SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Ventricular assist (bypass) device

Device Trade Name: CentriMag Circulatory Support System

Device Procode: DSQ

Applicant's Name and Address: Abbott
6035 Stoneridge Drive
Pleasanton, CA 94588

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P170038

Date of FDA Notice of Approval:

II. INDICATIONS FOR USE

The CentriMag Circulatory Support System is indicated for temporary circulatory support for up to 30 days for one or both sides of the heart to treat post-cardiotomy patients who fail to wean from cardiopulmonary bypass, providing a bridge to decision when it is unclear whether the patient's heart will recover or whether the patient will need alternative, longer-term therapy.

III. CONTRAINDICATIONS

The CentriMag Circulatory Support System is contraindicated for use as a cardiotomy suction device. The system is also contraindicated for patients who are unable or unwilling to be treated with an appropriate anticoagulant such as Heparin or a comparable alternative.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the CentriMag Circulatory Support System labeling.

V. DEVICE DESCRIPTION

The CentriMag Circulatory Support System features a centrifugal flow pump with inflow and outflow ports that are at right angles to one another, and a magnetically levitated impeller (Full MagLev™ technology). When the impeller is rotated, a pressure gradient

develops between the center and outside edge of the pump, causing blood to flow from the inflow to the outflow port of the pump. The rotation of the impeller, as well as the resulting blood flow, is not sensitive to the pump height or position. The amount of flow through the pump depends on the speed of the impeller, and the difference between the inlet and outlet pressures. Factors affecting the flow include the following:

- Pump speed
- Preload pressure
- Afterload pressure
- Inflow cannula resistance and position
- Outflow cannula resistance and position
- Tubing (length, diameter, placement)

The core components that comprise the CentriMag Circulatory Support System are: CentriMag Pump, 2nd Generation CentriMag Primary Console, CentriMag Motor, Mag Monitor, Flow Probe, and CentriMag Drainage and Return Cannulae. When the pump is inserted into the motor and activated, the internal impeller is electromagnetically levitated and centered (Full MagLev™ technology). During patient support, the console is used to control pump speed, the resultant blood flow, and monitor the operation of the system. A cable connects the console to the motor, allowing flexibility in the pump motor and pump positioning.

The main components of the CentriMag Circulatory Support System are shown in Figure 1 and described in more detail below.

