Post Market Surveillance Plan

ABT-CIP-10382
CRD 1022

Hong Kong and Taiwan HM3 PMS
Post Market Surveillance of the HeartMate 3 Left Ventricular Assist System in Hong Kong and Taiwan

Version Number	A
Date	December 2, 2020
Device and Model	HeartMate 3 106524INT
Planned Number of Sites and Region(s)	4, Hong Kong and Taiwan
Abbott Medical Expert	Robert Kormos, MD 6300 Bee Cave Rd Building 2, suite 100 Austin, TX – 78746 Ph: 5122864310 Email: Robert.Kormos@abbott.com
Sponsor	Abbott – Heart Failure 168 Middlesex Turnpike Burlington, MA 01803 USA
Electronic Data Capture Software	Oracle Clinical
PMS plan Author of Current Version	Carlo Gazzola, BSc

Post Market Surveillance Plan

SITE PRINCIPAL INVESTIGATOR SIGNATURE PAGE

I have read and agree to adhere to the post market surveillance plan and all regulatory requirements applicable in conducting this post market surveillance.

Site Principal Investigator

Printed name:
Signature:
Date:

Post Market Surveillance Plan

TABLE OF CONTENTS

Post Market Surveillance Plan

Post Market Surveillance Plan

Post Market Surveillance Plan

TABLE OF FIGURES

TABLE OF TABLES

Post Market Surveillance Plan

COMPLIANCE STATEMENT:

This study will be conducted in accordance with this Post Market Surveillance plan, the Declaration of Helsinki, ISO 14155:2011 standard and the appropriate local legislation(s). The most stringent requirements, guidelines or regulations must always be followed. The conduct of the post market surveillance will be approved by the appropriate Institutional Review Board (IRB) of the respective clinical site and as specified by local regulations.

Post Market Surveillance Plan

1.0 INTRODUCTION

The purpose of this post-market surveillance (PMS) is to collect data on clinical and functional outcomes with the HeartMate 3™ (HM3) left ventricular assist system (LVAS) as a treatment for advanced heart failure, refractory to optimal medical management in Hong Kong and Taiwan. The PMS is being sponsored by Abbott – the manufacturer of the HM3 LVAS.

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

1.1 Background and Rationale

1.1.1 Background

Patients with heart failure suffer significant morbidity and mortality. Heart Failure results when the pumping efficiency of the heart is diminished to the point of lack of end-organ perfusion. Since, allogenic heart transplantation is limited by insufficient supply of donor organs, left ventricular assist devices (LVADs) have become a mainstay of advanced heart failure treatment for patients on the waiting list and those not eligible for transplantation.

The HM3 is a durable, centrifugal-flow pump that has shown to improve the clinical and functional outcomes of advanced heart failure patients.[1] The pump is approved in multiple geographies for both short- and long-term left ventricular support for New York Heart Association (NYHA) class IIIB/IV heart failure patients.[2,3] Hemocompatibility related adverse events have been one of the main reasons for the slow adoption of LVADs for the treatment of heart failure, in spite of the improvements seen in quality-of-life (QoL) and functional outcomes. The HM3 was designed to have an improved hemocompatibility profile, with a frictionless fully magnetically levitated rotor, wider blood flow passages, and a programmed intrinsic pulse to reduce stasis.[4]

The CE Mark trial (clinicaltrials.gov identifier: NCT02170363) for the HM3 LVAD was a prospective, multicenter, single arm trial that enrolled 50 subjects at 10 sites. This was the first clinical investigation of the HM3 left ventricular assist system (LVAS). Six-month outcomes from this trial demonstrated 92% (95% confidence interval 83-97%) survival and led to the CE Mark approval of the HM3. Analysis of longer term data demonstrated a 2-year survival of 74 ± 6%.[5,6] At 2-years, QoL and functional outcomes remained significantly improved relative to baseline: the mean EQ-5D QoL scored improved from 48.2 to 70.6; 82% of the subjects were in NYHA class I/II compared to 32% at baseline; the mean 6-minute walk distance increased from 239 to 347 m. No instances of device thrombosis were observed in this cohort at 2 years.[6] Subjects will be followed for 5 years as a condition of CE Mark approval.

After CE Mark approval, the ELEVATE (Evaluating the HeartMate 3 with Full MagLev Technology in a Post-Market Approval Setting; clinicaltrials.gov identifier: NCT02497950) registry was initiated to collect real-world data on consecutive HM3 patients at 26 centers in Europe, Israel, Singapore, and Kazakhstan. The study enrolled 463 primary implant patients, 19 pump exchange patients, and collected only outcome data on an additional 58 patients who

were unable to provide consent due to a study outcome (n=57 death, n=1 explant). The ELEVATE trial reported, for the primary implant cohort at 2-years, actuarial survival of 83.4%, and adverse events of stroke in 10%, suspected pump thrombosis in 1.5%, and bleeding in 34%. Mean EQ-5D score increased from 35 to 67 and 6MWT distance improved from 104 to 350 m.[7] Subjects will be followed until the last patient completes the 5 year follow-up or experiences an outcome.

The MOMENTUM 3 study (Multi-center Study of MagLev Technology in Patients Undergoing MCS Therapy with HeartMate 3: clinicaltrials.gov identifier: NCT02224755) was a prospective, randomized, multicenter, non-blinded, clinical trial that enrolled 1,028 patients at 69 sites in the US. The study randomized patients to receive either the HM3 or HMII LVAD. The study design incorporated an initial safety phase that evaluated 30 subjects at 5 sites prior to study expansion.[8] The primary objective of the trial was to evaluate the safety and efficacy of using the HM3 LVAD in indicated patients at two timepoints: 6 months (short-term n=294) and 2 years (long-term n=366). The primary endpoint was a composite of survival free of disabling stroke or survival free of reoperation to replace or remove the device (for reasons other than recovery).[9] The secondary endpoint, which the study was powered to assess, was freedom from pump exchange through 2-years of follow-up in the full cohort of 1,028 patients. All study endpoints were successfully met.[9-11] The MOMENTUM 3 trial reported the full cohort HM3 actuarial survival at 2-years as 79.0% and stroke rates of 9.9%, suspected pump thrombosis rates of 1.4%, and bleeding rates of 43.7%.[11] Mean EQ-5D-5L score improved from 50 to 76. Performance on the 6-minute walk test improved from 136 to 323 m, and 80% of the subjects were determined to be NYHA class I or II relative to 0% at baseline.

1.1.2 Rationale for Conducting this Post Market Surveillance Study

The objective of this PMS is to assess clinical and functional outcomes under Hong Kong and Taiwanese standard of care for advanced heart failure patients implanted with the HM3 LVAS. PMS participants will be followed until the 24 months follow-up visit or until they experience an outcome, whichever comes first.

2.0 POST MARKET SURVEILLANCE OVERVIEW

2.1 Objective

The primary objective of this prospective, post-market surveillance study is to evaluate the functional and clinical outcomes with the HM3 LVAS, in the setting of Hong Kong and Taiwanese standard of care of advanced heart failure patients implanted with this device.

Secondary objective of this PMS is to assess the adverse events occurring during the surveillance period.

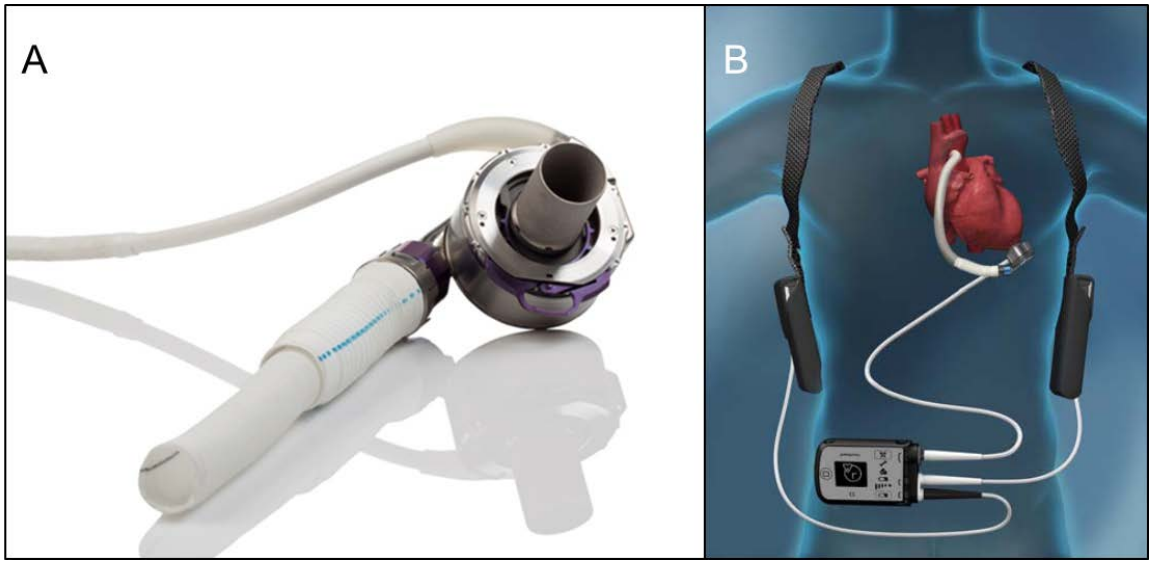
Assessments will include: 6-minute walk test (6MWT), NYHA heart failure severity classification, rates of survival, transplant, pump exchange or explant, device malfunctions, reoperations, rehospitalizations and the incidence of adverse events including, but not limited to, neurological dysfunction, bleeding, infections and device thrombosis. The definitions for the adverse events are in Appendix II and are INTERMACS definitions as used in the MOMENTUM3 study.

Post Market Surveillance Plan

2.2 Device(s) Used in the Post Market Surveillance

This PMS will be assessing functional and clinical outcomes with the HM3 as a treatment for advanced heart failure in the setting of Hong Kong and Taiwan standard-of-care.

Figure 1. The HM3 Left Ventricular Assist System. It comprises of the LVAD (A) with an inflow cannula, outflow graft, modular driveline cable, power source (i.e. batteries or power module that connects to an AC outlet), and a system controller (B).



2.2.1 Indication for Use

Please refer to the country specific IFU for the local indications for use. The HeartMate 3 Left Ventricular Assist System is indicated for providing short- and long-term mechanical circulatory support (e.g. as bridge to transplant or myocardial recovery, or destination therapy) in patients with advanced refractory left ventricular heart failure.

2.2.2 Description of the Device(s) Under Investigation

The HM3 LVAS consists of a centrifugal left ventricular assist device (LVAD) with an outflow graft and modular driveline cable, a pump controller and a power source (i.e. portable Batteries, Power Module, or Mobile Power Unit). The HM3 LVAD is comprised of an Inflow Cannula, a Pump Cover, a Lower Housing, a Screw Ring to attach the Pump Cover to the Lower Housing, a Motor, the Outflow Graft, and a Pump Cable.

