to Appendix I)
- Assessment of medications
- Kansas City Cardiomyopathy Questionnaire-12 (KCCQ-12) (refer to Appendix E)
- Brief Illness Perception Questionnaire (refer to Appendix F)
- Cardiac Health Security Survey (refer to Appendix G)
- Assessment of enrollment eligibility (inclusion/exclusion criteria)

The study coordinator or designee will administer patient-reported outcome questionnaires. It is important that the subject understands the meaning of all words and instructions in each questionnaire and answers all the questions. The subject will be instructed to ask any questions about the questionnaire if further explanation is needed. The research coordinator or designee will review the questionnaires to verify that all questions have been answered. The measures used will be the Kansas City Cardiomyopathy Questionnaire-12 (KCCQ-12), the Brief Illness Perception Questionnaire, and the Cardiac Health Security Survey. The Patient Reported Outcomes will be obtained at screening and each follow up visit post implant (with the exception of the 1 month follow-up visit) for 2 years. Patients who were enrolled in the study prior to addition of patient reported outcome questionnaires, and therefore did not complete baseline questionnaires, are not required to complete questionnaires at the follow-up visits.

Eligible subjects will be scheduled for the Implant procedure. Subjects on anticoagulation therapy (e.g. warfarin) may be instructed by the Investigator to discontinue use 1-2 days prior to pressure sensor placement. The investigator should consider utilizing enoxaparin (Lovenox) per the site's standard of care as bridge therapy to Sensor placement in subjects who were on anticoagulation therapy.

For subjects at risk for gastro-intestinal bleeding during the period in which dual antiplatelet therapy is given, the investigator should consider a proton pump inhibitor such as omeprazole (Prilosec). Subjects at risk include the elderly, those with a history of gastroduodenal ulcers, gastroesophageal reflux disease, esophagitis, intestinal polyps or cancer. Subjects who smoke or who are using steroids or non-steroidal anti-inflammatory drugs may also be at risk.

8.2. Right Heart Catheterization and Implant Procedure (Baseline Visit)

Before the RHC, the following procedures/assessments will be performed:

- Abbreviated physical examination (i.e., vital sign assessments and significant changes since Screening Visit) and weight
- Confirmation of enrollment eligibility (other than angiographic criteria)
- PT/PTT with International Normalized Ratio (INR) of 1.5 or less for subjects previously on warfarin
- Assessment of heart failure medications
- Record any medical history updates since screening visit.

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The patient will then undergo a standard RHC. A selective, hand injected pulmonary angiogram will be performed via the pulmonary artery catheter to identify a suitable pulmonary artery branch for sensor implantation. Subjects must have an appropriately sized (≥ 7mm diameter) pulmonary artery branch. Subjects who do not meet this inclusion criteria will not receive the PA Sensor implant and will be considered ineligible for the study. These subjects will be documented as consented not implanted and will be followed for 30 days for safety. Patients with a suitable target pulmonary artery branch will undergo:

- Wireless implantable hemodynamic sensor implant
- Pulmonary artery catheter measurements (pulmonary systolic, pulmonary diastolic, pulmonary mean, cardiac output) done 3 times consecutively with sensor measurements for setting of sensor baseline.
- Provide post-procedure vascular access site care per standard procedure
- At the Investigator's discretion, subjects should be discharged once stable with respect to the procedure and their heart failure.
- Please see User's Manual for implant details

Subjects who are currently on anticoagulant therapy (warfarin, or any FDA approved anticoagulant) will restart treatment. The subject's INR should be checked periodically to ensure that it is in the therapeutic range. Those subjects not on chronic warfarin will be placed on anticoagulant/antiplatelet therapy as indicated in the device User's Manual. Refer to the User's Manual for further details.

8.3. Study Follow-Up Visits 1, 2, 3, 4, and 5 (Months 1, 6, 12, 18, and 24)

Implanted subjects will be evaluated at Month 1 (± 7 days) and at Months 6, 12, 18, and 24 (± 30 days) and the following procedures/assessments will be performed:

- Updated medical and surgical history
- Assessment of AEs that occurred since the last visit
- Abbreviated physical examination (significant changes since previous visit) including vital signs (heart rate, respiratory rate, blood pressure), and weight
- Assessment of NYHA functional class
- Kansas City Cardiomyopathy Questionnaire (KCCQ-12)
- Brief Illness Perception Questionnaire
- Cardiac Health Security Survey
- Heart failure medication review
- PA pressure measurements may be obtained at the Investigator's discretion

Subjects will be reminded to obtain pulmonary artery pressure measurements utilizing the CardioMEMS HF System as directed. Subjects will be reminded of the current ACC/AHA guidelines regarding sodium and fluid restrictions.

The study coordinator or designee will administer patient-reported outcome questionnaires. It is important that the subject understands the meaning of all words and instructions in each questionnaire and answers all the questions. The subject will be instructed to ask any questions about the questionnaire if further explanation is needed. The research coordinator or designee will review the questionnaires to verify that all questions have been answered. The Patient Reported Outcomes will be obtained at 6, 12, 18 and 24 months. Patients who were enrolled in the study prior to addition of patient reported outcome questionnaires, and therefore did not complete baseline questionnaires, are not required to complete questionnaires at the follow-up visits.

8.4. Subject Home PA Pressure Readings

Prior to hospital discharge, subjects will be instructed on how to take their own pulmonary artery pressure measurements, utilizing the CardioMEMS HF System. Subjects will provide returned demonstration on: setting up the unit, connecting the system to a phone line, proper positioning for obtaining the optimum sensor signal, taking and transmitting the daily pressure measurements. The unit will transmit the data to a database using the system's modem.

The home measurements will be taken while the subject is lying down (supine) in bed positioned on a padded, flat antenna. It is recommended that subjects obtain home measurements in a supine position however, if the subject is unable to lie flat, measurements can be obtained in a sitting or reclined position. It is important the anatomical position is consistent for every measurement.

The home electronics system is small enough for placement on a bedside table. The unit will provide audio and visual prompts for the subject to guide them through signal acquisition. Once the subject is positioned and a signal is acquired, the subject will be notified of the successful reading and the data is automatically transmitted to a remote database. St. Jude Medical will provide instructions for use and a help line will be available. Please refer to subject's Patient System Guide for more detailed information.

8.5. PA Pressure Readings in the Hospital

If a subject is hospitalized, seen in the emergency room (ER) or has a clinic visit, the CardioMEMS HF System may be used to obtain pulmonary artery pressure measurements at the investigators discretion. Following sensor implant, subsequent RHC procedures or pulmonary artery catheter insertions must be performed under fluoroscopic guidance.

Resetting of the sensor baseline will be performed as deemed necessary by Sponsor. Baseline resetting may require an echocardiogram or a RHC procedure.

Following the sensor implant, should a RHC procedure or PA catheter evaluation be clinically warranted, comparative pulmonary artery pressures utilizing the CardioMEMS HF System should also be obtained utilizing the hospital electronics unit.

8.6. Criteria for Withdrawal

Subjects may be withdrawn from the study for any of the following reasons:

1. Subject withdraws his/her consent
2. Investigator determines that other treatment is warranted to protect the health and safety of the subject

3. Investigator determines that the subject is noncompliant with study related procedures
4. Subject is lost to follow-up: site must document attempts made to contact the subject for an early discontinuation visit (e.g., 2 – 3 phone calls, followed by 1 certified letter, documentation of repetitive missed study visits, etc.)

The Investigator will notify the Sponsor and document on the appropriate case report form (CRF) the reason/circumstances for early discontinuation. All subjects who withdraw from the study should have the following study exit procedures performed if possible:

- Updated medical and surgical history
- Assessment of AEs that occurred since the last visit
- Abbreviated physical examination (only significant changes since Enrollment) including vital signs (temperature, heart rate, respiratory rate, blood pressure), and weight
- Assessment of NYHA functional class
- Kansas City Cardiomyopathy Questionnaire(KCCQ-12)
- Brief Illness Perception Questionnaire
- Cardiac Health Security Survey
- Heart failure Medication Review
- PA pressures may be obtained at the Investigator's discretion

All reasonable efforts should be made to retain subjects in the clinical trial until its completion. If a patient moves from the geographic area of their investigator, St. Jude Medical will attempt to place the patient with another investigator.

8.7. Deviations from CIP

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

In some cases, failure to comply with the CIP may be considered failure to protect the rights, safety and well-being of subjects; such non-compliance exposes subjects to unreasonable risks. Examples: failure to adhere to the inclusion/exclusion criteria, failure to report SAEs within given timeframe as per CIP, etc. Investigators should seek to minimize such risks by adhering to 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 site will submit the CRF to the Sponsor.

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

SAFETY ANALYSES

9.1. Primary Safety Endpoints

Primary safety endpoints will be evaluated at 2 years:

1) Freedom from device/system related complications

2) Freedom from pressure sensor failure

9.1.1. Device / System-related Complication Criteria

A device / system-related complication is an adverse event that is, or is possibly, related to the system (wireless pressure sensor or external electronics) and has at least one of the following characteristics:

- is treated with invasive means (other than intramuscular medication or a right heart catheterization which is used for diagnostic purposes)
- results in the death of the subject
- results in the explant of the device

9.1.2. Sensor Failure Criteria

A Sensor failure occurs when no readings can be obtained from it after troubleshooting the system to rule out any problems with the external electronics.

EFFECTIVENESS ANALYSES

10.1. Primary Effectiveness Endpoint

- The primary effectiveness endpoint will compare the annualized HF hospitalization rate at 1 year in the study to the HF hospitalization rate in the year prior to enrollment.

10.2. Supplemental Analyses

10.2.1. Mortality

The mortality rate at 1 year in study will be analyzed.

10.2.2. HF Hospitalization or Death

The annualized HF hospitalization or death rate at 1 year in the study will be compared to the HF hospitalization rate in the year prior to enrollment.

10.2.3. Patient Compliance

Patient device usage over the course of the trial will be examined.

10.2.4. Training Evaluation

The effectiveness of the training program will be examined by community and academic hospitals.

10.2.5. Subgroup Analyses

The effectiveness analyses will be evaluated in each of the following subgroups: Women, Men, Reduced Ejection Fraction (< 40%), Preserved Ejection Fraction (≥ 40%), Ischemic Etiology, Non-ischemic Etiology, With ICD/CRT-D, and Without ICD/CRT-D.

10.2.6. Quality of Life Evaluations

Patient reported outcomes will be evaluated using Quality of Life Questionnaires. The measures used will be the **Kansas City Cardiomyopathy Questionnaire-12 (KCCQ-12)**, the **Brief Illness Perception Questionnaire**, and the **Cardiac Health Security Survey**.