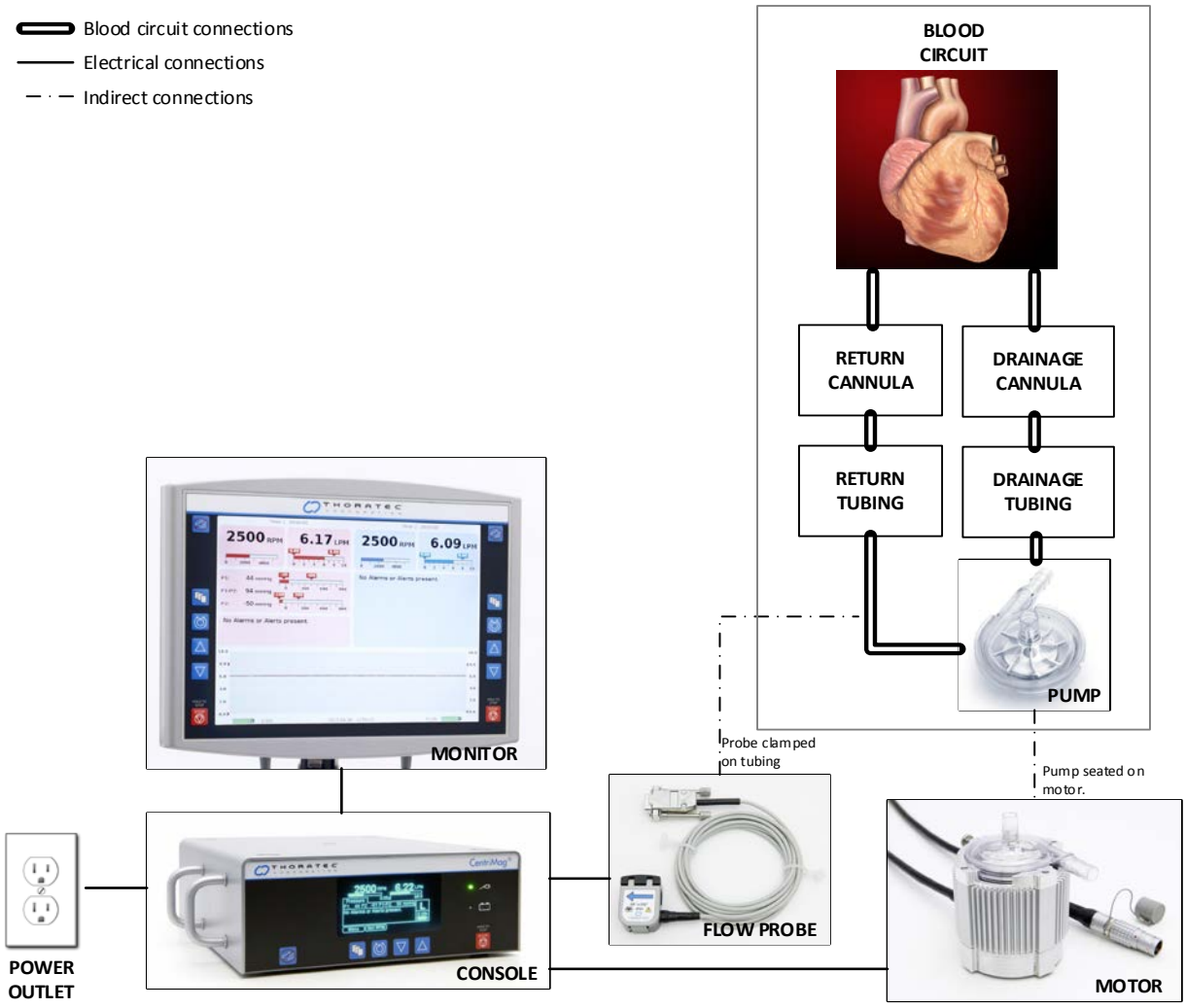

Figure 1: CentriMag Circulatory Support System

A. System Overview

Table 1: CentriMag System Components and Accessories

Blood Contacting Components	External Components	Accessories
• CentriMag Blood Pump • CentriMag Drainage and Return Cannulae	• 2nd Generation CentriMag Console • CentriMag Motor • Mag Monitor • Flow Probe • Rechargeable Lithium Ion Battery • Cables	• CentriMag System Cart • CentriMag System Transporter • Pressure Transducer

B. Major Components of the CentriMag Circulatory Support System

1. CentriMag Blood Pump

The CentriMag Circulatory Support System uses a sterile, single-use, disposable, polycarbonate, CentriMag Centrifugal Blood Pump which uses magnetic levitation technology. The blood flow is dependent upon the amount of blood entering the Pump, the Pump speed (RPM), the extracorporeal circuit resistance, and drainage and return blood pressures.

2. CentriMag Motor

The CentriMag Motor holds the CentriMag pump and drives the rotor inside the Blood Pump. The motor can be positioned next to the patient using an optional motor bracket. The motor turns the magnet (and rotor) within the CentriMag Blood pump at a speed that is set on the drive console by the user.

3. 2nd Generation CentriMag Console

The 2nd Generation CentriMag Primary Console uses single phase AC power. When used to control the CentriMag Blood Pump, the pump is capable of a flow rate of up to 10 LPM or maximum pressure head of 600 mmHg. In addition, each Console contains a rechargeable internal battery that can maintain console functionality in the event of a loss of AC power.

4. Mag Monitor

The optional Mag Monitor provides a redundant user interface containing a display and control buttons that allows the user to view system data directly on the console or the monitor. The Mag Monitor may be used with one or two consoles when a patient is supported in either a univentricular or biventricular support mode. In the biventricular mode, one Monitor is connected to two consoles.