The HM3 LVAD has a displacement volume of 80 milliliters and weighs 200 grams. All blood contacting surfaces are composed of titanium (LVAD body and centrifugal rotor) or gelatin-impregnated woven polyester (outflow graft). The HM3 LVAD is designed to reduce adverse events associated with LVAD thrombosis. Primary design features include full magnetic

levitation and large flow gaps, which minimize the shear stress imparted onto the blood elements.

The HM3 Controller is an extracorporeal interface device that receives power from the Power Module, Mobile Power Unit, or portable Batteries, and appropriately delivers that power to the HM3 LVAD. It is the primary user interface and has several important functions including:

- operating condition display,
- source of audible and visible alarms,
- communication link for transferring event/period log and alarm information, and
- battery backup in the case of full power disconnection.

The HM3 LVAD and Controller are sterilized using 100% ethylene oxide. Please refer to each device's respective local IFU for additional information regarding the device used in this PMS study. Modifications made to the device or manufacturing practices in response to issues identified during the MOMENTUM 3 IDE study are described in Appendix IV.

3.0 POST MARKET SURVEILLANCE DESIGN

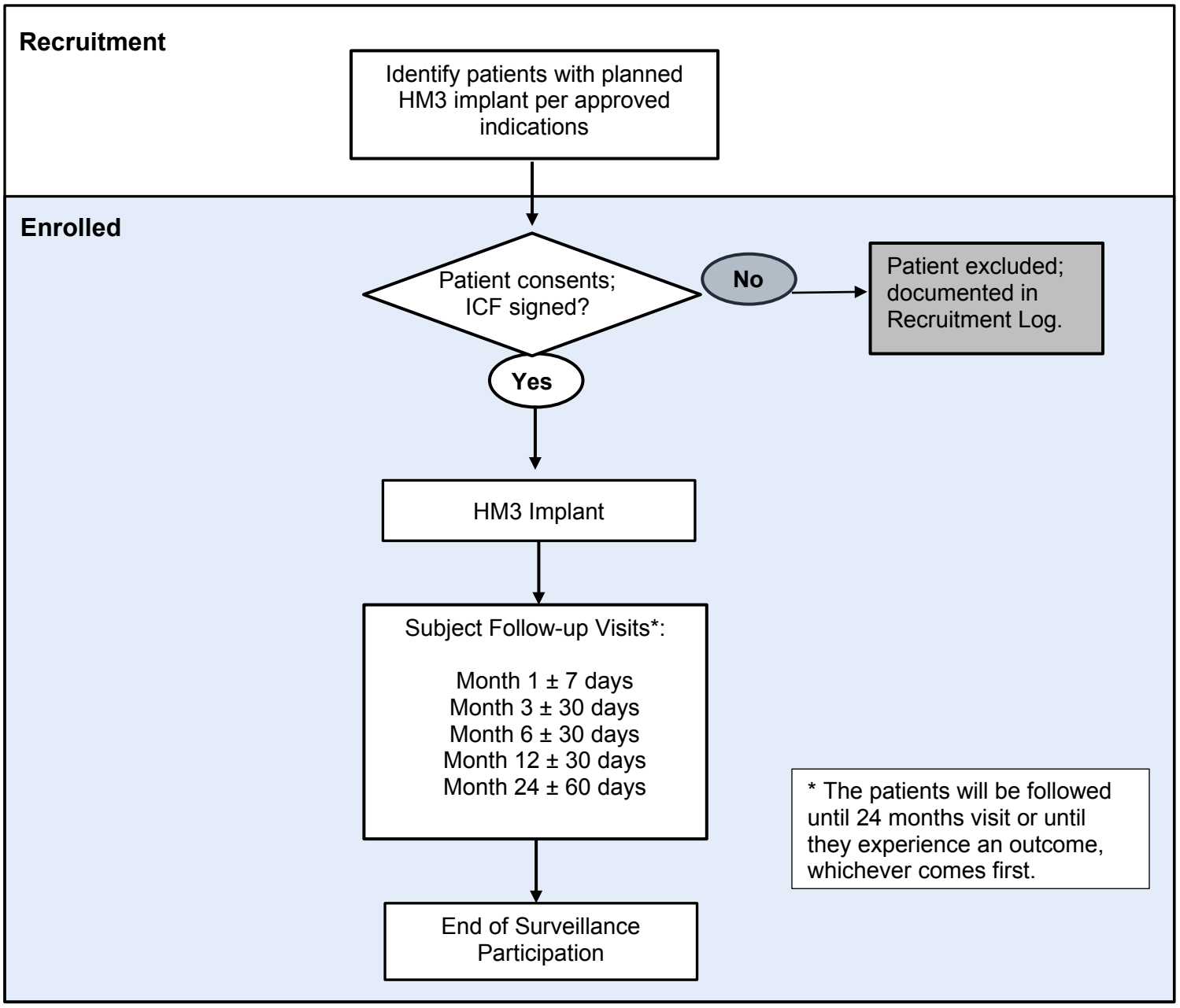
This prospective, single arm, post market surveillance is designed to evaluate clinical and functional outcomes with the HM3 LVAS as a treatment for advanced heart failure. The PMS will enroll approximately 30 patients, that meet the HM3 commercially approved labelling indications, from approximately 4 sites in Hong Kong and Taiwan.

3.1 Procedures and Follow-up Schedule

The PMS Design and follow-up requirements of this post market surveillance study are described below. Follow-up visits will occur at Baseline/Enrollment, HM3 Implant, 1, 3, 6, 12 and 24 months unless the subject experiences an outcome. All visits are relative to HM3 implant.

Post Market Surveillance Plan

Figure 2: Post Market Surveillance Flowchart



3.2 Measures Taken to Avoid and Minimize Bias

Participant selection bias will be minimized by training the PMS sites to provide all patients, that meet the HM3 commercially approved labelling indications, the opportunity to participate in this PMS. A log should be maintained of any subjects that are not included in this Registry and reasons for non-inclusion.

3.3 Suspension or Early Termination of the Post Market Surveillance

While no formal statistical rule for early termination of this PMS is defined, the Sponsor reserves the right to discontinue the PMS at any stage or reduce the follow-up period with suitable written notice to the investigator.

Should the Sponsor discontinue the post market surveillance, sites will follow subjects per routine hospital practice with device-related adverse events (AEs) reported to the Sponsor as per vigilance/commercial reporting requirements. The investigator shall return all post market surveillance materials to the Sponsor and provide a written statement to the IRB (if applicable). All applicable post market surveillance documents shall be subject to the same retention policy as detailed in Section 11.5 of the PMS plan.

If the Sponsor suspends or prematurely terminates the post market surveillance at an individual site in the interest of safety, the Sponsor will inform all other Principal Investigators.

If suspension or premature termination occurs, the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, and return patients to their standard medical treatment, if appropriate.

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

If a suspended investigation is to be resumed, a prior approval should be obtained from the IRB and a notification should be sent to the regulatory bodies.

4.0 POST MARKET SURVEILLANCE OUTCOMES

The objective of this PMS is to gather clinical and functional outcomes data from a country specific patient population that meets the HM3 commercially approved labelling indications.

The primary outcomes that will be evaluated in this post market surveillance include: functional status as measured with the 6MWT, NYHA classification of heart failure severity, quality of life measured with the EQ-5D-5L questionnaire, rates of survival, transplants, pump explant or exchange, device malfunction, reoperations, rehospitalizations and incidence of adverse events. Adverse events include, but are not limited to, neurological dysfunction, bleeding, device thrombosis and infections, that meet the definitions in Appendix II; device malfunctions will be recorded under the general category of Device Deficiencies (section 7.1.3) and is further explained in Appendix II.

Post Market Surveillance Plan

5.0 SUBJECT SELECTION AND WITHDRAWAL

5.1 Subject Population

This post market surveillance will enroll advanced heart failure patients of all genders with a planned HM3 implant, that meet the HM3 commercially approved labelling indications. Patients must provide written informed consent prior to sites conducting any investigation-specific procedures not considered standard of care.

5.2 Subject Recruitment/Screening and Informed Consent

5.2.1 Subject Recruitment and Screening

A member of the site's post market surveillance team, previously trained to the PMS plan, must evaluate patients for the PMS eligibility criteria (Section 5.3), and if applicable, will enter the patients into a site-specific recruitment log. A patient who does not satisfy all eligibility criteria prior to informed consent is considered a recruitment failure and should not be enrolled in the post market surveillance.

Sites will ask the patients meeting the eligibility criteria to sign an Informed Consent form following the established Informed Consent process (described in Section 5.2.2) if they wish to participate in the post market surveillance. Sites will enter these patients into the recruitment log.

5.2.2 Informed Consent

The Investigator or his/her authorized designee (if applicable) will conduct the Informed Consent process, as required by applicable regulations and the center's IRB. This process will include a verbal discussion with the patient on all aspects of the post market surveillance that are relevant to the patient's decision to participate, such as details of post market surveillance procedures, anticipated benefits, and potential risks of post market surveillance participation. Sites must inform patients about their right to withdraw from the post market surveillance at any time and for any reason without sanction, penalty, or loss of benefits to which the patient is otherwise entitled. Withdrawal from the post market surveillance will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the patient and will respect patient's legal rights. Financial incentives will not be given to patients. Patients may be compensated for time and travel directly related to the participation in the post market surveillance. The site shall provide the patient with the Informed Consent form written in a language that is understandable to the patient and that has been approved by the center's IRB. The patient shall have adequate time to review, ask questions, and consider participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the patient understands the information provided. If the patient agrees to participate, they must sign and date the Informed Consent form, along with the person obtaining the consent prior to any post market surveillance-specific procedures. The site will file the signed original in the patient's hospital or research charts and provide a copy to the patient.

Sites should report any failure to obtain informed consent from a patient to the Sponsor within 5 working days and to the reviewing center's IRB according to the IRB's reporting requirements.

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

This PMS will not permit informed consent via legally authorized representatives. Therefore, incapacitated individuals, including the mentally handicapped or individuals without legal authority or individuals under the age of 18 or local age of legal consent, are excluded from the PMS population. Furthermore, individuals unable to read or write are excluded from the PMS population.

5.3 Eligibility Criteria

All patients at the participating sites that are determined to meet the HM3 commercially approved labelling indication and have a planned HM3 implant are eligible to participate in this PMS. Assessment for eligibility criteria is based on medical records of the site and interview with a candidate patient.

5.4 Subject Enrollment

A patient is considered enrolled in the post market surveillance from the moment the patient provides written informed consent.

5.5 Subject Withdrawal and Discontinuation

All subjects enrolled in the study shall remain in the post market surveillance until they performed the 24 month follow-up or they experience an outcome (death, transplant, HM3 explant or exchange, or withdrawal), whichever comes first; however, a subject's participation in any clinical investigation is voluntary and the subject has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but not be limited to, the following:

- Physician or subject voluntary withdrawal
- Subject lost-to follow-up as described below
- Non-compliance with the PMS plan
- Subject is not on primary HM3 support

Sites must notify the Sponsor of the reason(s) for subject discontinuation. Investigators must also report this to their respective IRB as defined by their institution's procedure(s).