ADVERSE EVENTS

Clinical Investigation Plan

11.1. Adverse Event (AE)

An AE is any untoward medical occurrence (e.g., noxious or pathological changes) in a subject compared with pre-existing conditions that may occur during any part of the clinical study. An AE is defined as being independent of assumption of any causality (e.g., primary or concomitant disease or study design). AEs should be evaluated by the Investigator and maintained in the research records at the site. AEs should be reported to the Sponsor on a CRF.

11.2. Serious Adverse Event (SAE)

For this study, an SAE is defined as any untoward medical occurrence that:

- results in death
- is immediately life-threatening – an event in which the subject was at risk of death at the time of the event
- requires admission and hospitalization (> 24 hours) or prolongation of existing hospitalization
- results in disability/incapacity
- results in a congenital anomaly/birth defect
- requires intervention to prevent one of the above

SAEs, as determined by the Investigator, must be reported to the Sponsor.

The cause of death of any subject after enrollment must be documented on the AE CRF and reported as an SAE. The information should include the date expired, cause of death, and what attempts were made to treat the condition.

If it is not certain that an event meets the above definition, contact the Project Manager.

11.3. Device-Relatedness

An AE or SAE that is definitely or possibly related to the device or the insertion procedure should be considered device-related. A serious adverse device effect (SADE) is an event that meets any of the above SAE criteria and is considered related to the device or the insertion procedure by the Investigator. All other events considered related to the device or insertion procedure are non-serious adverse device effects (ADEs).

If it is not certain that an event meets the above definitions, contact the Project Manager.

11.4. Procedures for Reporting Adverse Events (AEs)

It is the responsibility of the Investigator or Sub-Investigator(s) to perform periodic assessments of all AEs as well as identifying SAEs. Safety surveillance and reporting starts as soon as the patient is enrolled in the clinical investigation. 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 investigation or the subject withdraws from the clinical investigation.

AEs, ADEs, SAEs and SADEs that occur during the study should be treated by established standards of care that will protect the life and safety of the subjects.

Any AEs/ADEs are to be reported as soon as possible after knowledge of the event. SAEs/SADEs 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

3 calendar days. If an SAE/SADE is not reported within the required time, it will be considered a protocol deviation. The date the site staff became aware of an event meeting the criteria of an SAE must be recorded in the source documentation.

The Sponsor will ensure that all applicable events and device deficiencies are reported to the relevant authorities as per regulations. The sites should notify the Sponsor of reportable AEs by creating and saving the applicable CRF within the electronic data capture (EDC) system. The description of the AE, date of the AE, treatment and resolution of the AE will be reported, as applicable per regulations, to the relevant authorities. Additional information may be requested, when required, by the Sponsor in order to support the reporting or adjudication of AEs. The Investigator must notify the IRB, if appropriate, in accordance with national and local laws and regulations, of the AEs reported to the Sponsor. Additional information with regard to an adverse event should be updated within the appropriate CRF.

11.5. Criteria and Guidelines for Non-reportable Events

The following events are not reportable to the Sponsor:

- Symptoms of previously reported events and/or scheduled procedures, such as:
  - Cataract surgery
  - Colonoscopy
  - Flaring of gout (when gout is already reported/pre-existing condition)
  - Symptoms of HF (when primary HF is already reported)

11.6. Anticipated Adverse Events

11.6.1. Anticipated AEs

Events associated with the CardioMEMS™ PA Sensor or the implant procedure (in conjunction with RHC) or post-implantation complications are considered anticipated and include the following:

- Infection
  - Upper respiratory infection
  - Bronchitis
  - Pneumonia
  - Acute Bronchitis
  - Groin abscess
  - Methicillin-resistant staphylococcal aureus infection
  - Pulmonary Infiltration
  - Sepsis
- Arrhythmias
  - Ventricular tachycardia
  - Atrial fibrillation
  - Ventricular arrhythmia
  - Ventricular fibrillation
  - Atrial fibrillation with rapid ventricular response
  - Atrial flutter
  - Cardiac dysrhythmias
  - Tachycardia
  - Wide complex tachycardia
- Bleeding
  - Epistaxis

  - Hemoptysis
  - GI bleed
  - Bleeding
  - Blood in stool
  - Catheter site bleeding
  - Catheter site ecchymosis
  - Hematuria
  - Nose bleeds
- Hematoma
  - Hematoma
  - Catheter site hematoma
  - Vessel puncture site hematoma
- Thrombus
  - Arterial thrombosis (limbs)
  - Blood clot
- Myocardial infarction
- Transient ischemic attack
- Stroke
- Death
- Sensor embolization
- Pulmonary artery perforation

11.6.2. Anticipated ADEs/SADEs

The following is a list of possible anticipated ADEs/SADEs:

- Hemoptysis
- Sensor not deploying
- Transient ischemic attack
- Atypical chest pain
- Sepsis leading to death
- Atrial arrhythmia leading to death
- Arterial embolism (upper extremity)
- PA (in-situ) thrombus
- Catheter site bleeding
- Catheter site ecchymosis
- Catheter site hematoma
- Vessel puncture site pain
- Cardiac monitoring abnormal
- Heart rate irregular
- Serum creatinine increased
- Dyspnea
- Congestive HF
- Ventricular tachycardia
- Dizziness
- Vessel perforation
- Sensor failure/malfunction
- Sensor migration

- System not transmitting

Refer to the CardioMEMS™ PA Sensor and Delivery Catheter, Model CM2000 User Manual for more information. If it is not certain that an event meets the above definitions, contact the Project Manager.

For unexpected failure modes or unexpected adverse events, the site should follow their standard reporting practices for medical device reporting (MDR). As defined in 21 CFR 803, a MDR reportable event (or reportable event) means: An event that device user facilities become aware of that reasonably suggests that a device has or may have caused or contributed to a death or serious injury. A device user facility must report to sponsor and the FDA (no later than 10 days after awareness date) deaths and serious injuries that a device has or may have caused or contributed to, establish and maintain adverse event files, and submit summary annual reports to FDA.

STATISTICAL ANALYSIS

The data will be summarized using univariate statistics (e.g., N, mean, standard deviation, median, minimum and maximum) or frequency (e.g., N, %) as appropriate.

The primary time point for safety analyses is 24 months post enrollment. Enrollment is defined as having a successful Sensor implant. The primary time point for effectiveness analyses is 12 months post enrollment.

Unless otherwise specified, all statistical tests will be 2-sided with a significance level of 0.05.

12.1. Populations for Analysis

Safety Population: The Safety Population consists of all subjects who received a Sensor implant or underwent the implant procedure but were never implanted, regardless of study completion status. All safety analyses will be performed on the Safety population.

Subjects who are found not to have an appropriately sized pulmonary artery branch and did not receive the Sensor implant will be considered ineligible for the study. However, these subjects will be followed for 30 days for safety and all safety related data for these subjects will be provided.

Effectiveness Population: The effectiveness population consists of all subjects who received a Sensor implant regardless of study completion status. All effectiveness analyses will be performed on the effectiveness population.

12.2. Sample Size Considerations

Effectiveness Sample Size Determination

For the primary effectiveness endpoint of HF hospitalization rate during 1 year, 300 patients will provide greater than 90% power to meet the efficacy goal (upper confidence limit less than the HF hospitalization rate in the year prior to enrollment), using a one-sample, two-sided Poisson confidence interval with alpha of 0.05.

Safety Sample Size Determinations

For the two-year primary safety endpoint of freedom from device-related complications, using an exact two-sided test for one-sample binomial proportions with alpha of 0.05, a sample size of 619 subjects will provide greater than 90% power to detect a difference as small as 5% from the null proportion rate of 0.80 (i.e., objective performance criterion of 80%). For sensor failures at 2 years, a sample size of 663 subjects provides greater than 90% power to detect a difference as small as 3.5% from the null proportion rate of 0.90 (i.e., objective performance criterion of 90%).

Thus, the sample size for this study is driven by the safety endpoints. The 2 year attrition rate in CHAMPION was 49.1% (228/550). To ensure sufficient patients are enrolled to adequately evaluate safety and efficacy, 1200 subjects will be enrolled.

Note that at least 35% of the 1200 enrolled patients (420) must be women resulting in approximately 206 women completing the trial (assuming a 49% attrition rate). This sample size will provide greater than 90% power to meet the goal for effectiveness. Regarding freedom from device-related complications and freedom from sensor failures, 206 women will provide greater than 90% power to detect a difference as small as 0.06 from the null proportion rate of 0.90.

12.3. Missing Data

Missing data will be tracked in the Electronic Data Capture system; queries will be generated and provided to the site. In addition, a St. Jude Medical representative, or designee will routinely perform monitoring visits at each site. During the monitoring visits, missing data queries will be addressed until resolution. Missing data that are not resolved will not be imputed unless specified in the sections below.

12.4. Subject Accountability and Baseline Information

Descriptive summaries will be generated to describe the disposition of all enrolled subjects.

12.5. Demographic and Baseline Information

Descriptive summaries will be generated for all relevant baseline variables. These variables include, but are not limited to, demographic data and conditions at the time of enrollment.

12.6. Safety Analyses

The safety analyses will be performed using the Safety Population. The data will be summarized using univariate statistics (e.g., N, mean, standard deviation, median, minimum and maximum) or frequency (e.g., N, %) as appropriate.

12.6.1. Primary Safety Endpoints

The primary safety analyses will be based on the following objective performance criteria: a) the lower limit of the two-sided 95% confidence interval on the freedom from device / system-related complication rate at 24 months is greater than 80% and b) the lower limit of the two-sided 95% confidence interval on the freedom from pressure sensor failure rate at 24 months is greater than 90%. These primary safety endpoints will be tested hierarchically in order to control for multiplicity. First, the freedom from device / system-related complication rate will be tested. If the result is statistically significant (i.e., $p<0.050$), then the freedom from pressure sensor failure rate will also be tested for significance (i.e., $p<0.050$). The study will be judged to have provided positive safety results if both tests of the primary safety analysis endpoints are statistically significant (i.e., $p<0.050$).

Mathematically stated, the primary safety hypotheses are:

a) H_0: $P_{\text{(Freedom from device / system-related complications at 24 months)}} \leq 80\%$

   H_a: $P_{\text{(Freedom from device / system-related complications at 24 months)}} > 80\%$

b) H_0: $P_{\text{(Freedom from pressure sensor failure at 24 months)}} \leq 90\%$

   H_a: $P_{\text{(Freedom from pressure sensor failure at 24 months)}} > 90\%$

Plotting and analysis of safety endpoints will also be displayed using Kaplan-Meier methods.