5. CentriMag Drainage and Return Cannulae

The CentriMag Drainage (Venous) and CentriMag Return (Arterial) Cannulae Kits are designed for use with the CentriMag Circulatory Support System. Each kit consists of either the Drainage (Venous) or Return (Arterial) Cannula and several accessories used in the surgical placement procedure. The cannula and all kit accessories are sterile, single-use, disposable devices.

6. CentriMag Flow Probe

The clamp-on flow probe (em-tec Adult Flow Probe 3/8" x 3/32'') is a reusable, non-patient contacting ultrasonic Flow Probe which is optimized to detect flows from 0-10 LPM.

7. Accessories

The System Cart is a mechanical, mobile cart intended to hold the CentriMag Console, Mag Monitor and Motor during operation, and facilitates transportation of patients within the hospital.

The CentriMag Transporter is designed to hold an entire CentriMag System and if needed, oxygenator and oxygen bottles, to facilitate transportation of CentriMag patients by ground or air ambulance.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

The alternative acute therapies used in patients who have difficulty in weaning from cardiopulmonary bypass include pharmacologic agents (e.g. inotropes) and other mechanical circulatory support devices. Depending on their design, mechanical circulatory support devices may be placed through the peripheral vasculature or with open surgical procedures. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The CentriMag Circulatory Support System is commercially available in the following countries:

Argentina	Germany	Romania
Australia	Greece	Russian Federation
Austria	Hong Kong	Saudi Arabia
Belgium	India	Serbia
Brazil	Iran	Singapore
Bulgaria	Israel	Slovenia
Canada	Italy	South Africa
Cayman Islands	Kazakhstan	Spain
Chile	Kuwait	Sri Lanka
Columbia	Mexico	Sweden
Costa Rica	Netherlands	Switzerland
Czech Republic	Palestine	Taiwan
Denmark	Peru	Thailand
Dominican Republic	Poland	Turkey
Finland	Portugal	United Arab Emirates
France	Qatar	United Kingdom

The CentriMag Circulatory Support System has not been withdrawn from marketing in any country for any reason related to safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- Death
- Bleeding
- Respiratory Failure
- Infection
- Cardiac Arrhythmias
- Renal Failure / Dysfunction
- Right Heart Failure
- Neurologic Dysfunction
- Hemolysis
- Hepatic Dysfunction
- Hypotension
- Venous Thromboembolism
- Hypertension
- Cardiac Tamponade
- Psychiatric episode
- Pericardial Fluid Collection
- Device Malfunction
- Wound Dehiscence
- Arterial non-CNS thromboembolism
- Limb Ischemia
- Myocardial Infarction
- Aneurysm

For details on the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

Biocompatibility Studies

Toxicology and biocompatibility evaluations and testing for the CentriMag Blood Pump and CentriMag cannulae were conducted in accordance with ISO 10993-1: Biological Evaluation of Medical Devices Part 1: Evaluation and Testing. Summaries of test results are provided inTable 2, for the blood pump and Table 3 for the cannulae.

The Blood Pump is an external communicating device in prolonged (24 hours to 30 days) contact with circulating blood. The Cannulae are partially implanted devices, also in prolonged contact with tissue and blood.