No additional follow-up is required, or data recorded from subjects once withdrawn from the post market surveillance, except for the status (deceased/alive).

In case of subject withdrawal of consent, the site should make attempts to schedule the subject for a final post market surveillance visit. At this final follow-up visit, the subject will undergo the following assessments:

- Adverse events since the last follow-up
- Transplant, explant/exchange or device deficiency since the last follow-up
- Subject outcomes

Lost-to-Follow-up

If the subject misses two consecutive scheduled follow-up time points and the attempts at contacting the subject detailed below are unsuccessful, then the subject is considered lost-to-follow-up. Site personnel shall make all reasonable efforts to locate and communicate with the subject (and document these efforts in the source documents), including the following, at each contact time point:

- A minimum of two telephone calls on different days over the specified follow-up windows to contact the subject should be recorded in the source documentation, including date, time and initials of site personnel trying to make contact.
- If these attempts are unsuccessful, the site should send a letter (certified if applicable) to the subject.
- If a subject misses one or more non-consecutive follow-up contact time points, it will be considered a missed visit. The subject may then return for subsequent visits. If the subject misses two consecutive time points and the above-mentioned attempts at communicating with the subject are unsuccessful, the subject will be considered lost-to-follow-up.

Note: Telephone contact with general practitioner, non-PMS cardiologist or relative without the presence of the subject or indirect documentation obtained via discharge letters will not be considered as subject contact.

5.6 Number of Subjects

All consecutive patients at the participating sites with a planned HM3 implant, that meet the HM3 commercially approved labelling indications, will be enrolled in the PMS. We expect, approximately 30 subjects will be enrolled.

5.7 Total Expected Duration of the Post market surveillance

Subject follow-up will occur at the time of Baseline/Enrollment, HM3 Implant, and at 1, 3, 6, 12 and 24 months post HM3 implant, unless the subject experiences an outcome. The total duration of the Post Market Surveillance is estimated to be 36 months.

Post Market Surveillance Plan

6.0 TREATMENT AND EVALUATION OF ENDPOINTS

6.1 Baseline/Enrollment

The assessments listed in **Table 1** should be performed prior to the HM3 implant.

Table 1: Pre-implant Baseline Assessments

Study Activity	Data Collection
Informed Consent	Explain post market surveillance study and obtain informed consent as described in section 5.2.2
Demographics	Age, height, gender, ethnic origin, blood type
General and Cardiac Medical History	• Etiology and duration of heart failure • Therapeutic intent (BTT/BTC/DT)[1] • Arrhythmias • Valve repair/replacement • History of organ transplant, stroke, TIA, smoking, bleeding[2], valve disease, hypertension, MI, peripheral non-CNS thrombosis/thromboembolism, substance abuse (drug/alcohol), drug/radiation toxicity, peripheral vascular disease, carotid artery disease, coronary artery disease, coronary stents, CABG, cancer, allergies, renal insufficiency/failure and psychiatric, head, ear, nose, throat, dermatological, coagulation, inflammatory, gastrointestinal, genitourinary, respiratory or endocrine disorders, cardiac arrest, aortic stenosis. • Cardiac rhythm management device • Intra-aortic balloon pump • Other pre-implant circulatory support • CardioMEMS™, MitraClip™
Vital Signs	Weight, blood pressure and method, and heart rate
Medications	Inotropes, Anticoagulation/Antiplatelet (aspirin, Persantine, Plavix, warfarin, Other), antibiotics, vasodilators, diuretics, anti-arrhythmic, ACEi, ARB and beta blockers.
Laboratory Assessments[3]	Hemoglobin, hematocrit, white blood cell count, platelets, creatinine, estimated glomerular filtration rate, liver function tests (AST, ALT, total bilirubin, albumin, pre-albumin), blood urea nitrogen, INR, LDH.

Post Market Surveillance Plan

Study Activity	Data Collection
Right Heart Catheterization[4]	Central venous pressure (CVP) or right atrial pressure (RAP), systolic, diastolic and mean pulmonary artery pressure (PAS, PAD, PAM), pulmonary capillary wedge pressure (PCWP), cardiac output (CO), and cardiac index (CI)
Echocardiogram[4]	Type of assessment, LVEF, LVEDD, LVESD, AI, MR, TR, PR, including severity and/or grade, and presence of LV or LA thrombus, and aortic valve opening ratio
Functional Capacity	6-minute Walk Test[5], NYHA Class, INTERMACS Profile
Quality of Life	EQ-5D-5L quality of life questionnaire

[1] BTT – bridge to transplant; BTC – bridge to transplant candidacy; DT – destination therapy.
[2] Bleeding includes diverticular disease, diagnosed arteriovenous malformations (AVMs), GI ulcer(s), anemia and/or erythropoietin treatment.
[3] Most recent results obtained within 30 days prior to implant will be permitted as baseline data.
[4] If collected per standard of care, most recent results within 30 days prior to implant.
[5] If subject is able, else reason must be provided if not performed.

6.2 Implant

The data in **Table 2** will be collected for each subject's HM3 implant procedure.

Table 2. Data to be collected at the time of HM3 implant.

Study Activity	Data Collection
HM3 System Information	VAD serial number, reference number and date of implant of entire implanted system
Implant Data	• Presence of intracardiac (LA or LV) thrombus • Concurrent procedures • Administration of factor VII, vitamin K or anti-fibrinolytic • Pump position • Apical cuff attachment method • Drive line related information • Transfusion of whole blood, packed red blood cells [PRBC], fresh frozen plasma [FFP], platelets, cryoprecipitate, or Cell Saver • Intraoperative medications • Cardiopulmonary bypass (CPB) time

	• ECMO • Total implant time • Location of outflow anastomoses • Additional post-implant MCS • Hematocrit value
Pump Parameters	Pump speed, flow, power and pulsatility index

6.3 Follow-Up Visit Assessments

The assessments listed in **Table 3** will be performed at all other visits (i.e. at 1, 3, 6, 12 and 24 months) post HM3 Implant, unless the subject experiences an outcome; for the purposes of this PMS a month is defined as 30 days. The required assessments, follow-up schedule, and associated visit windows (**Table 4**) are generally aligned with SOC LVAD patient follow up. All follow-up visits are based on the HM3 implant date.

Table 3. Follow-up visit assessments.

Study Activity	Definition
Subject Status	Whether the subject is on HM3 LVAD support, if not, what was the outcome the patient experienced (i.e. death, transplant, withdrawn, pump exchange or explant)
Vital Signs	Weight, blood pressure and method of blood pressure measurement, and heart rate
Pump Parameters	Pump speed, flow, power and pulsatility index
Medications	Inotropes, anticoagulation/antiplatelet (Aspirin, Persantine, Plavix, warfarin, Other), antibiotics, vasodilators, diuretics, anti-arrhythmic, ACEi, ARB and beta blockers.
Laboratory Assessments	Hemoglobin, hematocrit, white blood cell count, platelets, creatinine, estimated glomerular filtration rate, liver function tests (AST, ALT, total bilirubin, albumin, pre-albumin), blood urea nitrogen, INR, LDH.
Echocardiogram[1]	LVEF, LVEDD, LVESD, AI, MR, TR, PR, including new onset, severity and/or grade, and presence of LV or LA thrombus, and aortic valve opening ratio
Functional Capacity	6-minute Walk Test and NYHA Class
Quality of Life	EQ-5D-5L quality of life questionnaire

[1] *If collected per SOC.*

The follow-up visit must occur within the designated window (**Table 4**). The assessments for a single visit do not have to occur on the same date, but must occur within the designated window, or will be considered a protocol deviation. The Sponsor understands that some lab results may be received several days after the visit has occurred, in these instances the date

the blood draw occurred will be considered as the date of the lab assessment. All subjects should be asked, at each follow up visit, if they were seen at an outside facility. If so, medical records from any facility that has seen the patient must, with the subject's consent, be requested and reviewed for potential adverse events.

Table 4. Follow-up visit windows.

Visit 0	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
Baseline/ Enrollment	Implant	Month 1 ± 7 days	Month 3 ± 30 days	Month 6 ± 30 days	Month 12 ± 30 days	Month 24 ± 60 days
Patients will be followed until the 24 months visit or they experience an outcome.						

6.4 Unscheduled Visits

6.4.1 Adverse Events

Relevant data related to adverse events will be collected as they occur. For additional details regarding adverse events, including mandated reporting timelines, refer to section 7.

6.4.2 Reoperations

Data related to any cardiac or non-cardiac reoperations, occurring after enrollment will be collected. Reoperations must be reported to the Sponsor through the EDC system within three days of awareness of the event or, at the latest, if the operation was unknown to the implanting site (i.e. occurring at another facility), during the next follow-up visit. For pump exchanges, additional implant data will be collected, including exchange status and pump exchange type.

6.4.3 Rehospitalizations

All rehospitalizations with associated reasons will be captured during the follow-up period for all subjects. While hospitalized, the follow-up visit assessments will continue to be performed according to the follow-up schedule. Hospitalizations must be reported to the Sponsor through the EDC system within three days of awareness or discovery of the event or, at the latest, if the hospitalization is unknown to the implanting site (i.e. occurring at another facility), during the next follow-up visit.

6.5 Subject Outcomes

Subjects will be followed until the 24-month follow-up is completed or until they experience an outcome, whichever occurs first. Outcomes include death, heart transplantation, HM3 exchange or explant, and withdrawal from the PMS. Outcomes must be reported to the Sponsor through the EDC system immediately upon discovery of the event.

6.6 Schedule of Events

All of the post market surveillance assessments and their schedule are listed in **Table 5**.

Post Market Surveillance Plan

Table 5. Schedule of assessments.

Assessment	Baseline/ Enrollment	HM3 Implant	Month 1[1] (± 7 days)	Month 3[1] (± 30 days)	Month 6[1] (± 30 days)	Month 12[1] (± 30 days)	Month 24 (± 60 days)	As Occurs or Unscheduled
Eligibility Assessment	X							
Informed Consent	X							
Demographics	X							
General and Cardiac Medical History	X							
Right Heart Catheterization	X[2]							X[2]
HM3 Information		X						X[3]
Implant Data		X						X[3]
Vital Signs	X		X	X	X	X	X	X
Laboratory Assessments	X		X	X	X	X	X	X
Echocardiogram	X[2]		X[2]	X[2]	X[2]	X[2]	X[2]	X[2]
Medications	X		X	X	X	X	X	X
Functional Capacity	X		X	X	X	X	X	X[2]
EQ-5D-5L Quality of Life Questionnaire	X		X	X	X	X	X	X[2]
Pump Parameters		X	X	X	X	X	X	X
Subject Status			X	X	X	X	X	X
Subject Outcome								X
Rehospitalizations								X
Adverse Events								X
Device Deficiencies[4,5]								X
Modified Rankin Score (MRS) Assessment[6]								X
Reoperations (excluding primary implant)								X
Protocol Deviations	X	X	X	X	X	X	X	X
COVID-19 questions (if applicable)	X	X	X	X	X	X	X	X

Note: Patients will be followed until the 24 months visit or they experience an outcome, whichever comes first.
[1]One month = 30 days.
[2]If performed as standard of care.
[3]Implant data for HM3 to HM3 exchange(s) and only relevant information for non-HM3 exchange.
[4]Device deficiencies that result in adverse events only. Please see section 7.3.2 for further information.