Safety will also be assessed throughout the study by the frequency of Adverse Events (AEs), Adverse Device Effects (ADEs), Serious AEs (SAEs), and Serious Adverse Device Effects (SADEs), and device / system-related complications by relationship to the device via Medical Dictionary for Regulatory Activities (MedDRA) system organ classification. Physical examination, and subject survival data through 24 months will be tabulated across study period assessments.

12.7. Effectiveness Analyses

Effectiveness analyses will be conducted in the effectiveness population. The data will be summarized using univariate statistics (e.g., N, mean, standard deviation, median, minimum and maximum) or frequency (e.g., N, %) as appropriate.

12.7.1. Primary Effectiveness Endpoint

The primary time point for analyses is 12 months post-enrollment. The primary effectiveness endpoint will compare the annualized HF hospitalization rate parameter, γ, at 1 year versus the HF hospitalization rate in the year prior to enrollment using a two-sample, two-sided Poisson confidence interval. If the two-sided, upper 95% confidence interval for the PAS rate parameter is less than that in the year prior to enrollment, then the primary effectiveness endpoint will be met.

Mathematically stated, the primary effectiveness hypothesis is:

H_0: $\gamma_{\text{(12 month HF Hospitalization Rate)}} \geq \gamma_{\text{(HF hospitalization rate in year prior to enrollment)}}$

H_a: $\gamma_{\text{(12 month HF Hospitalization Rate)}} < \gamma_{\text{(HF hospitalization rate in year prior to enrollment)}}$

where $\gamma_{\text{(12 month HF Hospitalization Rate)}}$ = the HF hospitalization rate parameter at 1 year in the PAS and $\gamma_{\text{(HF hospitalization rate in year prior to enrollment)}}$ = the HF hospitalization rate in the year prior to enrollment.

12.7.2. Supplemental Analyses

Mortality

The mortality rate over 1 year in study will be reported. Plotting and analysis of survival data will be displayed using Kaplan-Meier methods.

HF Hospitalization or Death

The annualized HF hospitalization or death rate parameter, λ, at 1 year will be compared to the HF hospitalization rate in the year prior to enrollment using a two-sample, two-sided Poisson confidence interval. If the two-sided, upper 95% confidence interval for the PAS rate parameter is less than that in the year prior to enrollment, then the hypothesis will be met.

Mathematically stated, the hypothesis is:

H_0: $\lambda_{\text{(12 month HF Hospitalization or Death Rate)}} \geq \lambda_{\text{(HF hospitalization rate in year prior to enrollment)}}$

H_a: $\lambda_{\text{(12 month HF Hospitalization or Death Rate)}} < \lambda_{\text{(HF hospitalization rate in year prior to enrollment)}}$

where $\lambda_{\text{(12 month HF Hospitalization or Death Rate)}}$ = the HF hospitalization or death rate parameter at 1 year in the PAS and $\lambda_{\text{(HF hospitalization rate in year prior to enrollment)}}$ = the HF hospitalization rate in the year prior to enrollment.

Patient Compliance

Patient device usage over the course of the trial will be examined. The total number of PA pressure readings taken will be reported as a percentage of patient days at home.

Clinical Investigation Plan

Training Evaluation

To assess the effectiveness of the training program, the safety and effectiveness results will be reported for:

1) Academic Hospitals
2) Community Hospitals

Subgroup Analyses

The effectiveness analyses will be evaluated in each of the following subgroups:

1) Women
2) Men
3) Reduced Ejection Fraction (< 40%)
4) Preserved Ejection Fraction (≥ 40%)
5) Ischemic Etiology
6) Non-ischemic Etiology
7) With ICD/CRT-D
8) Without ICD/CRT-D

Quality of Life Evaluations

Patient improvement in Quality of Life will be reported. The difference between the Quality of Life scores at 6 months, 12 months, 18 months, and 24 months will be compared to the baseline values using general linear mixed models. Quality of Life will be measured using the Kansas City Cardiomyopathy Questionnaire-12 (KCCQ-12), the Brief Illness Perception Questionnaire, and the Cardiac Health Security Survey.

PAS SUB-STUDY

This section describes the design, hypotheses, populations, endpoints and analysis of the PAS sub-study. All other sections of the protocol pertain to the main PAS cohort unless specifically stated otherwise.

13.1. Sub-study Design

This is a prospective/retrospective multicenter single arm sub-study within the main PAS cohort.

13.2. Sub-study Hypotheses

The safety hypotheses are:

a) H_0: $P_{\text{(Freedom from device / system-related complications at 24 months)}} \leq 80\%$

   H_a: $P_{\text{(Freedom from device / system-related complications at 24 months)}} > 80\%$

b) H_0: $P_{\text{(Freedom from pressure sensor failure at 24 months)}} \leq 90\%$

   H_a: $P_{\text{(Freedom from pressure sensor failure at 24 months)}} > 90\%$

The effectiveness hypothesis is:

H0: $\Upsilon_{\text{(12 month heart failure [HF] Hospitalization Rate)}} \geq \Upsilon_{\text{(12 month HF Hospitalization Rate in CHAMPION trial Control group)}} + \Delta$

Ha: $Y_{(12\ month\ HF\ Hospitalization\ Rate)} < Y_{(12\ month\ HF\ Hospitalization\ Rate\ in\ CHAMPION\ trial\ Control\ group)} + \Delta$

where Y (12 month HF Hospitalization Rate) = the HF hospitalization rate parameter at 1 year in the PAS, Y (12 month HF hospitalization rate in CHAMPION trial Control group) = the HF hospitalization rate in Part 1 of the premarket Control group, and Δ = non-inferiority (NI) margin of 0.10. The CHAMPION study Part 1 Control group had a HF hospitalization rate of 0.75 with a lower 95% confidence limit of 0.64. Therefore, a NI margin of 0.10 was chosen to account for the typical variability in HF hospitalization rates occurring between clinical trials. If the null hypothesis is rejected, it can be concluded that there was not a worsening in HF hospitalization rate in the PAS compared to the CHAMPION study Control group (i.e. non-inferiority is established).

13.3. Sub-study Population (device and control group)

These patients must be selected by an independent committee to be clinically similar to the CHAMPION study Control cohort and will be selected from the PAS Main Cohort.

The independent committee will identify optimally medicated adults from the main cohort with New York Heart Association (NYHA) Class III Heart Failure (HF) who have experienced a HF hospitalization within the past 12 months. This will be based on pre-enrollment information, and not on any information regarding what happened to the patient post-enrollment.

Efforts should be taken to have a fair representation of women (actual number not set as there may be unknown biases regarding optimal medication for women and men).

The Control patients from Part 1 of the CHAMPION study will set the performance goal.

13.4. Sub-study Sample Size

The Control group HF hospitalization rate for Part 1 of the CHAMPION study at 1 year was 0.75.

Using an exact one-sample, 2-sided Poisson 95% confidence interval with alpha of 0.05, 114 patients will provide 85% power to show a difference between the estimated Treatment rate of 0.52 and the Control rate of 0.75. Likewise, 130 patients are required to achieve 90% power to show a difference between the estimated Treatment rate of 0.52 and the Control rate of 0.75.

The 2 year attrition rate in CHAMPION was 49.1%, therefore 256 patients (130/(100%-49.1%) = 256) is the minimum sample size for this analysis. However, the Independent Committee will identify all patients that are optimally managed and are clinically similar to the Control group in CHAMPION. Therefore, the eligible patients for this sub-cohort and the resultant sample size may be greater.

13.5. Sub-study Endpoints

13.5.1. Sub-study Safety Endpoints

Safety endpoints will be evaluated at 2 years:

1) Freedom from device/system related complications compared to OPC of 0.80

2) Freedom from pressure sensor failure compared to OPC of 0.90

13.5.2. Device / System-related Complication Criteria

A device / system-related complication is an adverse event that is, or is possibly, related to the system (wireless pressure sensor or external electronics) and has at least one of the following characteristics:

- is treated with invasive means (other than intramuscular medication or a right heart catheterization

which is used for diagnostic purposes)

- results in the death of the subject
- results in the explant of the device

13.5.3. Sensor Failure Criteria

A Sensor failure occurs when no readings can be obtained from it after troubleshooting the system to rule out any problems with the external electronics.

13.5.4. Sub-study Effectiveness Endpoint

Heart failure (HF) hospitalization rate over 1 year in the PAS study compared to the 1 year HF hospitalization rate in Part 1 of the CHAMPION study Control cohort.

13.5.5. Sub-study Supplemental Analyses

Training Evaluation

To assess the effectiveness of the training program, the safety and effectiveness results will be reported for:

1) Academic Hospitals
2) Community Hospitals

Subgroup Analyses

The effectiveness analyses will be evaluated in each of the following subgroups:

1) Women
2) Men
3) Reduced Ejection Fraction (< 40%)
4) Preserved Ejection Fraction (≥ 40%)
5) Ischemic Etiology
6) Non-ischemic Etiology
7) With ICD/CRT-D
8) Without ICD/CRT-D

13.6. Sub-study Enrollment Plan

These patients must be selected by an Independent Committee to be clinically similar to the CHAMPION study Control cohort and will be selected from the main cohort of the PAS.

13.7. Sub-study Length of Follow-up

The follow-up length for the PAS will be 24 months.

13.8. Sub-study Frequency of Follow-up Assessments

Follow-up assessments will be made at Month 1, Month 6, and every 6 months thereafter for 2 years. Follow-up visits will include a physical exam, evaluation of NYHA Class, AE assessment, heart failure medications review, and assessment of any hospitalizations that may have occurred between visits.

13.9. Sub-study Statistical Plan

13.9.1. Analysis of Sub-study Safety Endpoints

The safety analyses will be based on the following objective performance criteria:

a) the lower limit of the two-sided 95% confidence interval on the freedom from device / system-related complication rate at 24 months is at least 80%, and

b) the lower limit of the two-sided 95% confidence interval on the freedom from pressure sensor failure rate at 24 months is at least 90%.

These safety endpoints will be tested hierarchically in order to control for multiplicity. First, the freedom from device / system-related complication rate will be tested. If the result is statistically significant (i.e., $p<0.05$), then the freedom from pressure sensor failure rate will also be tested for significance (i.e., $p<0.05$). The study will be judged to have provided positive safety results if both tests of the safety analysis endpoints are statistically significant (i.e., $p<0.05$).

13.9.2. Analysis of Sub-study Effectiveness Endpoints

The effectiveness evaluation will compare the annualized HF hospitalization rate at 1 year to the 1 year HF hospitalization rate in Part 1 of the CHAMPION trial Control patients. The estimate of the rate will be tested with a NI margin of 0.10 and presented with 95% Poisson confidence intervals.

13.9.3. Schematic Diagram of the Sub-study and Main PAS Study

See Appendix M for a schematic diagram of the Main PAS Study and the PAS Sub-study.