Table 2: Biocompatibility – CentriMag Blood Pump

Test	Purpose	Results
Cytotoxicity (ISO 10993-5): Minimal Essential Media (MEM) Elution	Determine if test article extracts cause cell death, inhibition of cell growth, or other cytotoxic effects on cells.	Pass. The test article sample did not induce cytotoxicity (score = 0) at 24, 48 and 72 ± 4 hours and is considered non-cytotoxic.
Sensitization (ISO 10993-10): Guinea Pig Maximization (0.9% sodium chloride extract)	Evaluate the potential of a material or product to cause a sensitizing effect or allergenic reaction over an extended period of exposure.	Pass. No significant difference between the test article and the negative control article was noted throughout the procedure. The studies demonstrated no evidence of sensitization from the saline extracts of the device.
Sensitization (ISO 10993-10): Guinea Pig Maximization (Cottonseed Oil Extract)	Evaluate the potential of a material or product to cause a sensitizing effect or allergenic reaction over an extended period of exposure.	Pass. No significant difference between the test article and the negative control article was noted throughout the procedure. The studies demonstrated no evidence of sensitization from the cottonseed oil extracts of the device.
Irritation /Intracutaneous Reactivity (ISO 10993-10): Rabbit Intracutaneous Reactivity	Determine if the test article extracts would cause local irritation in the dermal tissues of the test subjects.	Pass. All test article extracts were determined to show no evidence of significant irritation or toxicity when injected intracutaneously into rabbits.
Acute Systemic Toxicity (ISO 10993-11): Injection test	Evaluate any acute systemic reaction from doses of extracts of the medical device.	Pass. All test article extracts were determined to show no mortality or evidence of systemic toxicity as compared to the control extracts. The test article was determined to be systemically non-toxic.
Material Mediated Pyrogenicity (ISO 10993-11): USP Rabbit Pyrogen Study	Determine if the test article extracts cause a febrile response (temperature rise) in intravenously injected rabbits.	Pass. The total rise of rabbit temperatures during the 3-hour observation period was within acceptable USP limits. The test article was judged as non-pyrogenic.
Subchronic Toxicity (ISO 10993-11): 30-Day Toxicity Study in the Rat, Parenteral extract Administration	Determine if the test article extracts would cause systemic toxicity due to potential leachable components, with both intravenous and intraperitoneal extraction injections over 30 days in rats.	Pass. There were no microscopic changes considered to be a test article related response. Parenteral administration of the test article extract did not produce systemic toxicity in rats.
Hemocompatibility (ISO 10993-4): C3a Complement Activation Assay	The objective of this test was to evaluate interactions of materials with blood.	Pass. Under the conditions of the SC5b-9 assay, the test article exhibited activation at 5162 ng/mL which was 0.0% of the normalized SC5b-9 concentration produced by CVF. The test article results in the SC5b-9 assay were not statistically significant ($p>0.05$) when compared to the reference material and is considered satisfactory under the test conditions employed. The test article was not considered to be a potential activator of the complement system.
Hemocompatibility (ISO 10993-4): ASTM Hemolysis Study (Direct Contact and Extract)	The objective of this test was to evaluate interactions of materials with blood.	Pass. The hemolytic index for the test article in direct contact with blood was 0.0% and the hemolytic index for the test article extract was 0.2%. Both the test article in direct contact with blood and the test article extract were non-hemolytic.

Test	Purpose	Results
Hemocompatibility (ISO 10993-4): SC5b-9 Complement Activation Assay	The objective of this test was to evaluate interactions of materials with blood.	Pass. The concentration of SC5b-9 in the test article sample was 9,185.8 ± 291.7 ng/mL [mean ± standard deviation] and was not statistically higher than the activated NHS control and was not statistically higher than the negative control. As a result, the test article was not considered to be a potential activator of the complement system.
In Vivo Thrombogenicity	The objective is to evaluate the potential of the device (blood pump) in contact with circulating blood to produce thrombi or clots for a 30-day duration of use.	Pass. See rational for no additional preclinical testing. Extensive clinical experience of the CentriMag Blood Pump suggests a favorable safety profile for its intended use. Pre-clinical animal test results indicate that through 30 days of use, the blood pump generated no concerning amount of thrombus formation.
Genotoxicity (ISO 10993-3): Reverse Mutation Assay (Ames test; saline extract)	Evaluate the potential mutagenic activity of a test sample extracts in strains of Salmonella typhimurium.	Pass. The sample did not exhibit a mutagenic or toxic response. Sample negative controls did not exhibit a toxic or mutagenic response. Sample positive controls did exhibit a mutagenic response. Negative and positive controls were satisfactory.
Genotoxicity (ISO 10993-3): Reverse Mutation Assay (Ames test; cottonseed oil extract)	Evaluate the potential mutagenic activity of a test sample extracts in strains of Salmonella typhimurium.	Pass. The sample did not exhibit a mutagenic or toxic response. Sample negative controls did not exhibit a toxic or mutagenic response. Sample positive controls did exhibit a mutagenic response. Negative and positive controls were satisfactory.
Genotoxicity (ISO 10993-3): Mouse Lymphoma Assay	Evaluate the test article for mutagenic potential using the mouse lymphoma forward gene mutation assay.	Pass. The $RPMI_0$ and EtOH test article extracts did not cause a two-fold or greater increase in the mean mutant frequency of the L5178Y/TK+/- cell line either in the presence or absence of metabolic activation. The test article was not mutagenic.
Genotoxicity (ISO 10993-3): Mouse Peripheral Blood Micronucleus Study – SC and SO Extracts*	Determine the potential of the test article to induce micronuclei formation in a mouse peripheral blood micronucleus model.	Pass. The test article extracts did not induce micronuclei in mice.
Chemical Characterization (ISO 10993-18)	Evaluate the toxicological profile of the leachable compounds.	Pass. No discrete chemical entities detected at toxicologically significant levels.