Post Market Surveillance Plan

Assessment	Baseline/ Enrollment	HM3 Implant	Month 1[1] (± 7 days)	Month 3[1] (± 30 days)	Month 6[1] (± 30 days)	Month 12[1] (± 30 days)	Month 24 (± 60 days)	As Occurs or Unscheduled

[5]*Device malfunction is included within the definition of Device Deficiency.*
[6] *Required only if a stroke has occurred*

7.0 Adverse Events

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

7.1 Definition

7.1.1 Adverse Event

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

As part of ISO14155 Section 3.2, the Adverse Event definition has the following notes:

Note 1: This definition includes events related to the medical device under investigation or the comparator.

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

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

7.1.2 Serious Adverse Event

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

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

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

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

7.1.3 Device Deficiency

Device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling. This includes the failure of the device to meet its performance specifications or otherwise perform as intended. Note: performance specifications include all claims made in the labeling of the device.

7.2 Device Relationship

Determination of whether there is a reasonable possibility that the device under investigation caused or contributed to an AE is to be **determined by the Investigator** and recorded on the appropriate Case Report Form (CRF). Determination should be based on the assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility and patient condition (pre-existing condition). If an AE or Device Deficiency is determined to be pump-related or possibly related, pump parameters should be reported in the appropriate CRF.

7.3 Adverse Event and Device Deficiency Reporting

7.3.1 Adverse Event Reporting

Safety surveillance and reporting starts as soon as the patient is enrolled in the post market surveillance. Safety surveillance and reporting will continue until sites perform the last follow-up visit, the subject is deceased, the subject concludes participation in the post market surveillance, or the subject withdraws from the post market surveillance. Sites will collect all adverse event data, including deaths and device deficiency data, throughout the period defined above and will report these events to the Sponsor on a CRF. Sites should update additional information regarding an adverse event on the appropriate CRF.

Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported.

The Sponsor will provide an offline form to allow the investigator to report SAEs in the event the entry cannot be made in the EDC. This does not replace the EDC reporting system. Sites must still enter all information in the EDC system as soon as feasible.

Non-cardiac related abnormal laboratory values will not be considered AEs unless:

1. the investigator determined that the value is clinically significant, OR
2. the abnormal lab value required intervention, OR
3. the abnormal lab value required subject withdrawal from the post market surveillance

Post Market Surveillance Plan

All adverse events will be collected on each subject throughout the follow up period – until the subject reaches an outcome or withdraws or until the surveillance ends. Causes of death will be captured for all subjects who expire during follow up.

SAE Reporting

The investigator must report all SAEs to the Sponsor as soon as possible but no later than outlined below.

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

Sites must record the date the site staff became aware that the event met the criteria of an SAE in the source document. The Investigator will further report the SAE to the local IRB according to the institution's IRB reporting requirements.

7.3.2 Device Deficiency Reporting

Device deficiencies should be reported on the appropriate CRF form only if they are associated with any adverse events.

The investigator should report device deficiencies associated with AEs to the Sponsor as soon as possible but no later than outlined below.

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

Device deficiencies should be reported to the IRB per the investigative site's local requirements.

An offline form will be made available to allow the investigator to report device deficiencies, if the entry cannot be made in the EDC system. This does not replace the EDC reporting system. All information must still be entered in the EDC system as soon as feasible.

In case a device deficiency occurred before the patient ID number has been assigned, the device deficiency should be reported to the Sponsor via the offline reporting form.

Irrespective of the device deficiency requirement per this investigation, the site must submit all device deficiencies to Sponsor Product Performance Group in order to be captured in the Sponsor complaints database.

7.3.3 Adverse Event and Device Deficiency Reporting to Country Regulatory Authorities by the Sponsor

The Sponsor will report SAEs and reportable device deficiencies to the country regulatory authority, per local requirements. All reportable events will be reported to the Competent Authority per the applicable regulations by the Product Performance Group (PPG).

8.0 STATISTICAL CONSIDERATIONS

8.1 Analysis Populations

Data from all enrolled subjects will be used in the analyses. Subjects will be followed until they experience an outcome (death, transplant, HM3 exchange/explant or withdrawal) or the 24 month follow-up visit is completed, whichever occurs first.

8.2 Statistical Analyses

In general, continuous data will be presented with measures of central tendency (e.g. mean, median) and deviation (e.g. standard deviation, inter-quartile range). Discrete events will be presented as frequency and percentage.

8.2.1 Primary Efficacy Endpoint

Primary efficacy endpoint is defined as the overall survival to transplant, myocardial recovery or on device support free of debilitating stroke (Modified Rankin Score >3) or reoperation for pump replacement during the 2-year surveillance period; this will be assessed using the Kaplan-Meier product-limit method along with a competing outcomes graph. Subjects who are urgently transplanted due to a HeartMate 3 malfunction will be considered to have experienced a primary endpoint event, as will subjects who expire, suffer a debilitating stroke or have their HeartMate 3 exchanged due to a device failure. Subjects who are transplanted (except as described above), explanted for recovery, withdraw from the trial or are lost to follow-up will be censored at that time in the analysis.

8.2.2 Primary Safety Endpoint

Primary safety endpoint is measured by all pre-defined adverse events. Cumulative occurrence of adverse events during the surveillance period will be presented as percent of patients with adverse events and events per patient year of support.

8.2.3 Secondary Efficacy and Safety Endpoints

8.2.3.1 Six-minute Walk Test

Subjects may not be able to walk due to heart failure, especially at baseline. Subjects unable to walk due to heart failure will receive a score of 0 meters. For all other reasons, missing data will

remain missing and will not be included in the analysis. The 6-minute Walk test will be conducted at all follow-up visits until the end of the surveillance period. The overall mean, median, standard deviation, minimum and maximum will be presented for all follow-up visits. Differences in walking distance between each visit and baseline will be calculated and assessed for improvements using paired, nonparametric Wilcoxon signed-rank test. In addition, box plots will be used to show changes in walking distance over time.

8.2.3.2 NYHA

Subjects' NYHA Functional Status will be assessed at all scheduled follow-up visits until the end of the surveillance period. Percent of subjects in each NYHA class will be presented for all follow-up visits. For comparison, patients will be grouped into NYHA Class I/II (No limitation and Slight limitation of physical activity) vs. NYHA Class III/IV (Marked limitation and Inability to carry out physical activities). McNemar's test will then be used to assess if there is an increase in proportion of Class I and II subjects at each visit comparing to the baseline. In addition, bar charts will be used to show changes in NYHA classification over time.

8.2.3.3 EQ-5D-5L quality of life (QoL) questionnaire

Subject's quality of life will be measured by the EQ-5D-5L QoL questionnaire at baseline and all visits after HM3 implant until the end of surveillance period. The overall mean, median, standard deviation, minimum and maximum will be presented for all follow-up visits. Differences in QoL Score between each visit and baseline will be calculated and assessed for improvements using paired, nonparametric Wilcoxon signed-rank test. In addition, box plots will be used to show changes in QoL over time.

8.2.3.4 Rehospitalization and Reoperation

Frequency and reason will be reported for rehospitalization and reoperation. Freedom from rehospitalization and reoperation will be assessed using the Kaplan-Meier product-limit method.

8.2.3.5 Device Malfunctions

All suspected HM3 device malfunctions will be reported. Data on device malfunctions will be analyzed and tables will be created that report the following:

- The component of the device involved
- Days to the malfunction
- Action taken in response to the malfunction
- Reoperations due to malfunction
- Death due to malfunction

Note: Device malfunctions will be collected under the general category of Device Deficiencies (section 7.1.3) and the term is defined further in Appendix II.

8.3 Sample Size Calculation

Sample size is based on an estimate of the number of consecutive patients likely to be implanted with a HM3 at the participating sites during the surveillance period.

8.4 Timing of Analysis

All endpoints will be assessed at the end of the surveillance period.

8.5 Subgroup Analysis

No subgroup analyses are planned for this PMS.

8.6 Procedures for Accounting for Missing Data

Data collected outside of the study visit window will be excluded from the analysis. Except for 6-minute Walk Test stated above, missing data will not be imputed.

8.7 Planned Interim Analysis

No interim analyses are planned for this PMS.

8.8 Deviations from Statistical Plan

The Sponsor will document any major changes to the analysis plan in an amendment to the SAP and any less significant changes to the planned analyses in the final report.

9.0 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The investigator/institution will permit direct access to source data/documents for performing post market surveillance-related monitoring, audits, IRB review and regulatory inspections.

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

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

10.1 Selection of Clinical Sites and Investigators

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

10.2 PMS plan Amendments

The Sponsor will provide approved PMS plan amendments to the Investigators prior to implementing the amendment. The Principal Investigator is responsible for notifying the IRB or

equivalent committee of the PMS plan amendment (administrative changes) or obtaining IRB's approval of the PMS plan amendment (changes in subject care or safety), according to the instructions provided by the Sponsor with the PMS plan amendment.

Sites must document in writing acknowledgement/approval of the PMS plan amendment by the IRB prior to implementation of the PMS plan amendment. Sites must also provide copies of this documentation to the Sponsor.

10.3 Training

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

10.4 Monitoring

Sponsor and/or designee will monitor the post market surveillance over its duration according to the PMS plan-specific monitoring plan which will include the planned extent of source data verification.

Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

- The investigator understands and accepts the obligation to conduct the post market surveillance according to the PMS plan and applicable regulations and has signed the Clinical Trial Agreement.
- The Investigator and his/her staff should have sufficient time and facilities to conduct the post market surveillance and should have access to an adequate number of appropriate subjects to conduct the post market surveillance.
- Sites must have source documentation (including original medical records) to substantiate proper informed consent procedures, adherence to PMS procedures, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.
- The Investigator/site will permit access to such records and will maintain a monitoring visit sign-in log at the site. The Investigator will agree to dedicate an adequate amount of time to the monitoring process. The Investigator and/or research coordinator will be available for monitoring visits. It is expected that the Investigator will provide the monitor with a suitable working environment for review of post market surveillance-related documents.

Post Market Surveillance Plan

10.5 Deviations from PMS plan

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

The Sponsor will not grant any waivers for PMS plan deviations. Sites must report all deviations to the Sponsor using the Deviation CRF. The Sponsor will monitor the occurrence of deviations from the PMS plan for evaluation of investigator compliance to the PMS plan and regulatory requirements and handle according to written procedures. Investigators will inform their IRB or equivalent committee of all PMS plan deviations in accordance with their specific IRB or equivalent committee reporting policies and procedures.