REPORTING OF INTERIM AND PRIMARY ANALYSES

In addition to the primary safety and effectiveness analyses, updates from the PAS will be submitted to FDA as a PMA supplement every 6 months for the first two years of the study (annually thereafter) and updated in the device labeling. This information will include the following: study enrollment and follow-up status; demographic information; safety and effectiveness results; mortality; serious adverse events; days alive outside of the hospital for heart failure; patient compliance; sensor performance; and medication changes in response to PA pressure. Please refer to Appendix L: Reporting of Interim Analyses.

The primary safety analyses will be reported after all patients complete 24 months post enrollment or discontinue early. The primary effectiveness analyses will reported after all patients complete 12 months post enrollment or discontinue early.

CLINICAL EVENTS COMMITTEE

An independent clinical events committee (CEC) will be formed to review clinical data. The committee will be comprised of physicians, who will not participate in the enrollment or treatment of subjects in this trial. All endpoints or suspected endpoints will be reviewed by this committee according to the CEC Committee charter. Any event listed in the CEC Committee charter reported in an SAE report or the CRF will trigger the accumulation of a portfolio of pertinent documents from the hospital admission. These documents will be collected and copies distributed to members of the CEC Committee. The

interpretation of the event as classified and adjudicated by the clinical events committee will be used in the final effectiveness and safety analyses.

The composition and function of the CEC Committee is described in Appendix K.

DATA COLLECTION, STUDY MONITORING, AND DATA DISCLOSURE

16.1. Data Collection and Reporting

Electronic CRFs (eCRFs) will be utilized. Site staff will enter the information required by the protocol onto eCRFs using a validated St. Jude Medical system that conforms to FDA requirements for electronic data capture. All data fields will be completed where appropriate. However, if data are not available (i.e., missed visit, etc.), the site will receive instruction regarding electronic documentation. As data are entered, automated cross-check programs will search for any data discrepancies in the eCRFs. Appropriate error messages will be generated, allowing for the modification or verification of the entered data. Queries will generally be sent to the study site using an electronic data query system that includes an automated audit trail of the corrections.

Monitoring personnel of St. Jude Medical, or its designee, will review the eCRFs for completeness and accuracy and will instruct site personnel to make any corrections or additions. The Investigator, or designee, will certify that the data are complete and accurate by applying an electronic signature to the eCRF. Any subsequent alterations, corrections, or additions will be reviewed and electronically signed by the Investigator prior to database lock.

16.2. Site Qualification

For sites that did not participate in the CHAMPION protocol, a site visit will be performed by St. Jude Medical or designee prior to the start of the study to review the protocol in detail, to ensure the availability of appropriate trial personnel, adequate resources and to assess their ability to properly conduct the study according to ICH-GCP guidelines and local requirements.

16.3. Training

Detailed training to cover aspects of the hemodynamic management of heart failure (HF), identification of prospective patients, HF sensor implant procedures, the use of the heart failure electronic units and the use of the CardioMEMS HF website to view the patient's hemodynamic parameters will occur for all sites prior to enrollment of patients.

The CardioMEMS HF System training program is comprised of specific modules designed to provide essential didactic and field training. Each module consists of training materials, reference information, checklists, and training documentation forms. Training materials used will include equipment demonstrations, PowerPoint presentations, manuals, posters, brochures, and videos.

The training may be carried out in any sequence. Specific requirements for certification are defined within each module. The five training modules are:

Module 1: Hemodynamic Management of Heart Failure

Module 2*:* CardioMEMS™ HF Sensor Implant Procedure

Module 3: CardioMEMS™ HF Electronic Systems

Module 4: CardioMEMS™ HF Website

Module 5: Patient Training

Didactic and hands-on training on an anatomic model will be provided before the first Sensor implant. St. Jude Medical representative will be present during the first 3 Sensor implant procedures at each site.

Clinical Investigation Plan

After successful completion of implant training, the Investigator will receive documentation of training. Following the required training, a St. Jude Medical representative will be available to support the site staff with additional training needs as necessary.

A Sensor implant identification card will be provided to the patient following the implant procedure. This card will include the date of the Sensor implant and the location of the Sensor. Prior to discharge, the patient will be trained on taking their pulmonary artery pressures at home utilizing the CardioMEMS HF System. Subjects will be instructed to take PA sensor pressure measurements daily or as instructed by their physician. Subjects will be reminded of the current ACC/AHA guidelines regarding sodium and fluid restrictions. Patients will be instructed to contact a St. Jude Medical technical support representative if they are having any problems using the CardioMEMS HF System.

The Investigator and/or designee will be trained on use of the CardioMEMS HF Patient Database for the first 3 patients. Investigators will demonstrate knowledge of hemodynamic management of heart failure and will be provided documentation of training. Investigators or designee may contact a St. Jude Medical representative if they have any questions regarding the CardioMEMS HF System.

16.4. Study Monitoring

St. Jude Medical or designee will monitor the study to meet the sponsor's monitoring Standard Operating Procedures (SOPs), ICH-GCP guidelines, and applicable regulatory requirements and to ensure that study initiation, conduct, and closure are adequate.

Clinical Monitors will periodically audit CRFs/eCRFs and corresponding source medical records for each subject. The monitoring visits provide the Sponsor with the opportunity to evaluate the progress of the study, to verify the accuracy and completeness of CRFs/eCRFs, to resolve any inconsistencies in the study records, and to assure that all protocol requirements, applicable regulatory or country-specific regulations, other requirements, and Investigator's obligations are being fulfilled.

The Investigator and his/her staff will be expected to cooperate with St. Jude Medical personnel or agents of St. Jude Medical and to be available during the monitoring visits to answer questions sufficiently and to provide any missing information.

The Investigator(s)/institution(s) will permit direct access to source data/documents for trial-related monitoring, audits, IRB and regulatory inspection(s).

16.5. Source Data Verification

Source data verification ensures accuracy and credibility of the data obtained. During monitoring visits reported data are reviewed with regard to being accurate, complete, and verifiable from source documents (e.g., subject files, physician notes, discharge summaries, operative records, etc.).

16.6. Definition of Source Data

Source data includes all information in source documents (original records, certified copies of original records, and original data recorded on customized worksheets) and includes all original recordings or certified copies of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial.

16.7. Data Disclosure and Subject Confidentiality

Subject medical information obtained as a result of this study is considered confidential and disclosure to third parties other than those noted below is prohibited. All reports and communications relating to subjects in this study will identify each subject only by their initials and number. Medical information resulting from a subject's participation in this study may be given to the subject's personal physician or to

the appropriate medical personnel responsible for the subject's welfare. Data generated as a result of this study are to be available for inspection upon request by FDA or other government regulatory agency auditors, the Sponsor and the IRB.

The information developed in this clinical study will be used by the Sponsor in the clinical development of the study device and therefore may be disclosed by the Sponsor as required for disclosure as to other clinical Investigators, to other companies, to the FDA and to other government agencies.

ETHICAL CONSIDERATIONS AND STUDY ADMINISTRATION

17.1. Human Subjects Protection

Subject's informed consent has to be obtained and documented in accordance with local regulations, ICH-GCP requirements, and the ethical principles that have their origin in the principles of the Declaration of Helsinki.

Before initiation of this study, the Investigator or designee and the Sponsor will jointly develop the consent form. Written IRB approval of the protocol and the consent form must be provided to the Sponsor prior to enrollment of subjects. This approval must refer to the consent form and to the study title and protocol number as given by the Sponsor on the cover page of the protocol.

Prior to participation in the study, the written informed consent form must be signed and personally dated by the subject, or his/her legal representative, and by the person who conducted the informed consent discussion (Investigator or designee). The subject or his/her legal representative must receive a copy of the signed and dated informed consent form. As part of the consent process, each subject must consent to direct access to his/her medical records for trial-related monitoring, auditing, IRB review, and regulatory inspection.

The informed consent form should be updated or amended whenever new information becomes available that may be relevant to the subject. The subject should then sign the revised informed consent form as directed by the IRB.

A list of IRB voting members, their titles or occupations, and their institutional affiliations or a federal wide assurance number should be provided to the Sponsor before study initiation.

The IRB must be notified of completion of the study and a final report must be provided to the IRB. A copy of these reports must be forwarded to the sponsor. The Investigator must maintain an accurate and complete record of all submissions made to the IRB, including a list of all reports and documents submitted. Adverse experiences which are reported to the FDA and/or to other regulatory agencies, as Expedited Safety Reports, must be submitted promptly to the IRB.

At least once per year, the IRB must review and give written approval to continue the study. A copy of this written approval, referring to the study by protocol title and number, as given by the Sponsor, must be provided to the Sponsor.

This trial will be conducted in accordance with FDA regulations and ICH-GCP.

17.2. Protocol Amendments

The Investigator will not modify the protocol without first obtaining concurrence in writing from the Sponsor. If an amendment is required, this must be made in written form and receive approval according to the appropriate SOP. All changes to the protocol must be submitted to the IRB. Protocol modifications that impact subject safety or the validity of the study must be approved by the IRB and submitted to the FDA before initiation.

17.3. Retention of Records

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FDA and ICH-GCP guidelines require that an Investigator retain subject identification codes, subject files, and source data for the maximum period of time permitted by the hospital, institution, or private practice, but not less than 2 years.

17.4. Finance, Insurance, and Publication

Insurance coverage will be handled according to local requirements.

Finance, insurance, and publication rights are addressed in separate agreements as appropriate.