*SC: normal saline (0.9% NaCl), SO: sesame oil

Table 3: Biocompatibility – CentriMag Arterial and Venous Cannula Kits

Test	Purpose	Results
Cytotoxicity (ISO 10993-5): Study Using the ISO Elution Method (MEM Extract)	Determine if test article extracts cause cell death, inhibition of cell growth, or other cytotoxic effects on cells.	Pass. The test article scored 0 at 24 and 48 ± 4 hours, 1 at 72 ± 4 hours and is considered non-cytotoxic.

Test	Purpose	Results
Sensitization (ISO 10993-10): Guinea Pig Maximization Test (SC and SO Extracts*)	Evaluate the potential of a material or product to cause a sensitizing effect or allergenic reaction over an extended period of exposure.	Pass. The test article extracts showed no evidence of causing delayed dermal contact sensitization in the guinea pig. The test article was not considered a sensitizer in the guinea pig maximization test.
Intracutaneous Reactivity/Irritation (ISO 10993-10): ISO Intracutaneous Study in Rabbits – SC and SO Extracts	Determine the localized irritation potential of extracts from the medical device.	Pass. The test article met the requirements of the test since the difference between each test article extract overall mean score and corresponding control extract overall mean score was 0.0 and 0.1 for the SC and SO test article extracts, respectively.
Acute Systemic Toxicity (ISO 10993-11): Systemic Toxicity Study in Mice – SC and SO Extracts	Evaluate any acute systemic reaction from doses of extracts of the medical device.	Pass. There was no mortality or evidence of systemic toxicity from the extracts injected into mice. Each test article extract met the requirements of the study.
Material Mediated Pyrogenicity (ISO 10993-11): USP Rabbit Pyrogen Study	Determine if the test article extracts cause a febrile response (temperature rise) in intravenously injected rabbits.	Pass. The total rise of rabbit temperatures during the 3-hour observation period was within acceptable USP limits. The test article was judged as non-pyrogenic.
Subchronic Toxicity (ISO 10993-11): ISO 30 Day Toxicity Study in the Rat, SC and SO Extracts	Determine if the test article extracts would cause systemic toxicity due to potential leachable components, with both intravenous and intraperitoneal extraction injections over 30 days in rats.	Pass. There were no microscopic changes considered to be a test article related response. Parenteral administration of the test article extract did not produce systemic toxicity in rats.
Hemocompatibility (ISO 10993-4): C3a Complement Activation Assay	The objective of this test was to evaluate interactions of materials with blood.	Pass. The C3a concentration of the test article sample was 10,468.9 ± 984.5 ng/mL [mean ± standard deviation] and was not statistically higher than the activated NHS control and was not statistically higher than the negative control. As a result, the test article was not considered to be a potential activator of the complement system.
Hemocompatibility (ISO 10993-4): SC5b-9 Complement Activation Assay	The objective of this test was to evaluate interactions of materials with blood.	Pass. The concentration of SC5b-9 in the test article sample was 8,399.3 ± 389.1 ng/mL [mean ± standard deviation] and was not statistically higher than the activated NHS control and was not statistically higher than the negative control. As a result, the test article was not considered to be a potential activator of the complement system.
Hemocompatibility (ISO 10993-4): ASTM Hemolysis Study (Direct Contact and Extract)	The objective of this test was to evaluate interactions of materials with blood.	Pass. The hemolytic index for the test article in direct contact with blood was 0.0% and the hemolytic index for the test article extract was 0.8%. Both the test article in direct contact with blood and the test article extract were non-hemolytic.
Material Thrombogenicity:		
• Platelet and Leukocyte (P & P) tests (assessment of platelets adhesion / activation)	The purpose of this test was to determine if the test article could induce thrombus formation.	Equivocal. A comparative P&L study was conducted in accordance with ASTM 2888-13. The platelet counts of the test article were considered equivocal to the negative control.
• Partial Thromboplastin Time (assessment of the coagulation system)	The objective of this test was to determine the potential of the test article to cause an effect on the coagulation cascade via the intrinsic coagulation pathway.	Pass. A comparative PTT test was performed in accordance with the ASTM F2382 (2017). The results indicate that the test article clotting times were lower and statically different than the negative control and reference material ($p < 0.05$).