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

- Visiting the investigator and/or delegate
- Telephoning the investigator and/or delegate
- Corresponding with the investigator and/or delegate

Repeated non-compliance with the signed agreement, the PMS plan, or any other conditions of the post market surveillance may result in further escalation in accordance with the Sponsor's written procedures, including securing compliance or, at its sole discretion, the Sponsor may terminate the investigator's participation in the post market surveillance.

10.6 Quality Assurance Audit

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

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

11.0 DATA HANDLING AND RECORD KEEPING

Sponsor and/or its affiliates will maintain documentation of the systems and procedures used in data collection for the duration of the post market surveillance. CRF data collection will be performed through a secure web portal and only authorized personnel will access the EDC system using a unique username and password to enter, review or correct data. Passwords and

electronic signatures will be strictly confidential. The data will be subjected to consistency and validation checks within the EDC system and supplemental review by the Sponsor. At the end of the post market surveillance, completed CRF images with the date-and-time stamped electronic audit trail indicating the user, the data entered, and any reason for change (if applicable) will be provided to the investigational sites, if requested.

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

11.1 Protection of Personally Identifiable Information

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

The Sponsor requires the investigational sites to enter only pseudonymous Personal Information (key-coded) necessary to conduct the post market surveillance, such as the patient's medical condition, treatment, dates of treatment, etc., into Sponsor's data management systems. The Sponsor discloses as part of the post market surveillance informed consent process that some Sponsor representatives still may see Personal Information at the participating sites for technical support of the participating physicians on the device implant or procedures, monitoring and quality control purposes. All parties will observe confidentiality of Personal Information always throughout the post market surveillance. All reports and data publications will preserve the privacy of each subject and confidentiality of his/her information.

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

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

11.2 Data Management Plan

A Data Management Plan (DMP) will describe procedures used for data review, data cleaning, and issuing and resolving data discrepancies. If appropriate, the Sponsor may update the DMP

throughout the duration of the post market surveillance. The Sponsor will track and document control all revisions.

11.3 Source Documentation

Regulations require the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. To comply with these regulatory requirements, sites should include the following information in the subject record at a minimum and if applicable to the post market surveillance:

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

11.4 Case Report Form Completion

Site research personnel trained on the PMS plan and CRF completion will perform the primary data collection clearly and accurately based on source-documented hospital and/or clinic chart reviews. The investigator will ensure accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor on the CRFs and in all required reports. Sites will collect data on all subjects who sign an informed consent form until they experience an outcome or the 24 month visit is completed. Only authorized site personnel will be permitted to enter the CRF data through the EDC system deployed by the Sponsor. The Sponsor will use an electronic audit trail to track any subsequent changes of the entered data.

11.5 Record Retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the post market surveillance as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any post market surveillance records.

12.0 ETHICAL CONSIDERATION

12.1 Institutional Review Board Approval

The Principal Investigator at each investigational site will obtain IRB approval for the PMS plan and ICF/other written information provided to the patient prior to consenting and enrolling patients in this post market surveillance. The site must receive the approval letter prior to the start of this post market surveillance and provide a copy to the Sponsor.

Sites will submit any amendments to the PMS plan as well as associated ICF changes to the IRB and written approval obtained prior to implementation, according to each institution's IRB requirements.

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

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

Sites will not perform any investigative procedures, other than those defined in this PMS plan, on the enrolled subjects without the written agreement of the IRB and the Sponsor.

13.0 POST MARKET SURVEILLANCE CONCLUSION

The post market surveillance will be concluded when:

- All sites are closed, AND
- The final report has been provided to investigators or the Sponsor has provided formal documentation of post market surveillance closure.

14.0 PUBLICATION POLICY

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

Post Market Surveillance Plan

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

15.0 RISK ANALYSIS

15.1 Anticipated Clinical Benefits

In addition to improved functional status and quality of life, advanced heart failure patients may experience the following clinical benefits from use of the HM3 LVAD as compared to the HeartMate II LVAD[11]:
1. improved survival free from stroke of any type or severity
2. significantly lower risk of pump thrombosis
3. lower risk of need for reoperation for pump replacement
4. a lower risk of rehospitalization and device malfunction

15.2 Foreseeable Adverse Events and Anticipated Adverse Device Effects

Risks associated with the specified device and procedure, together with their likely incidence, are described in Appendix IV.

15.3 Residual Risks Associated with the Device Under Investigation, as Identified in the Risk Management Report / Risk Analysis Report

Risk analysis of the HM3 device has been performed in accordance with Abbott's risk management and mitigation process, demonstrating systematic identification of hazards associated with the design and use of this device. Based upon bench testing and prior Abbott sponsored clinical study data, all risks have been mitigated as far as possible through application of risk controls documented in the risk management file. The overall risk benefit analysis concludes that the risks are outweighed by the benefits.

Residual risks are likewise disclosed in the IFU in the form of clear instructions of what actions to take or to avoid, in order to avoid a hazardous situation of harm from occurring (contra-indications, warnings, and precautions). The anticipated AEs disclosed in the IFU (and PMS plan Appendix IV) provide further information to enable the user, and potentially the patient, to make an informed decision that weights the residual risk against the benefit of using the device.

15.4 Risks Associated with Participation in this Post Market Surveillance

All anticipated adverse events with the HM3 and the implant procedure are disclosed in Appendix IV. All the Study assessments (listed in Tables 1-4) are standard of care and would be performed even if the patient is not enrolled in this post market surveillance study.

Post Market Surveillance Plan

15.5 Steps Taken to Control or Mitigate Risks

In-depth recommendations, special precautions and instructions regarding subject selection, device handling, physician training, device placement and system removal are included in the IFU. Mitigations and treatment for all adverse events will be performed per the current practice standards/standards of care as determined by the Investigator.

Device Design

The HM3 has several features to mitigate the risks to the patients including, but not limited to the following:

- Alarms audibly and visibly indicate problems, such as low flow, to the patients, when appropriate. The alarms are also modulated in duration depending on the severity of the problem (Hazard vs. Advisory alarms).
- The power cables (i.e. driveline) have been designed to be difficult to unintentionally disconnect.
- The device was designed to be in compliance with international regulations on fire and shock hazards, biocompatibility, electromagnetic emissions and interference, and sterilization. These are outlined in the IFU.
- The IFU for the HM3 describes the validated implant technique.
- The LVAS is supplied with additional accessories to facilitate activities of daily living (e.g. shower bag) and the proper use of the device for different scenarios is explained in the IFU.
- The IFU has checklists of items that need to be checked periodically to ensure proper device function and to identify problems before they become critical.
- The HM3 LVAD has wide blood-flow paths and an artificial pulse feature to prevent stasis within the pump and thereby minimize the risk of thrombus formation.
- The HM3 LVAD has no mechanical bearings, which minimizes the damage to the components of the blood when flowing through the pump.
- The driveline cable was made modular via an inline connector to be able to replace the external segment without having to replace the entire system, thereby obviating pump exchange for driveline damage on the Controller side of the inline connector.
- Where appropriate, blood contacting surfaces have been texturized to prevent the formation of clots.

Please refer to the IFU for further information on the safety features of the HM3 LVAS.

Investigator Selection and Training:

It is also stated in the IFU that the devices can only be used by physicians who have received appropriate training on the proper use of the device. This statement is interpreted to mean that the physician users must complete Sponsor-provided HM3 training prior to clinical use and are expected to be aware of the known and foreseeable safety risks associated with the use of the devices including the surgical and/or non-surgical treatment of these conditions. Emergency surgical back-up should be available as per the institution's standard procedures. Cases may be supported by Abbott field personnel.

Ensuring Strict Adherence to the PMS plan

Post Market Surveillance Plan

The post market surveillance will be carefully monitored by the Sponsor monitor (or designee) to ensure adherence to the PMS plan. Adverse events and device deficiencies will be reported to the Sponsor/designee and will be monitored internally for safety surveillance purposes.

Study Participation Risk Mitigation

Subject risk from participation will be mitigated by ensuring that only experienced LVAD personnel will be involved in the care of research subjects. In addition to providing local product specific IFU, staff involved in this post market surveillance study will have undergone product and PMS plan training prior to initiating study-related activities, and all subjects will be closely monitored throughout the surveillance period at pre-specified time points to assess their clinical status.

Specific information applicable to this PMS are listed below.

- It is suggested that patients possess a minimum 5th grade educational level.
- All users, including clinicians, patients, and caregivers, will be trained on HM3 system operation and safety before use.
- Clinical procedures, including adjustments to LVAS settings, should be conducted under the direction of the prescribing physician (Authorized Personnel) only.

15.6 Risk to Benefit Rationale

Participation in this post market surveillance study does not have any additional benefits or risks beyond what a patient may otherwise experience with the approved HM3 LVAS. However, this PMS will allow the collection of country specific data to incorporate within the continuing Risk Management activities of the Sponsor.

Post Market Surveillance Plan

APPENDIX I: ABBREVIATIONS AND ACRONYMS

Abbreviation	Term
ACEi	Angiotensin Converting Enzyme inhibitor
AE	Adverse Event
AI	Aortic Insufficiency
ALT	Alanine Aminotransferase
ARB	Angiotensin II Receptor Blockers
AST	Aspartate Aminotransferase
BTC	Bridge-to-Candidacy
BTT	Bridge-to-Transplant
CABG	Coronary Artery Bypass Graft
CI	Cardiac Index
CK	Creatinine Kinase
CK-MB	Creatinine Kinase Muscle/Brain
CNS	Central Nervous System
CO	Cardiac Output
CPB	Cardiopulmonary Bypass
CRF	Case Report Form
CT	Computed Tomography
CVP	Central Venous Pressure
DMP	Data Management Plan
DT	Destination Therapy
EDC	Electronic Data Capture
EPPY	Events Per Patient Year
eGFR	Estimated Glomerular Filtration Rate
FDA	Food and Drug Administration
GI	Gastrointestinal
HIE	Hypoxic-ischemic injury
HM3	HeartMate 3
ICF	Informed Consent Form
ICH	Intracranial Hemorrhage
IFU	Instructions for Use
INR	International Normalized Ratio
INTERMACS	Interagency Registry for Mechanically Assisted Circulatory Support
IRB	Institutional Review Board
LA	Left Atrium
LAA	Left Atrial Appendage
LDH	Lactate dehydrogenase

Post Market Surveillance Plan

Abbreviation	Term
LV	Left Ventricle
LVAD	Left Ventricular Assist Device
LVAS	Left Ventricular Assist System
LVEDD	Left Ventricular End Diastolic Diameter
LVEF	Left Ventricular Ejection Fraction
LVESD	Left Ventricular End Systolic Diameter
MCS	Mechanical Circulatory Support
MCSD	Mechanical Circulatory Support Device
MI	Myocardial Infarction
MOMENTUM3	Multi-center Study of MagLev Technology in Patients Undergoing MCS Therapy With HeartMate 3™ IDE Study
MR	Mitral Regurgitation
MRI	Magnetic Resonance Imaging
MRS	Modified Rankin Score
MFDS	Ministry of Food and Drug Safety
NYHA	New York Heart Association
PAD	Diastolic Pulmonary Artery Pressure
PAS	Systolic Pulmonary Artery Pressure
PAM	Mean Pulmonary Artery Pressure
PMS	Post Market Surveillance
PR	Pulmonary Regurgitation
PRBC	Packed Red Blood Cells
PCWP	Pulmonary Capillary Wedge Pressure
RAP	Right Atrial Pressure
RHF	Right Heart Failure
RVAD	Right Ventricular Assist Device
SAE	Serious Adverse Event
SOC	Standard of Care
TE	Thromboembolism
tPA	Tissue Plasminogen Activator
TR	Tricuspid Regurgitation
UNOS	United Network for Organ Sharing
VAD	Ventricular Assist Device
VT	Ventricular Tachycardia

Post Market Surveillance Plan

APPENDIX II: DEFINITIONS

ADVERSE EVENTS

1. Bleeding

An episode of SUSPECTED INTERNAL OR EXTERNAL BLEEDING that results in one or more of the following:

a. Death,
b. Reoperation,
c. Hospitalization,
d. Transfusion of red blood cells as follows:

➢ If transfusion is selected, then apply the following rules:

During first 7 days Post-implant

- ≥ 50 kg: ≥ 4U packed red blood cells (PRBC) within any 24 hour period during first 7 days post-implant.
- <50 kg: ≥20 cc/kg packed red blood cells (PRBC) within any 24 hour period during the first 7 days post-implant

After 7 days Post-implant*

- Any transfusion of packed red blood cells (PRBC) after 7 days following implant with the investigator recording the number of units given. (Record number of units given per 24 hour period).