Clinical Investigation Plan

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Clinical Investigation Plan

APPENDICES

APPENDIX A: Anticipated Study Timeline

Timeline	2014			2015												2016					
	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun
Study Month			*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*	*15*	*16*	*17*	*18*	*19*
Cumulative Sites with IRB Approval			5	10	15	20	25	30	35	40	45	50	60	70	80	90	100	110	120	130	140
Cumulative Enrollment			5	12	20	30	41	53	67	82	99	117	141	168	198	231	267	305	346	390	437
	Study Initiation																				
		First Enrollment																			

Timeline	2016						2017											
	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Study Month	*20*	*21*	*22*	*23*	*24*	*25*	*26*	*27*	*28*	*29*	*30*	*31*	*32*	*33*	*34*	*35*	*36*	*37*
Cumulative Sites with IRB Approval	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150
Cumulative Enrollment	486	528	570	612	654	696	738	780	822	864	906	948	990	1032	1074	1116	1158	1200
																Enrollment Complete		

Timeline	2018	. . .	2019						2020		
	Jan	. . .	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar
Study Month	*38*	. . .	*56*	*57*	*58*	*59*	*60*	*61*	*62*	*63*	*64*
Sites with IRB Approval by Month	-	. . .	-	-	-	-	-	-	-	-	-
Cumulative Sites with IRB Approval	-	. . .	-	-	-	-	-	-	-	-	-
Monthly Enrollment	-	. . .	-	-	-	-	-	-	-	-	-
Cumulative Enrollment	-	. . .	-	-	-	-	-	-	-	-	-
						Study Follow-up Complete					
								Study Report Complete & Submit to FDA			

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APPENDIX B: Schedule of Events

	Screening	Baseline (Implant)	Month 1	Months 6 and every 6 Months thereafter until Study Termination
Procedures		(within 30 days of Screening)	Visit 1 (30 ± 7 days)	Visits 2-5 or Study Termination (± 30 day window)
Informed Consent	X			
Demographics	X			
Past Medical & Surgical History	X			
Inclusion/Exclusion Criteria Review	X	X		
GFR	X			
Kansas City Cardiomyopathy Questionnaire (KCCQ-12)	X			X
Brief Illness Perception Questionnaire	X			X
Cardiac Health Security Survey	X			X
INR (if indicated)		X		
Pulmonary artery measurement		X		
Physical Examination (including weight)	X[1]	X[2]	X[2]	X[2]
NYHA HF Classification	X		X	X
Pulmonary Artery Angiography		X		
Sensor Implant		X		
Sensor Measurements		X	X (Investigator discretion)	X (Investigator discretion)
Adverse Events Assessment		X	X	X
Medication Assessment (heart failure)	X	X	X	X

[1] Includes weight, height and vital signs (temperature, blood pressure, pulse, respirations).
[2] Includes weight, vital signs and significant changes from previous physical examination

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APPENDIX C: NYHA Functional Classification for Heart Failure

The New York Heart Association (NYHA) Functional Classification provides a simple way of classifying heart disease (originally cardiac failure), useful for pre-operative and post-operative assessment. It places subjects in one of four categories, based on how much they are limited during physical activity:

Class I (Mild): Subjects with no limitation of activities; they suffer no symptoms.

Class II (Mild): Subjects with slight, mild limitation of activities and suffer mild symptoms (slight swelling of extremities).

Class III (Moderate): Subjects with marked limitation of activity; they are comfortable only at rest.

Class IV (Severe): Subjects who are unable to do any physical activity without discomfort; they suffer with HF symptoms at rest and are confined to bed or chair.

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APPENDIX D: Management of Hemodynamic Parameters

The CardioMEMS HF System allows intermittent assessment of pulmonary artery systolic, diastolic and mean pulmonary artery pressures. Hemodynamic information obtained by the system should be used for clinical decision making in addition to symptoms, weights or physical examination (traditional markers of volume).

Pulmonary Artery Pressure Ranges:	
PA Systolic	15 - 35 mmHg
PA Diastolic	8 - 20 mmHg
PA Mean	10 - 25 mmHg

Initially, thresholds will be set automatically at the acceptable range. The physician can adjust the thresholds specifically for each patient. These threshold notifications are intended to guide the physician to review the CardioMEMS HF Website. Every attempt should be made to keep the pulmonary artery pressures within the specified pulmonary artery pressure ranges utilizing the guidelines. In order to clinically manage patient's PA pressures, the physician must review the PA pressure measurements on a frequent basis, for example, some patients may require a daily review of their PA pressure measurements, while some patients may need a weekly review. The physician or designee has unlimited access to the CardioMEMS HF Website.

An elevation of pressures beyond the patient's pressure ranges should be considered a volume overloaded status and should be managed according to the hyper-volemic guidelines (see below). Diuretics and vasodilators should be adjusted based on the patient's baseline diuretic requirement, knowledge of the patient's prior response to these agents, and clinician judgment to accomplish the pressure goals set forth in this guideline.

A decrease in the pulmonary pressures below the patient's pressure ranges should be considered a volume depletion event and managed according to the hypo-volemia guidelines (see below) (see below). Diuretic therapy should be held and the chronic dose should be lowered.

In addition to these specific guidelines, the physician should also incorporate the recommendations set forth in the ACC/AHA 2013 Guidelines for the Diagnosis and Management of Heart Failure in the Adult.

The PA pressure readings should be used in addition to weights, signs and symptoms, laboratory values and other traditional markers of volume in the management of heart failure. It is important to review the trend of PA pressures. As with all other diagnostic information, physicians should consider the entire medical history of each patient when initiating or modifying therapies.

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Elevated PA Pressures (Hyper-volemic)

Hyper-volemic Definitions

- Subject symptoms: Congestive symptoms (wet)
- CardioMEMS HF System Parameters: above the acceptable range
- Daily trends: elevated trend data outside the acceptable range
- Weekly trends: elevation in trend data

Treatment Recommendations

- Add or increase diuretic (and appropriate electrolyte replacement)
    a. Increase or add loop diuretic
    b. Change to another loop diuretic
    c. Add thiazide diuretic (with caution)
    d. IV doses of loop diuretic
    e. Serum electrolyte evaluation with change in baseline medication
    f. Re-assess pulmonary artery pressure utilizing the CardioMEMS HF System at least 2 – 3 days per week until optivolemic
- Add or increase vasodilators including long-acting nitrates
- Re-educate in salt intake and fluid restriction
- If subject has signs and symptoms of poor perfusion (cold) in addition to being hyper-volemic:
    a. Consider admission if clinical evidence suggests need for IV diuretics, telemetry monitoring or the IV therapeutic agents
    b. Consider invasive hemodynamic monitoring for determination of Cardiac Output, if indicated

Clinical Investigation Plan

Low PA Pressures (Hypo-volemic)

Hypo-volemic Definitions

- Subject symptoms: poor perfusion in absence of signs and symptoms of congestion
- CardioMEMS HF System Parameters: below the acceptable range
- Daily trends: decrease in trend data outside the acceptable range
- Weekly trends: decrease in trend data

Treatment Recommendations

- Lower or discontinue diuretic
    a. If on a thiazide diuretic with loop diuretic, lower or discontinue the dose of thiazide (and adjust electrolyte replacement)
    b. If on only loop diuretic, lower the dose or discontinue
    c. Consider liberalization of oral fluid restriction and salt restriction
- If postural hypotension, hold or lower vasodilators and/or oral nitrates, especially if hypotensive when sitting or supine
- If worsening renal function, hold or lower ACE/ARB dose, especially if hypotensive
- If subject had signs and symptoms of poor perfusion (cold) in addition to being hypo-volemic:

a. Consider admission if clinical evidence suggests need for IV fluid repletion, telemetry monitoring or the use of IV therapeutic agents
b. Consider invasive hemodynamic monitoring for determination of Cardiac Output, if indicated

Clinical Investigation Plan

Recommended Frequency of CardioMEMS HF System Review

Subject Status	Weekly	At least 2– 3 times per week until optivolemic	At least 2 – 3 times per week until pressure stabilizes
Acceptable PA Pressure (Opti-volemic)	X		
Elevated PA Pressure (Hyper-volemic)		X	
Low PA Pressure (Hypo-volemic)		X	
Medication modifications			X
Significant deviations in trend data			X

Clinical Investigation Plan

APPENDIX E: Kansas City Cardiomyopathy Questionnaire-12

Kansas City Cardiomyopathy Questionnaire (KCCQ-12)

The following questions refer to your **heart failure** and how it may affect your life. Please read and complete the following questions. There are no right or wrong answers. Please mark the answer that best applies to you.

1. **Heart failure** affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by **heart failure** (shortness of breath or fatigue) in your ability to do the following activities over the past 2 weeks.

Activity	**Extremely** Limited	**Quite a bit** Limited	**Moderately** Limited	**Slightly** Limited	**Not at all** Limited	Limited for other reasons or did not do the activity
a. Showering/bathing	O	O	O	O	O	O
b. Walking 1 block on level ground	O	O	O	O	O	O
c. Hurrying or jogging (as if to catch a bus)	O 1	O 2	O 3	O 4	O 5	O 6

2. Over the past 2 weeks, how many times did you have **swelling** in your feet, ankles or legs when you woke up in the morning?

Every morning	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
O 1	O 2	O 3	O 4	O 5

3. Over the past 2 weeks, on average, how many times has **fatigue** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
O 1	O 2	O 3	O 4	O 5	O 6	O 7

4. Over the past 2 weeks, on average, how many times has **shortness of breath** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
O 1	O 2	O 3	O 4	O 5	O 6	O 7

5. Over the past 2 weeks, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of **shortness of breath**?

Every night	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
O 1	O 2	O 3	O 4	O 5

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6. Over the past 2 weeks, how much has your **heart failure** limited your enjoyment of life?

It has **extremely** limited my enjoyment of life	It has limited my enjoyment of life **quite a bit**	It has **moderately** limited my enjoyment of life	It has **slightly** limited my enjoyment of life	It has **not limited** my enjoyment of life at all
O	O	O	O	O
1	2	3	4	5

7. If you had to spend the rest of your life with your **heart failure** the way it is right now, how would you feel about this?

Not at all satisfied	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Completely satisfied
O	O	O	O	O
1	2	3	4	5

8. How much does your **heart failure** affect your lifestyle? Please indicate how your **heart failure** may have limited your participation in the following activities over the past 2 weeks.

Activity	**Severely** Limited	Limited **quite a bit**	**Moderately** limited	**Slightly** limited	**Did not** limit at all	Does not apply or did not do for other reasons
a. Hobbies, recreational activities	O	O	O	O	O	O
b. Working or doing household chores	O	O	O	O	O	O
c. Visiting family or friends out of your home	O	O	O	O	O	O
	1	2	3	4	5	6

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APPENDIX F: Brief Illness Perception Questionnaire (English)

Brief Illness Perception Questionnaire

For the following questions, please circle the number that best corresponds to your views:

How much does your illness affect your life?										
0 no affect at all	1	2	3	4	5	6	7	8	9	10 severely affects my life
How long do you think your illness will continue?										
0 a very short time	1	2	3	4	5	6	7	8	9	10 forever
How much control do you feel you have over your illness?										
0 absolutely no control	1	2	3	4	5	6	7	8	9	10 extreme amount of control
How much do you think your treatment can help your illness?										
0 not at all	1	2	3	4	5	6	7	8	9	10 extremely helpful
How much do you experience symptoms from your illness?										
0 no symptoms at all	1	2	3	4	5	6	7	8	9	10 many severe symptoms
How concerned are you about your illness?										
0 not at all concerned	1	2	3	4	5	6	7	8	9	10 extremely concerned
How well do you feel you understand your illness?										
0 don't understand at all	1	2	3	4	5	6	7	8	9	10 understand very clearly
How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?										
0 not at all affected emotionally	1	2	3	4	5	6	7	8	9	10 extremely affected emotionally

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APPENDIX G: Cardiac Health Security Survey

CARDIAC HEALTH SECURITY

We want to understand what it is like for you to live with a medical condition. Below are some statements that describe personal beliefs about your condition. Please rate the extent to which you agree or disagree with each of the following statements by checking the most appropriate box.