Note: Hemorrhagic stroke is considered a neurological event and not as a separate bleeding event.

*Any transfusion of ≥ 2U packed red blood cells (PRBC) after 7 days following implant will be considered a serious bleed

2. Cardiac Arrhythmias

Any documented arrhythmia that results in clinical compromise (e.g., diminished VAD flow, oliguria, pre-syncope or syncope) that requires hospitalization or occurs during a hospital stay. Cardiac arrhythmias are classified as 1 of 2 types:

1) Sustained ventricular arrhythmia requiring defibrillation or cardioversion.

2) Sustained supraventricular arrhythmia requiring drug treatment or cardioversion.

3. Pericardial Fluid Collection

Accumulation of fluid or clot in the pericardial space that requires surgical intervention or percutaneous catheter drainage. This event will be subdivided into those with clinical signs of tamponade (e.g. increased central venous pressure and decreased cardiac/VAD output) and those without signs of tamponade.

4. Device Thrombosis

Device thrombosis is an event in which the pump or its conduits contain a thrombus that results in or could potentially induce circulatory failure. Suspected device thrombus is an event in which

clinical or MCSD parameters suggest thrombus on the blood contacting components of the pump, cannulae, or grafts. Signs and symptoms should include at least 2 of the 3 following criteria:

- Presence of hemolysis
- Worsening heart failure or inability to decompress the left ventricle
- Abnormal pump parameters

Suspected pump thrombus should be accompanied by 1 or more of the following events or interventions:

- Treatment with intravenous anticoagulation (e.g., heparin), intravenous thrombolytics (e.g., tPA), or intravenous antiplatelet therapy (e.g., eptifibatide, tirofiban)
- Pump replacement
- Pump explant
- Urgent transplant (UNOS status 1A)
- Stroke
- Arterial non-CNS thromboembolism
- Death

Confirmed device thrombus is an event in which thrombus is confirmed by Abbott returned product analysis to be found within the blood contacting surfaces of device inflow cannula or outflow conduit or grafts. This can also be reported via direct visual inspection or by incontrovertible contrast radiographic evidence or by the absence of an appropriate Doppler flow signal that results in or could potentially induce circulatory failure or result in thromboembolism.

5. Hemolysis*

A plasma-free hemoglobin value that is greater than 40 mg/dl, concomitant with a rise in serum LDH above three times the upper limit of normal, in association with clinical signs associated with hemolysis (e.g., anemia, low hematocrit, hyperbilirubinemia) occurring after the first 72 hours post-implant.

*Hemolysis in the presence of worsening heart failure or inability to decompress the left ventricle or abnormal pump parameters should be reported as suspected device thrombosis, not as hemolysis

6. Hepatic Dysfunction

An increase in any two of the following hepatic laboratory values (total bilirubin, aspartate aminotransferase/AST and alanine aminotransferease/ALT) to a level greater than three times the upper limit of normal for the hospital, beyond 14 days post-implant (or if hepatic dysfunction is the primary cause of death).

7. Hypertension

Blood pressure elevation of a mean arterial pressure greater than 110 mm Hg, despite anti-hypertensive therapy.

Post Market Surveillance Plan

8. Major Infection

A clinical infection accompanied by pain, fever, drainage and/or leukocytosis that is treated by anti-microbial agents (non-prophylactic). A positive culture from the infected site or organ should be present unless strong clinical evidence indicates the need for treatment despite negative cultures. The general categories of infection are listed below:

Localized Non-Device Infection

Infection localized to any organ system or region (e.g. mediastinitis) without evidence of systemic involvement (see sepsis definition), ascertained by standard clinical methods and either associated with evidence of bacterial, viral, fungal or protozoal infection, and/or requiring empirical treatment.

Percutaneous Site and/or Pocket Infection

A positive culture from the skin and/or tissue surrounding the drive line or from the tissue surrounding the external housing of a pump implanted within the body, coupled with the need to treat with antimicrobial therapy, when there is clinical evidence of infection such as pain, fever, drainage, or leukocytosis.

Internal Pump Component, Inflow or Outflow Tract Infection

Infection of blood-contacting surfaces of the LVAD documented by positive site culture.

Sepsis

Evidence of systemic involvement by infection, manifested by positive blood cultures and/or hypotension.

9. Myocardial Infarction

Two categories of myocardial infarction will be identified:

Peri-Operative Myocardial Infarction

The clinical suspicion of myocardial infarction together with CK-MB or Troponin > 10 times the local hospital upper limits of normal, found within 7 days following VAD implant together with ECG findings consistent with acute myocardial infarction. (This definition uses the higher suggested limit for serum markers due to apical coring at the time of VAD placement, and does not use wall motion changes because the apical sewing ring inherently creates new wall motion abnormalities.)

Non-Perioperative Myocardial Infarction

The presence at > 7 days post-implant of two of the following three criteria:

a) Chest pain which is characteristic of myocardial ischemia,

b) ECG with a pattern or changes consistent with a myocardial infarction, and

c) Troponin or CK (measured by standard clinical pathology/laboratory medicine methods) greater than the normal range for the local hospital with positive MB fraction (≥ 3% total CK).

Post Market Surveillance Plan

This should be accompanied by a new regional LV or RV wall motion abnormality on a myocardial imaging study.

10. Neurologic Dysfunction

Any new, temporary or permanent, focal or global neurological deficit, ascertained by a standard neurological history and examination administered by a neurologist or other qualified physician and documented with appropriate diagnostic tests and consultation note; or an abnormality identified by surveillance neuroimaging. The examining physician will classify the event as defined below:

- Transient ischemic attack*, defined as an acute transient neurological deficit conforming anatomically to arterial distribution cerebral ischemia, which resolves in < 24 hours and is associated with no infarction on brain imaging (head CT performed >24 hours after symptom onset; or MRI)
- Ischemic Stroke*: a new acute neurologic deficit of any duration associated with acute infarction on imaging corresponding anatomically to the clinical deficit, or a clinically covert ischemic stroke seen by surveillance imaging, without clinical findings of stroke or at the time of event recognition.
- Hemorrhagic Stroke*: a new acute neurologic deficit attributable to intracranial hemorrhage (ICH), or a clinically covert ICH seen by surveillance imaging, without clinical findings of ICH at the time of event recognition.
- Encephalopathy: Acute new encephalopathy** due to hypoxic-ischemic injury (HIE), or other causes, manifest as clinically evident signs or symptoms, or subclinical electrographic seizures found by complete neurological diagnostic evaluation to be attributable to acute global or focal hypoxic, or ischemic brain injury not meeting one of ischemic stroke or ICH events as defined above.
- Seizure of any kind
- Other neurological event (non-CNS event): examples include neuro muscular dysfunction or critical care neuropathy

*Modified Rankin Score will be used to classify the severity of all strokes

**Acute encephalopathy is a sign or symptom of some underlying cerebral disorder and is manifest as depressed consciousness with or without any associated new global or multifocal neurologic deficits in cranial nerve, motor, sensory, reflexes and cerebellar function.

11. Psychiatric Episode

Disturbance in thinking, emotion or behavior that causes substantial impairment in functioning or marked subjective distress requiring intervention. Intervention is the addition of new psychiatric medication or hospitalization. Suicide is included in this definition.

12. Renal Dysfunction

Two categories of renal dysfunction will be identified:

Post Market Surveillance Plan

Acute Renal Dysfunction

Abnormal kidney function requiring dialysis (including hemofiltration) in Subjects who did not require this procedure prior to implant, or a rise in serum creatinine of greater than 3 times baseline or greater than 5 mg/dL sustained for over 48 hours.

Chronic Renal Dysfunction

An increase in serum creatinine of 2 mg/dl or greater above baseline, or requirement for hemodialysis sustained for at least 90 days.

13. Respiratory Failure
Impairment of respiratory function requiring reintubation, tracheostomy or (the inability to discontinue ventilatory support within six days (144 hours) post-VAD implant. This excludes intubation for reoperation or temporary intubation for diagnostic or therapeutic procedures.

14. Right Heart Failure
Symptoms and signs of persistent right ventricular dysfunction requiring RVAD implantation or requiring inhaled nitric oxide or inotropic therapy for a duration of more than 1 week at any time after LVAD implantation.

15. Arterial Non-CNS Thromboembolism
An acute systemic arterial perfusion deficit in any non-cerebrovascular organ system due to thromboembolism confirmed by one or more of the following:
- Standard clinical and laboratory testing
- Operative findings
- Autopsy findings

This definition excludes neurological events.

16. Venous Thromboembolism Event
Evidence of venous thromboembolic event (e.g. deep vein thrombosis, pulmonary embolism) by standard clinical and laboratory testing.

17. Wound Dehiscence
Disruption of the exposed surfaces of a surgical incision, excluding infectious etiology, and requiring surgical repair.

18. Other

An event that causes clinically relevant changes in the Subject's health (e.g. cancer).

Post Market Surveillance Plan

MODIFIED RANKIN SCORE

Score	Definition
0	No observed neurological symptoms
1	No significant neurological disability despite symptoms; able to carry out all usual duties and activities
2	Slight neurological disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate neurological disability; requiring some help, but able to walk without assistance
4	Moderate severe neurological disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe neurological disability; bedridden, incontinent and requiring constant nursing care and attention as a result of a neurological deficit
6	Death

Post Market Surveillance Plan

DEVICE MALFUNCTIONS

A Device Malfunction occurs when any component of the MCS system ceased to operate to its designated performance specifications or otherwise fails to perform as intended. Performance specifications include all claims made in the Instructions for Use.