Strongly Disagree	Mostly Disagree	Neither Agree nor Agree	Mostly Agree	Strongly Agree
1	2	3	4	5

AVAILABILITY

1) I have the information that I need to be as healthy as possible.
2) I have the support that I need to be as healthy as possible.
3) I am not sure what to do to be healthy in the future.

ACTION

4) I don't know what symptoms of my condition that I should watch for.
5) I get mixed messages from different providers about what I need to do to take care of my health.
6) I don't know what to do if my condition worsens.

OUTCOME

7) If my health condition changes, I can get it back on track.
8) I can deal with my condition.
9) My condition is dangerous on a day-to-day basis.

FUTURE ORIENTATION

10) I look forward to better health in the future.
11) My health problems are not predictable.
12) It's hard to know when I will have "good days" or "bad days" as far as my health problems go.

WIHM SYSTEM EVALUATION AND IMPACT

13) Overall, I am satisfied with my pressure monitoring system.
14) Given the choice again, I would agree to get pressure monitoring system again.
15) The pressure monitoring system gives me a sense of control.
16) The pressure monitoring system provides me a sense of security.
17) My heart disease prevents me from planning activities in the future.
18) The pressure monitoring system provides my loved ones a sense of security.
19) The pressure monitoring system is a problem for me.
20) The pressure monitoring system was overwhelming to deal with.

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21) I lost interest in pressure monitoring.
22) I worry that my data is not secure.
23) The pros outweigh the cons for pressure monitoring.
24) I avoid making plans because I am afraid that I will not feel well enough to participate.

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APPENDIX H: BMI Calculator

To calculate subjects Body Mass Index using the website below:

http://www.nhlbisupport.com/bmi/bmi-m.htm

Enter the subjects Weight and Height and then calculate BMI (print screen for source documentation)

Formulas used to calculate Body Mass Index:

English BMI Formula

BMI = Weight in pounds/ (height in inches x height in inches) x 703

Metric BMI Formula

BMI = Weight in kilograms/ (height in meters x height in meters)

Note that BMI may also be calculated within the eCRF.

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APPENDIX I: Glomerular Filtration Rate

To calculate subjects Glomerular Filtration Rate use the website below:

http://www.nephron.com/cgi-bin/CGSI.cgi

Enter the subjects Creatinine level, Age, Race, Gender then calculate (print screen for source documentation)

GFR (mL/min/1.73 m^2) = 186 x$(S_{cr})^{-1.154}$ x $(Age)^{-0.203}$ x (0.742 if female) x (1.210 if African American)

Note that GFR may also be calculated within the eCRF.

Clinical Investigation Plan

APPENDIX J: Protocol Definitions

Enrollment – After meeting study inclusion criteria and following successful Sensor implant, subjects are considered enrolled

Hospitalization – Greater than or equal to 24 hours in a hospital

HF Hospitalization – hospitalization determined to be related to heart failure as determined by the CEC

Active Infection- Febrile, elevated WBC, left shift, on antibiotics, positive cultures (blood, sputum or urine)

PI – Appropriate clinician designated as the Principal Investigator on the "Investigator Agreement" received and approved by St. Jude Medical. For study related procedures/visits PI refers to the PI or his/her designee.

Source documents – Primary study documentation including electronic, paper, phone messages, etc. containing study-pertinent information such as visit information, clinical history, medications, (S)AE reporting, etc. These documents are originals and should be treated as such. Information from these documents will be transferred from and compared against information reported in study CRFs

Sub-investigator – Clinical personnel designated as a sub-investigator on the "Investigator Agreement" received and approved by St. Jude Medical

Worksheets –Source documents used for calculation of clinical values such as BMI or EGFR from screening to end of study. Worksheets may also be used during the sensor implant or follow-up visits to capture information not captured in the medical record. In order for these worksheets to be considered valid, the Investigator must sign and date the worksheet.

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APPENDIX K: Composition, Function, and Procedures of the Clinical Events Committee (CEC)

The hospitalizations and deaths in this study will be monitored by a Clinical Events Committee (CEC). The committee will be comprised of physicians, who will not participate in the enrollment or treatment of subjects in this trial. The CEC members have agreed with the study design and protocol. CEC members are independent and cannot be removed based on difference of opinion on study-related matters with St. Jude Medical, Investigators, or any St. Jude Medical contractor.

The members of the CEC are responsible for reviewing the safety data and providing an assessment of the data according to their individual expertise. The CEC Committee will evaluate all SAEs to determine whether or not the SAE is device / system-related. The interpretation of events as classified and adjudicated by the clinical events committee will be used in the final effectiveness and safety analyses.

The role and procedures of the CEC Committee will be detailed in the CEC charter.

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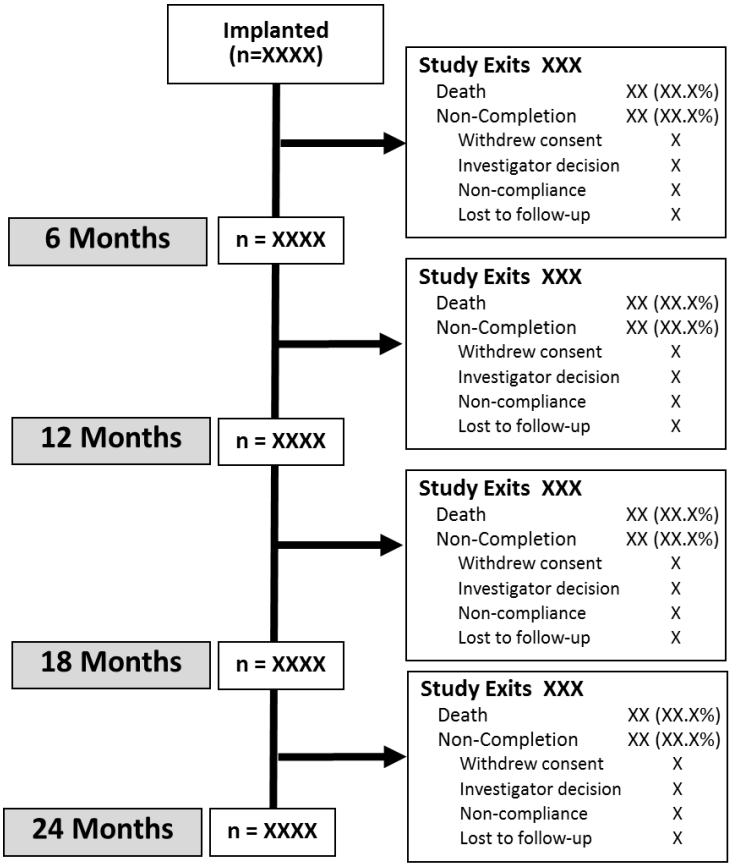
APPENDIX L: Reporting of Interim Analyses

Updates from the PAS will be submitted to FDA as a PMA supplement every 6 months for the first two years of the study (annually thereafter). This information will include the following information:

Study enrollment and follow-up status



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Demographic information

	Premarket Study	PAS Aggregate	PAS Male	PAS Female
Average Age (years)	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X
Male	XX.X%	XX.X%	XX.X%	XX.X%
Caucasian	XX.X%	XX.X%	XX.X%	XX.X%
Average BMI	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X
Average LVEF	XX.X ± XX.X%	XX.X ± XX.X%	XX.X ± XX.X%	XX.X ± XX.X%
LVEF < 40%	XX.X%	XX.X%	XX.X%	XX.X%
Ischemic Cardiomyopathy	XX.X%	XX.X%	XX.X%	XX.X%
Average PA Systolic (mmHg)	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X
Average PA Diastolic (mmHg)	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X
Average PA Mean (mmHg)	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X
Average PA Wedge (mmHg)	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X
Average Cardiac Output (L/min)	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X
Average Cardiac Index (L/min/m^2)	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X	XX.X ± XX.X

Safety

	6 Months N=XXXX		12 Months N=XXXX		18 Months N=XXXX		24 Months N=XXXX	
	N	Percent	N	Percent	N	Percent	N	Percent
DSRCs	XXX	XX.X%	XXX	XX.X%	XXX	XX.X%	XXX	XX.X%
Pressure Sensor Failures	XXX	XX.X%	XXX	XX.X%	XXX	XX.X%	XXX	XX.X%

Heart Failure Hospitalizations

	6 Months N=XXXX	12 Months N=XXXX	18 Months N=XXXX	24 Months N=XXXX
HF Hospitalizations	XXX	XXX	XXX	XXX
HF Hospitalization Rate: Events/patient years Events/patient days	 X.XX X.XX	 X.XX X.XX	 X.XX X.XX	 X.XX X.XX
HF Hospitalization Proportion	XX.X%	XX.X%	XX.X%	XX.X%

Mortality

	6 Months N=XXXX		12 Months N=XXXX		18 Months N=XXXX		24 Months N=XXXX	
	Deaths	Percent	Deaths	Percent	Deaths	Percent	Deaths	Percent
All Cause Deaths	XXX	XX.X%	XXX	XX.X%	XXX	XX.X%	XXX	XX.X%
Cardiac Deaths	XXX	XX.X%	XXX	XX.X%	XXX	XX.X%	XXX	XX.X%
Non-Cardiac Deaths	XXX	XX.X%	XXX	XX.X%	XXX	XX.X%	XXX	XX.X%

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Serious Adverse Events

	6 Months N=XXXX		12 Months N=XXXX		18 Months N=XXXX		24 Months N=XXXX	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
All Patients with an Event	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX	XX (XX.X%)	XXX
System Organ Class I	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
…								

Days alive outside of hospital for heart failure

	6 Months N=XXXX	12 Months N=XXXX	18 Months N=XXXX	24 Months N=XXXX
	N	N	N	N
Days Alive outside of Hospital	XXX	XXX	XXX	XXX

Weekly Patient Pressure Reading Compliance

	Compliance %
Mean ± StdDev	XX.X ± XX.X%
Median	XX.X%

Sensor Performance

	N	Percent
Number of Patients	XXX	XX.X%
Number of RHCs with comparative readings	XXX	XX.X%

Results will presented using Bland-Altman comparing Sensor vs. Swan-Ganz.