Internal Component Malfunction: Malfunction of any device system component that is implanted within the patient. A malfunction to these components may require further surgery to repair or replace.

External Component Malfunction: Malfunction of a device system component that is used external to the patient and can be replaced or repaired without the need for further surgery.

Post Market Surveillance Plan

NEW YORK HEART ASSOCIATION (NYHA) CLASSIFICATION

NYHA Classification	Definition
I	Cardiac disease without resulting limitations of physical activity. Ordinary physical activity does not cause undue fatigue, palpitations, dyspnea or anginal pain.
II	Cardiac disease resulting in slight limitation of physical activity. Subjects are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.
IIIA	Cardiac disease resulting in marked limitations of physical activity. Subjects are comfortable at rest. Less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain.
IIIB	Cardiac disease resulting in marked limitations of physical activity. Subjects are comfortable at rest. Mild physical activity causes fatigue, palpitation, dyspnea, or anginal pain.
IV*	Cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

*For all post-enrollment NYHA assessments, any patient who is inotrope dependent will be considered NYHA Class IV.

Post Market Surveillance Plan

INTERMACS PROFILE

INTERMACS Profile*	Definition
1	Critical cardiogenic shock describes a patient who is “crashing and burning”, in which a patient has life-threatening hypotension and rapidly escalating inotropic pressor support, with critical organ hypoperfusion often confirmed by worsening acidosis and lactate levels.
2	Progressive decline describes a patient who has been demonstrated “dependent” on inotropic support but nonetheless shows signs of continuing deterioration in nutrition, renal function, fluid retention, or other major status indicator. Patient profile 2 can also describe a patient with refractory volume overload, perhaps with evidence of impaired perfusion, in whom inotropic infusions *cannot be maintained* due to tachyarrhythmias, clinical ischemia, or other intolerance.
3	Stable but inotrope dependent describes a patient who is clinically stable on mild-moderate doses of intravenous inotropes (or has a temporary circulatory support device) after repeated documentation of failure to wean without symptomatic hypotension, worsening symptoms, or progressive organ dysfunction (usually renal). It is critical to monitor nutrition, renal function, fluid balance, and overall status carefully in order to distinguish between a patient who is truly stable at Patient Profile 3 and a patient who has unappreciated decline rendering this person a Patient Profile 2. This patient may be either at home or in the hospital.
4	Resting symptoms describes a patient who is at home on oral therapy but frequently has symptoms of congestion at rest or with ADL. He or she may have orthopnea, shortness of breath during ADL such as dressing or bathing, gastrointestinal symptoms (abdominal discomfort, nausea, poor appetite), disabling ascites or severe lower extremity edema. This patient should be carefully considered for more intensive management and surveillance programs, by which some may be recognized to have poor compliance that would compromise outcomes with any therapy.
5	Exertion Intolerant describes a patient who is comfortable at rest but unable to engage in any activity, living predominantly within the house or housebound. This patient has no congestive symptoms, but may have chronically elevated volume status, frequently with renal dysfunction, and may be characterized as exercise intolerant.
6	Exertion Limited also describes a patient who is comfortable at rest without evidence of fluid overload, but who is able to do some mild activity. Activities of daily living are comfortable and minor activities outside the home such as visiting friends or going to a restaurant can be performed, but fatigue results within a few minutes of any meaningful physical exertion. This patient has occasional episodes of worsening symptoms and is likely to have had a hospitalization for heart failure within the past year.
7	Advanced NYHA Class 3 describes a patient who is clinically stable with a reasonable level of comfortable activity, despite history of previous decompensation that is not recent. This patient is usually able to walk more than a block. Any decompensation requiring intravenous diuretics or hospitalization within the previous month should make this person a Patient Profile 6 or lower.

Post Market Surveillance Plan

6-MINUTE WALK TEST

Purpose
The purpose of the 6-Minute Hallway Walk test (6MWT) is to walk as far as possible for 6-minutes, without running or jogging, as a way of measuring functional status.

Preparing for the test
1. Establish a 30-meter walking course in an enclosed corridor, preferably free of distractions and close to a wall so that if needed, the Subject may rest against it during the test (note: a treadmill is not an acceptable alternate method for this PMS).
2. Mark the course at 3-meter intervals using a method unnoticeable to the Subject.
3. Place noticeable markers at either end of the 30-meter course to indicate the turnaround points.
4. The distance covered during the preceding walk test will not be revealed to the Subject during the PMS.
5. A warm up prior to the test should not be performed.

Explaining the test procedure to the Subject
1. Clearly explain to the Subject what is required of him/her using the following instructions verbatim:

   THE PURPOSE OF THIS TEST IS TO WALK AS FAR AS POSSIBLE FOR SIX-MINUTES. YOU WILL START FROM THIS POINT AND FOLLOW THE HALLWAY TO THE MARKER AT THE END, THEN TURN AROUND AND WALK BACK. WHEN YOU ARRIVE BACK AT THE STARTING POINT, YOU WILL GO BACK AND FORTH AGAIN. YOU WILL GO BACK AND FORTH AS MANY TIMES AS YOU CAN IN THE SIX-MINUTE PERIOD. IF YOU NEED TO, YOU ARE PERMITTED TO SLOW DOWN, TO STOP, AND TO REST AS NECESSARY. YOU MAY LEAN AGAINST THE WALL WHILE RESTING, BUT RESUME WALKING AS SOON AS YOU ARE ABLE. HOWEVER, THE MOST IMPORTANT THING ABOUT THE TEST IS THAT YOU COVER AS MUCH GROUND AS YOU POSSIBLY CAN DURING THE SIX MINUTES. I WILL KEEP TRACK OF THE NUMBER OF LAPS YOU COMPLETE AND I WILL LET YOU KNOW WHEN THE SIX MINUTES ARE UP. WHEN I SAY STOP, PLEASE STAND RIGHT WHERE YOU ARE.

   DO YOU HAVE ANY QUESTIONS ABOUT THE TEST?

   PLEASE EXPLAIN TO ME WHAT YOU ARE GOING TO DO.

2. The Subject will re-state the instructions. If the Subject does not seem to understand, repeat the entire instructions.

   Conducting the test
   1. Position the Subject at the starting line.
   2. Repeat the sentence:

      THE MOST IMPORTANT THING ABOUT THE TEST IS THAT YOU COVER AS MUCH GROUND AS YOU POSSIBLY CAN DURING THE SIX MINUTES.

      ARE YOU READY?

      START NOW, OR WHENEVER YOU ARE READY.

   3. Start the timer as soon as the Subject takes the first step.

Post Market Surveillance Plan

4. During the test, the walking pace of the Subject should not be influenced. The test supervisor must walk behind the Subject – do not walk with, rush up behind, or rush past the Subject.
5. Each time the Subject returns to the starting line, record the lap.
6. While walking, encourage the Subject at one-minute intervals with the following phrases:

1 minute:	YOU ARE DOING WELL. YOU HAVE 5 MINUTES TO GO.
2 minutes:	KEEP UP THE GOOD WORK. YOU HAVE 4 MINUTES TO GO.
3 minutes:	YOU ARE DOING WELL. YOU ARE HALFWAY DONE.
4 minutes:	KEEP UP THE GOOD WORK. YOU HAVE ONLY 2 MINUTES LEFT.
5 minutes:	YOU ARE DOING WELL. YOU HAVE ONLY ONE MINUTE TO GO.

7. The Subject should be spoken to only during the 1-minute encouragements; no response should be made to the Subject's questions about the time and distance elapsed.
   a. If the Subject is not concentrating on the walking, the Subject can be reminded at a 1-minute mark:

      THIS IS A WALKING TEST, TALKING WILL UTILIZE YOUR ENERGY RESERVE AND INTERFERE WITH YOUR PERFORMANCE.

   When only 15 seconds remain, state:

      IN A MOMENT I AM GOING TO TELL YOU TO STOP. WHEN I DO, STOP RIGHT WHERE YOU ARE AND I WILL COME TO YOU.

8. When the timer reads 6-minutes, instruct the Subject to STOP and walk over to him/her. Consider bringing a chair if the Subject appears exhausted. Mark the spot where the Subject stopped.

   If the Subject wishes to stop walking during the test
   If the Subject is slowing down and expresses that he/she wants to pause, keep the timer running and state:

   REMEMBER, IF YOU NEED TO, YOU MAY LEAN AGAINST THE WALL UNTIL YOU CAN CONTINUE WALKING AGAIN.

   If the Subject wishes to stop before the 6-minutes are complete and refuses to continue (or you decide that he/she should not continue), provide a chair for the Subject to sit on and discontinue the test. Record the distance completed, the time the test was stopped and the reason for pre-maturely stopping.

   Immediately after the test
   1. Total the number of completed laps and add the additional distance covered in the final partial lap. Record the distance walked to the nearest meter.
   2. Observe the Subject sitting in a chair for at least 10 minutes after the test is completed.

Post Market Surveillance Plan

APPENDIX III: CONTACT INFORMATION

Contact information for each participating clinical site is available under separate cover by contacting the Sponsor at:

Evonne Poon
Clinical Project Manager
3 Fraser Street #23-28
DUO Tower
Singapore 189352
Ph: +65 6914 8433
Email: evonnesueyin.poon@abbott.com

Post Market Surveillance Plan

APPENDIX IV: ANTICIPATED ADVERSE EVENTS

1. Incidence of anticipated adverse events with the HM3, HM2 and HVAD at 2 years from Pivotal Trials and Real-World Data from the INTERMACS Database