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Medication changes in response to PA pressure

	# Medications	
Medication Changes in Response to PA Pressure	N	Percent
ACE/ARB	XXX	XX.X%
Aldosterone Antagonist	XXX	XX.X%
Beta-blocker	XXX	XX.X%
Diuretic-Loop	XXX	XX.X%
Diuretic-Thiazide	XXX	XX.X%
Hydralazine	XXX	XX.X%
Nitrate	XXX	XX.X%
Other	XXX	XX.X%
Total	XXX	XX.X%

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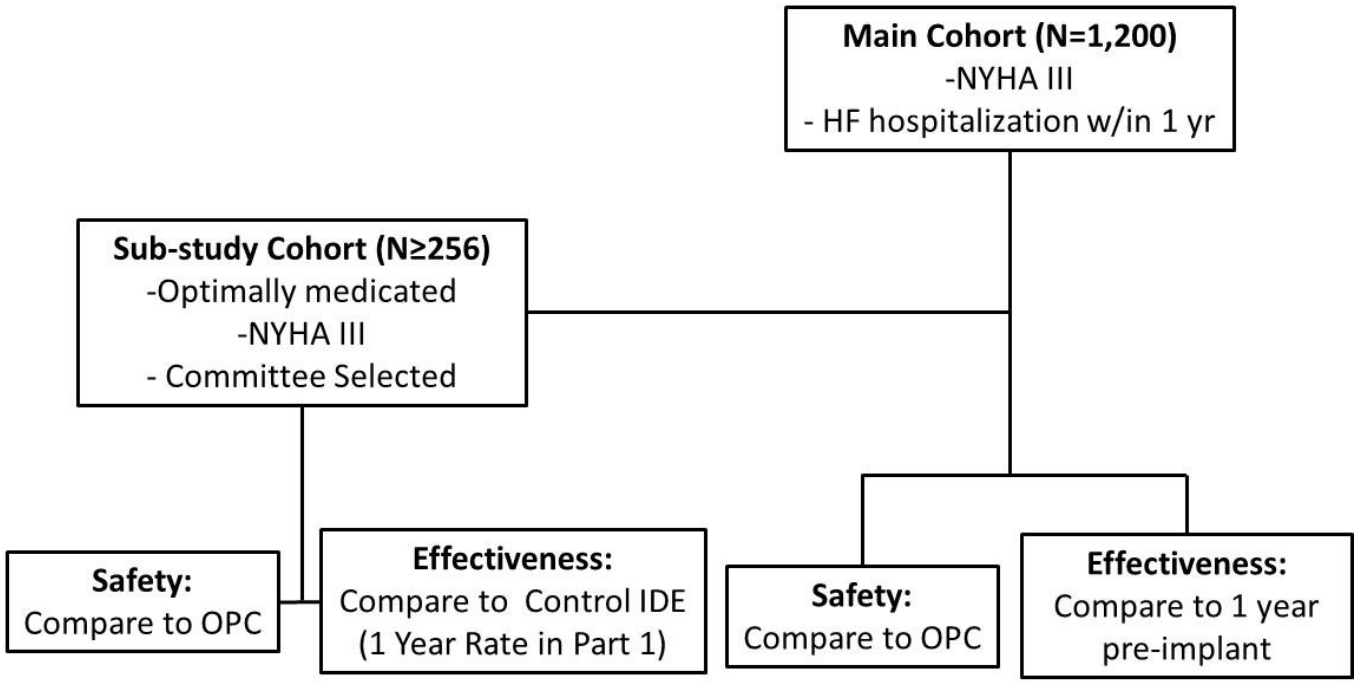
Appendix M: Schematic Diagram of Main PAS Study and Substudy



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Appendix N: informed consent template

CONSENT TO PARTICIPATE IN A CLINICAL STUDY

Title: CardioMEMS™ HF System Post Approval Study

Sponsor: St. Jude Medical, Inc.

Institution: (*Name)*
(Address)
(City, State zip)

Principal Investigator: (*Name, title)*
(Address)
(City, State zip)
(Phone)

INTRODUCTION

You have been diagnosed with heart failure. Heart failure (HF) is a disorder resulting from damage to the heart. Hypertension (high blood pressure) or coronary artery disease (narrowed or blocked blood vessels to the heart) are the most common causes of heart failure. This damage makes it difficult for the heart to pump enough blood to meet the demands of the body. Heart failure is a progressive disease that often gets worse over time.

Physicians treating heart failure patients rely on signs and symptoms, physical exams, and lab values to manage your therapy. In addition, special procedures are needed to evaluate the condition and performance of the heart. One of these procedures is a right heart catheterization. During this procedure, pressures in the heart and the blood vessels close to the heart are measured using a pulmonary artery catheter (a thin, flexible tube). A heart catheterization offers valuable information to the physician; however, it is limited to a one-time

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"snap-shot" of the pulmonary artery pressures related to heart function. CardioMEMS developed a technology that provides physicians with reliable, accurate daily trends of pulmonary artery pressure measurements. This technology proved to be extremely valuable in the management of care for heart failure patients.

The CardioMEMS HF System provides a method to measure pulmonary artery (PA) pressures by using a small wireless sensor (about the size of a paperclip) implanted into the pulmonary artery (a vessel close to your heart). Once implanted, the sensor communicates through radio frequency to an antenna contained in a pillow connected to an electronic unit and then transmits this valuable information to a secure website for your doctor to review. You will be able to take these PA pressure measurements yourself at home. In addition to these home readings, your PA pressures can also be obtained in the physician's office, clinic, or hospital. Your doctor can access the secure website to view your measurements allowing him/her to make earlier treatment changes (usually changes in medications) to manage your heart failure remotely.

The CardioMEMS HF System was evaluated during a recent clinical study. The CHAMPION trial was conducted at 64 study sites in the U.S. and enrolled 550 patients with NYHA Class III heart failure who had been hospitalized for heart failure in the previous year. All patients were implanted with a sensor and then assigned by chance to either the Treatment group (heart failure management on the basis of pulmonary artery pressure and standard of care) or the Control group (heart failure management on the basis of standard of care). CHAMPION met its primary endpoint of reduction in the rate of heart failure hospitalizations with Treatment patients having 28% fewer heart failure hospitalizations compared to Control patients at 6 months; the benefit was sustained with a 37% reduction over the entire study time period which averaged 15 months. Treatment patients also experienced an improvement in their quality of life compared to Control patients.

The FDA approved the CardioMEMS HF System for commercial use in the USA in May of 2014. Part of the FDA's responsibility to the public is to make sure that medical devices are safe and work correctly after they are approved. As such, the FDA has requested the sponsor of the device, St. Jude Medical, to conduct a Post Approval Study (PAS). This study can give patients, doctors, the sponsor, and the FDA valuable information on the safety, effectiveness and reliability of the CardioMEMS HF System.

You are being invited to participate in the CardioMEMS HF System Post Approval Study. This consent form will inform you of the risks and benefits of participating in this study. Before you agree to volunteer, you should know as much as possible so that you can make an informed decision about taking part in this Post Approval Study. It is important that you read the following information and ask as many questions as necessary.

This is a commercial device and participation in the PAS does not increase your health risks or require additional steps. A right heart catheterization is required to implant the sensor and the PA pressure-based medical management provided by your doctor will be the same, regardless of study participation.

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PURPOSE

The objective of this Post Approval Study is to demonstrate that data collected related to the use of the CardioMEMS HF System in a commercial setting are comparable with data collected in a controlled clinical trial.

This is a prospective, open-label clinical trial to be conducted at up to 150 clinical sites in the United States (US). There will be 1200 patients enrolled in the study.

CardioMEMS HF SYSTEM

The CardioMEMS HF System consists of a sensor, delivery system, external electronics (hospital and patient units) and the patient website. The System will be used in your home to transmit your pulmonary artery pressure measurements to a secure website for your physician to review and determine the best way to manage your heart failure. Your physician may also use the System in the clinic or in the hospital.

QUALIFICATIONS

You have been asked to consider participation in this study because:

- You are willing to review and sign an informed consent
- You are at least 18 years old
- You have been diagnosed with heart failure and have been classified as NYHA Class III
- You have experienced at least 1 hospitalization within the past 12 months because of your heart failure
- Your Body Mass Index (a calculation using your weight and height) is acceptable for the study
- You are willing to comply with the requirements of the study, including taking PA pressure readings from home as directed by your doctor

STUDY VISITS

Screening Visit

In order to participate in this study the following tests, examinations and reviews will need to be completed and the results must meet the study requirements:

- Physical examination including vital signs (temperature, heart rate, respiratory rate, blood pressure), weight, height, Body Mass Index calculation
- Medical and surgical history
- Demographics information (age, race, date of birth)
- New York Heart Association Classification for heart failure (a classification your doctor uses to describe your heart failure)
- Kansas City Cardiomyopathy Questionnaire (KCCQ-12)

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- Brief Illness Perception Questionnaire
- Cardiac Health Security Survey
- Laboratory tests (if necessary)
- Heart failure medication review

Your doctor will determine if you can participate in the study after your examination and lab tests have been reviewed. Once your study eligibility is confirmed, your physician's office will schedule the Sensor implant visit. You may be instructed to stop taking blood thinning medications 1-2 days before the implant procedure.

Implant Procedure (Baseline)

During the sensor implant visit, the following procedures will be performed:

- Physical examination including vital signs (temperature, heart rate, respiratory rate, blood pressure) and weight
- New York Heart Association Classification for heart failure
- Lab tests: Prothrombin Time (PT) with International Normalized Ratio (INR) if you have been prescribed warfarin
- Heart failure medication review
- Right heart catheterization and sensor implant procedure
- Review of adverse events that occurred (if any) since the baseline visit

The Sensor will be implanted during the heart catheterization procedure. The Sensor is about the size of small paper clip and has a thin curved wire at each end. It is placed inside your pulmonary artery (one of the vessels close to the heart) with a special delivery catheter.

Figure 1. CardioMEMS HF Sensor

You may receive a mild sedative before and/or during the procedure but you will be awake so you can follow instructions. An area on your groin will be cleansed with sterile soap and a local anesthetic (numbing) medicine will be injected at that site.

There are two parts to the procedure, the right heart catheterization (RHC) and the Sensor implant. The heart catheterization is performed first. A pulmonary artery catheter is inserted in your groin and then carefully threaded into your heart using an x-ray machine to produce pictures (fluoroscopy). Your heart rate and rhythm will be constantly monitored by an electrocardiogram (ECG). Once the catheter is in the pulmonary artery, a small amount of contrast material (dye) is injected and pictures are taken to make sure the catheter is in the right position and to make sure the branch of the pulmonary artery is the appropriate size. This procedure is called angiography.

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Next, a delivery catheter with the Sensor attached is carefully threaded to your pulmonary artery over a guide wire (a very small wire used to guide catheters). The Sensor is then positioned in the pulmonary artery and released from the delivery catheter. The delivery catheter will be removed and the pulmonary artery catheter positioned next to the Sensor. Once the Sensor is confirmed by x-ray to be in the correct position, it will stay inside the pulmonary artery permanently. The doctor will hold a monitor (called an antenna) to your back, chest or side to obtain the Sensor's signal. Pulmonary artery pressure readings will be recorded from both the Sensor and the pulmonary artery catheter. The heart catheter is removed and the Sensor will remain in your pulmonary artery

If the doctor is unable to safely pass the catheter into the pulmonary artery or if the pulmonary artery branch is not the appropriate size, you will not be able to receive the Sensor. Your doctor will follow your progress for 30 days and then afterward you will no longer participate in the study.