Anticipated Adverse Events	% of Subjects with Events		
	HEARTMATE 3	HEARTMATE II	HVAD
All-cause Death	HM3 CE MARK[5]: 24% MOMENTUM 3[11]: 19% INTERMACS 2019[12]: 16.0%	ENDURANCE: 32.2% MOMENTUM 3[11]: 19.7% INTERMACS 2019: 28.0%	ENDURANCE[13]: 39.2% INTERMACS 2019: 28.0%
Bleeding	HM3 CE MARK: 50% MOMENTUM 3: 43.7%	ENDURANCE: 60.4% MOMENTUM 3: 55.0%	ENDURANCE: 60.1%
Stroke	HM3 CE MARK: 24% MOMENTUM 3: 9.9% INTERMACS 2019: 7.0%	ENDURANCE: 12.1% MOMENTUM 3: 19.4% INTERMACS 2019: 18%	ENDURANCE: 29.7% INTERMACS 2019: 22.0%
Infection	INTERMACS 2019: 41.0%	INTERMACS 2019: 51.0%	INTERMACS 2019: 55.0%
Driveline	HM3 CE MARK: 24% MOMENTUM 3: 23.3%	ENDURANCE: 15.4% MOMENTUM 3: 19.4%	ENDURANCE: 19.6%
Sepsis	HM3 CE MARK: 22% MOMENTUM 3: 15.1%	ENDURANCE: 15.4% MOMENTUM 3: 14.9%	ENDURANCE: 23.6%
Suspected/Confirmed PT	HM3 CE MARK: 0.0% MOMENTUM 3: 1.4%	ENDURANCE: 10.7%[a] MOMENTUM 3: 13.9%	ENDURANCE: 6.4%[a]
Cardiac Arrhythmia	HM3 CE MARK[b]: 34% MOMENTUM 3: 35.9%	ENDURANCE: 40.9% MOMENTUM 3: 41.0%	ENDURANCE: 37.8%
Right Heart Failure	HM3 CE MARK: 14% MOMENTUM 3: 34.2% INTERMACS 2019: 37.0%	ENDURANCE: 26.8% MOMENTUM 3: 28.3% INTERMACS 2019: 34.0%	ENDURANCE: 38.5% INTERMACS 2019: 46%
Renal Dysfunction	HM3 CE MARK[b]: 10% MOMENTUM 3: 14.2%	ENDURANCE: 12.1% MOMENTUM 3: 11.1%	ENDURANCE: 14.9%
Hepatic Dysfunction	HM3 CE MARK[b]: 2.0% MOMENTUM 3: 4.9%	ENDURANCE: 8.1% MOMENTUM 3: 5.3%	ENDURANCE: 4.7%
Respiratory Failure	HM3 CE MARK[b]: 16.0% MOMENTUM 3: 21.6%	ENDURANCE: 25.5% MOMENTUM 3: 19.4%	ENDURANCE: 29.1%
Hypertension	HM3 CE MARK[b]: 2.0% MOMENTUM 3[d]: 8.2%	ENDURANCE: 16.8% MOMENTUM 3[d]: 9.3%	ENDURANCE: 15.9%
Pericardial Fluid Collection	HM3 CE MARK[b]: 2.0% MOMENTUM 3[d]: 4.9%	ENDURANCE[c]: 6.0% MOMENTUM 3[d]: 8.7%	ENDURANCE[c]: 2.7%
MI	HM3 CE MARK[b]: 0.0% MOMENTUM 3[d]: 1.2%	ENDURANCE[c]: 0% MOMENTUM 3[d]: 1.0%	ENDURANCE[c]: 1.4%
Hemolysis	HM3 CE MARK: 0.0% MOMENTUM 3[d]: 1.2%	ENDURANCE: 8.7% MOMENTUM 3[d]: 1.6%	ENDURANCE: 8.1%

Arterial Non-CNS TE	HM3 CE MARK [b]: 0.0% MOMENTUM 3 [d]: 1.0%	ENDURANCE: 6.7% MOMENTUM 3 [d]: 2.0%	ENDURANCE: 6.1%
Venous TE	HM3 CE MARK [b]: 0.0% MOMENTUM 3 [d]: 3.9%	ENDURANCE [c]: 3.4% MOMENTUM 3 [d]: 2.8%	ENDURANCE [c]: 2.7%

PT – pump thrombosis; TE – thromboembolic events; MI – myocardial infarction; Non-CNS – non central nervous system.

Pivotal study sample size: HM3 CE MARK: 50 patients implanted with the HM3; MOMENTUM 3: 1028 (8 patients died post randomization; data reported are from 515 HM3 and 505 HM2 patients); ENDURANCE: 446 (1 patient did not receive either device; data reported are from 296 HVAD and 149 HM2 patients).

[a] Pump thrombosis requiring pump exchange.

[b, c, d] From clinicaltrials.gov (NCT02170363, NCT01166347 and NCT02224755).

2. Device issues identified and addressed during MOMENTUM3 IDE study

Outflow graft twist

At the time this issue was identified, 35 of 5607 (0.62%) devices implanted worldwide were reported to have this issue. The outflow graft (OG) twist resulted in low blood flow and/or formation of thrombus within the OG. There were three deaths that were attributed to this issue. On May 22nd, 2018, the FDA categorized this as a Class I recall event. Analysis done by the Sponsor suggested that, over time, normal motion such as the heart beating, respiration and patient activity can cause small rotations between the OG bend relief component and the outflow graft metallic connector underneath. These forces, known as “in vivo loads”, are believed to cause the OG twisting. Additionally, it was determined that the twisting may occur more easily if the screw ring is not firmly hand tightened during implant. In response to the identification of this issue, initially a clip was designed to secure the OG to the pump housing and then later the pump housing design was modified to prevent the OG twist from occurring.

HM3 Driveline Communication Fault

On June 7, 2017, the Sponsor notified the MOMENTUM 3 DSMB chair and investigators of limited reports of errors in communication between the System Controller and pump of the HM3 LVAS. The root cause of the errors was traced to manufacturing variances from a single supplier that could lead to crystallization within the pump electronics.

The specifications and manufacturing processes for the HM3 pump have been updated to ensure this issue did not occur in future lots. In addition, the Sponsor retrieved potentially impacted HM3 implant kits from hospital shelves. The units that were removed from investigational sites were replaced with product not impacted by this field advisory.

To date, there have been no adverse effects related to this issue; however, it may lead to frequent advisory alarms that may need to be silenced. In the notification to investigators, the Sponsor provided recommendations for managing patients with advisory alarms. The Sponsor has received acknowledgment forms from all investigators indicating that they were made aware of the issue and the associated recommendations.

Post Market Surveillance Plan

APPENDIX V: CASE REPORT FORMS

Final draft CRFs will be sent under a separate cover.

Post Market Surveillance Plan

APPENDIX VI: INFORMED CONSENT FORM

A template informed consent form will be provided under a separate cover.

Post Market Surveillance Plan

APPENDIX VII: MONITORING PLAN

A copy of the Monitoring Plan can be obtained upon request from the Sponsor Clinical Project Manager for the post market surveillance.

Post Market Surveillance Plan

APPENDIX VIII: REVISION HISTORY

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

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

Amendment Number	Version	Date	Details	Rationale
Not Applicable	A	02/DEC/2020	First release of PMS plan	NA

Post Market Surveillance Plan

APPENDIX IX: PMS PLAN SUMMARY

Post Market Surveillance Study Name and Number	Hong Kong and Taiwan HM3 PMS CRD_1022
Title	Post Market Surveillance of the HeartMate 3 Left Ventricular Assist System in Hong Kong and Taiwan
Primary Objective	The primary objective of this prospective, post-market surveillance study is to assess the use of the HM3 LVAS in the setting of Hong Kong and Taiwanese standard-of-care for advanced heart failure patients implanted with this device. Secondary objective of this PMS is to assess the adverse events occurring during the surveillance period. Assessments will include: 6-minute walk test, New York Heart Association heart failure severity classification, EQ-5D-5L quality of life questionnaire, rates of survival, transplant, pump explant or exchange, device malfunctions, reoperations, rehospitalizations and incidence of adverse events including, but not limited to, neurological dysfunction, bleeding, device thrombosis, and infection.
Device Under Investigation	HeartMate 3™ Left Ventricular Assist System
Number of Subjects Required for Inclusion in Post market surveillance	All consecutive patients at the participating sites with a planned HM3 implant, that meet the HM3 commercially approved labelling indications are eligible to participate in this PMS. We expect approximately 30 patients will be enrolled during the surveillance period.
Post market surveillance Design	Prospective, single arm, open-label, multi-center, post market surveillance study
Subject Follow-up	Surveillance visits will occur at: • Baseline/Enrollment (prior to HM3 implant) • HM3 Implant • Month 1 ± 7 days • Month 3 ± 30 days • Month 6 ± 30 days • Month 12 ± 30 days • Month 24 ± 60 days Note: – The follow-up visits are relative to the date of HM3 implant. – A month is defined as 30 days. – the patients will be followed until they experience an outcome or the 24 month follow-up visit is completed, whichever comes first.

Post Market Surveillance Plan

APPENDIX X: REFERENCES

1 Colombo, P. C. *et al.* Comprehensive Analysis of Stroke in the Long-Term Cohort of the MOMENTUM 3 Study. *Circulation* **139**, 155-168, doi:10.1161/CIRCULATIONAHA.118.037231 (2019).

2 Schmitt, F. *et al.* 3 Tesla MRI: successful results with higher field strengths. *Der Radiologe* **44**, 31-47 (2004).

3 Cleveland, J. C., Goldstein, D. J., Uriel, N., Mehra, M. R. & Investigators, M. Forward "MOMENTUM" in left ventricular assist systems: advanced engineering meets biology. *Journal of thoracic disease* **9**, E653-E655, doi:10.21037/jtd.2017.06.72 (2017).

4 Bourque, K. *et al.* Design Rationale and Preclinical Evaluation of the HeartMate 3 Left Ventricular Assist System for Hemocompatibility. *ASAIO J* **62**, 375-383, doi:10.1097/MAT.0000000000000388 (2016).

5 Schmitto, J. D. *et al.* Long-term evaluation of a fully magnetically levitated circulatory support device for advanced heart failure—two-year results from the HeartMate 3 CE Mark Study. *European Journal of Heart Failure* **21**, 90-97, doi:10.1002/ejhf.1284 (2019).

6 Schmitto, J. D. *et al.* Long-term evaluation of a fully magnetically levitated circulatory support device for advanced heart failure-two-year results from the HeartMate 3 CE Mark Study. *Eur J Heart Fail* **21**, 90-97, doi:10.1002/ejhf.1284 (2019).

7 Garbade, J. *et al.* Postmarket Experience With HeartMate 3 Left Ventricular Assist Device: 30-Day Outcomes From the ELEVATE Registry. *Ann Thorac Surg* **107**, 33-39, doi:10.1016/j.athoracsur.2018.07.092 (2019).

8 Heatley, G. *et al.* Clinical trial design and rationale of the Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy With HeartMate 3 (MOMENTUM 3) investigational device exemption clinical study protocol. *J Heart Lung Transplant* **35**, 528-536, doi:10.1016/j.healun.2016.01.021 (2016).

9 Mehra, M. R. *et al.* A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure. *The New England journal of medicine* **376**, 440-450, doi:10.1056/NEJMoa1610426 (2017).

10 Mehra, M. R. *et al.* Two-Year Outcomes with a Magnetically Levitated Cardiac Pump in Heart Failure. *The New England journal of medicine* **378**, 1386-1395, doi:10.1056/NEJMoa1800866 (2018).

11 Mehra, M. R. *et al.* A Fully Magnetically Levitated Left Ventricular Assist Device - Final Report. *The New England journal of medicine* **380**, 1618-1627, doi:10.1056/NEJMoa1900486 (2019).

12 Teuteberg, J. J. *et al.* The Society of Thoracic Surgeons Intermacs 2019 Annual Report: The Changing Landscape of Devices and Indications. *Ann Thorac Surg* **109**, 649-660, doi:10.1016/j.athoracsur.2019.12.005 (2020).

13 Rogers, J. G. *et al.* Intrapericardial Left Ventricular Assist Device for Advanced Heart Failure. *The New England journal of medicine* **376**, 451-460, doi:10.1056/NEJMoa1602954 (2017).

14 Milano, C. A. *et al.* HVAD: The ENDURANCE Supplemental Trial. *JACC Heart Fail* **6**, 792-802, doi:10.1016/j.jchf.2018.05.012 (2018).