The procedure (RHC and Sensor implant) may last up to one hour. After the procedure is completed, you may be asked to lay flat on your back for a few hours, to prevent any bleeding from the catheter insertion site. At your doctor's discretion, you may be discharged the day of the procedure or you may be required to stay in the hospital overnight so that your condition may be observed and evaluated.

Following the implant procedure, your doctor will give you instructions on taking a blood thinning medication. If you are currently on warfarin therapy, you will be asked by your doctor to restart this medication. If you are not currently on warfarin therapy, you will be placed on clopidogrel (75 mg) daily for 1 month and aspirin (81 mg or 325 mg) daily. If necessary, laboratory tests on your blood will be done periodically so your doctor can make certain you are receiving the proper blood thinning medication during the trial.

After the procedure, your doctor or nurse will instruct you how to set-up and take PA pressure readings from your home using the patient electronics system (home readings typically take less than one minute to complete). It is important that you are comfortable with setting up your patient electronics system and that you understand how to take a reading. Should you need assistance with the System when you get home, you may call the St. Jude Medical helpline at 877-696-3754.

Your physician will have access to your hemodynamic information (PA pressure readings and heart rate) through the CardioMEMS HF System. He/she will evaluate your pulmonary artery pressures daily or weekly as required and use the information to better manage your heart failure. Therefore, it is very important that you take pressure readings as directed by your doctor.

You will be contacted by your doctor or his/her staff periodically during the study when adjustments in your medications are necessary. You should feel free to contact your physician or his/her staff as you would normally. It is important that you notify your study doctor immediately if you have any worsening symptoms of heart failure.

As a participant in the Post Approval Study, it is very important that you follow all the instructions from your doctor, including taking PA pressure readings and going to all of the scheduled follow-up visits.

Follow-Up Visits

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You will return to see your doctor for follow up study visits at 1 month following your implant procedure and 4 more times over the next 2 years (6 months, 12 months, 18 months, and 24 months). During the study visits, the following procedures will be performed:

- Updated medical and surgical history
- Assessment of adverse events if any occurred since your last visit
- Physical examination including vital signs (temperature, heart rate, respiratory rate, blood pressure), and weight
- Assessment of your NYHA functional class
- Kansas City Cardiomyopathy Questionnaire
- Brief Illness Perception Questionnaire
- Cardiac Health Security Survey
- Review of your heart failure medications
- Your doctor may obtain PA pressure measurements during the visit
- You will be reminded to take your PA pressure readings and will be provided counseling regarding the AHA guidelines for sodium and fluid restrictions in your diet.

STUDY DURATION

Your involvement in this Post Approval Study will last for two (2) years.

RIGHT TO WITHDRAW

Participation in this study is voluntary. You have the right to withdraw your consent and stop taking part in this study at any time without penalty and your doctor will continue to treat you regardless of your participation. However, we encourage you to talk to the research coordinator, nurse and your doctor about your decision before you withdraw.

Your participation may also be ended without your consent if your study doctor feels that it is in your best interest. The study Sponsor or the Ethics Committee may discontinue the study at any time for safety, administrative or other reasons.

RISKS

To date, the CardioMEMS HF System has been safely tested in 567 patients in the United States. During the CHAMPION trial, there were no failures of the device (sensor) and no other unanticipated complications. We do not know all of the risks. Some of the possible risks are also complications of the right heart catheterization and/or drugs associated with the procedure and blood thinning medications. Some of these risks include:

- Air embolism (air bubble in the bloodstream)
- Allergic reaction
- Abnormal heart rate or rhythm

- Bleeding
- Bruising
- Chest pain
- Myocardial infarction
- Nausea
- Stroke
- Infection
- Delayed wound healing
- Thrombus formation (blood clots)
- Hematoma (collection of blood internally)
- Venous trauma (injury to your veins)
- Valve damage
- Sensor not releasing from delivery system
- Pulmonary infarct (damage to the lung)
- Pulmonary embolism (blood clot to the lung)
- Death

Some of the side effects that you may experience will go away shortly after the procedure, but in other cases side effects can be serious, long lasting, and/or permanent.

Resetting of the sensor baseline may also be performed as deemed necessary by Sponsor or your physician. Baseline resetting may require an echocardiogram or a RHC procedure and would include the risks associated with those procedures.

BENEFITS

The results of the CHAMPION trial showed that through the use of the information obtained from the CardioMEMS HF System, physicians were able to adjust medications that allowed for a significant reduction in hospitalizations for heart failure. To experience the most benefit from the CardioMEMS HF System, it is important that you take readings daily or as instructed by you physician. Your participation in the Post Approval Study will also help your doctor, the sponsor, and the FDA evaluate the public health benefit for patients in the future.

ALTERNATIVE THERAPIES

An alternative is not to participate in this study and continue with your current care. If you choose not to be in the study and the CardioMEMS sensor is implanted, your doctor will still have access to the PA pressure data provided from the CardioMEMS HF System and use that information in addition to traditional standard of care methods to follow and treat your heart failure.

There are no other FDA approved therapies similar to the CardioMEMS HF System. Currently, patients' weights are monitored by simple or sophisticated scales and medications are adjusted

accordingly. There are also telephone or internet systems used for the monitoring of worsening heart failure symptoms.

NEW INFORMATION

If significant new information that may affect your participation in the study is discovered, your doctor will be given the information as soon as possible for review and discussion with you.

COSTS

The CardioMEMS HF System is an approved medical device covered by Medicare and most insurance providers. There are no additional costs to you for your participation in this study. The costs of the visits required for the study will be paid for by the sponsor.

INJURY

If you suffer an injury resulting directly from the study, the reasonable costs of medical treatment will be paid for you, to the extent such costs are not covered by your medical or hospital insurance or third-party or governmental programs providing such coverage.

ROLE OF THE SPONSOR'S REPRESENTATIVE

The role of the Sponsor (St. Jude Medical) representative in this study is to provide training and technical support. A representative of the sponsor may be present during the implant procedure. The sponsor's representative may assist your doctor to make sure your CardioMEMS HF System is working as expected. The representative will work under the direction of your doctor and may be aware of your medical history but will in no way compromise your confidentiality.

CONFIDENTIALITY AND PROTECTED INFORMATION

By signing this form, you allow access to your medical records to the study doctors and their staff, the Sponsor or its representative(s), representatives of the Institutional Review Board (IRB) and representatives from the regulatory agencies. If you decide to take part in this research study, your medical records and personal information will be kept confidential to the extent allowed by Federal, State, and local law. However, information from the study may be exported to countries where different data protection laws apply. The data protection laws in other countries may be less strict than those of your country.

The results of this study may be reported or published. However, you will never be identified by name nor will other personal identifying information about you be released in a publication. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Medical records and information regarding your health status are protected information. Because this information is protected, ***(Institution Name)*** is required by law to let you know what types of information about you may be requested and how your information will be used and disclosed for this study. The next few paragraphs give you additional information about how your medical records and health information will be used, disclosed, and stored. By signing this form, you also authorize and request all other health care providers who examine and/or treat you during your participation in this study and any necessary follow-up to this study, to release all relevant and necessary medical records to ***(Institution or Principal Investigator)*** at

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its request. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used and disclosed for other purposes.

Information from this study will be submitted to the study Sponsor and the US Food and Drug Administration (FDA). It may also be submitted to governmental agencies in other countries where the device may be considered for approval. In order to verify information collected in this study and to verify how the study was conducted, your medical records related to the study, the consent form signed by you, and any other regulatory documents associated with the study, will be inspected and may be copied by:

- The study doctor and study staff
- The Sponsor and/or their representative
- The IRB/IEC (ethics committee)
- The FDA

The Sponsor may store, access, use and disclose the information in any of the following ways:

- To analyze and make conclusions about the results of the study,
- In documents sent to the government agencies throughout the world including the U.S. Food and Drug Administration (FDA (or other similar bodies outside the United States) to request reviews/approvals relating to the System,
- For reporting undesirable events to the FDA (choose agency) and other government health agencies,
- To provide overall study results to other study doctors, including in publications,
- To conduct new medical research study, to reanalyze the study results in the future or to combine your information with information from other studies,
- To develop new medical products and procedures, and other product-development related activities.
- To remove identifying information (such as name, address, etc.) from the information and then use and disclose the resulting information for other purposes.

While using the information in these ways, the sponsor may give study data to its affiliated companies in the U.S. or other countries. The sponsor may also share the information with its business partners or companies it hires to provide study-related services.

Your authorization for the access, use and/or disclosure of your health information for the purposes described in this document does not expire. If you decide to participate in the research study, you are free to withdraw your authorization regarding the access, use and disclosure of your health information at any time. If you wish to revoke your authorization, you must write to _____ [insert appropriate address]. If you drop out of this study, the study sponsor and study doctor will continue to use and disclose any information about you **[or from you]** that were gathered before you dropped out in order to preserve the integrity of the research study.

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You have the right to request copies of the medical tests performed during the course of this study for as long as the study doctor has this information in his or her possession. However, by signing this form you agree that you might not have full access to review study related medical test records until after the study is complete.

CONTACT FOR QUESTIONS

Please be sure to ask your doctor any questions or concerns you may have about being in this study. Feel free to ask questions about the CardioMEMS HF System, the sensor, the implant procedure, risks, benefits, and alternative therapies available to you. If you have questions regarding any part of the study, contact ***(Principal Investigator)*** at ***(phone number).***

This study was reviewed by the ***(Institutional Review Board)***, a special group of people that are independent of the study doctor and the Sponsor. The purpose of this group is to protect the rights and safety of people who volunteer to take part in clinical studies such as this Post Approval Study. If you have any questions about your rights as a study patient or a complaint or concern about participating in this study, you may contact ***(IRB Chairman)*** at ***(phone number).***

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CONSENT TO PARTICIPATE

I choose to participate in the CardioMEMS HF System Post Approval Study. I have read all of the above information or it has been read to me. I have been given the opportunity to ask questions about this study and the required procedures. My questions have been answered to my satisfaction. After I sign the consent form, I understand I will receive a copy of it for my own records. I am aware that I do not give up any of my legal rights by signing this consent form.

Patient:

Signature of Patient Date Signed

Patient Name (print)

Consent Obtained By:

Signature Date Signed

Name (print)

Title

Witness (if applicable):

Signature Date Signed

Name (print)