Test	Purpose	Results
• SEM imaging (inner lumen surface assessment)	Evaluate the material and surface characteristics of blood contacting materials for thrombogenic potential.	Pass. The results of SEM analysis indicate the surface characteristics of the test article contain an equivalent or better hemocompatible profile than comparison devices.
Genotoxicity (ISO 10993-3): Bacterial Reverse Mutation Study – SC and 95% EtOH Extracts	Evaluate the potential mutagenic activity of a test sample extracts in strains of Salmonella typhimurium.	Pass. The EtOH and saline test article extracts were non-mutagenic to S. typhimurium tester strains TA98, TA100, TA1535, and TA1537, and to E. coli tester strain WP2uvrA.
Genotoxicity (ISO 10993-3): Mouse Lymphoma Assay	Evaluate the test article for mutagenic potential using the mouse lymphoma forward gene mutation assay.	Pass. The $RPMI_0$ and EtOH test article extracts did not cause a two-fold or greater increase in the mean mutant frequency of the L5178Y/TK+/- cell line either in the presence or absence of metabolic activation. The test article was not mutagenic.
Genotoxicity (ISO 10993-3): Mouse Peripheral Blood Micronucleus Study –SC and SO Extracts	Evaluate the potential of the test article to induce micronuclei formation in a mouse peripheral blood micronucleus model.	Pass. The test article extracts did not induce micronuclei in mice.
Implantation (ISO10993-6): Muscle Implantation Study in Rabbits, 4 Weeks	Evaluate the local tissue response to the test article implanted in muscle tissue in rabbits.	Pass. The macroscopic reaction was not significant as compared to the negative control article. Microscopically, test articles 1, 2, 3, and 5 were classified as non-irritants as compared to the negative control article. Microscopically, test articles 4 and 6 were classified as slight irritants as compared to the negative control article.
Chemical Characterization (ISO 10993-18)	Determine if the device has chemical compounds that can leach out during the medical use of the device under "worst case" conditions.	Pass. Test methods included FTIR for composition; GPC for molecular weight; LC/MS for organic additive identification, ICP-MS for inorganic additive identification; and solvent extraction for additive loading.

*SC: normal saline (0.9% NaCl), SO: sesame oil

B. Animal Studies

The CentriMag Circulatory Support System has been studied in six separate animal studies, five of which focused on the CentriMag blood pump and one of which focused on the CentriMag cannulae. In general, the animal studies demonstrated no signs indicative of device failures or other device-related abnormalities. The overall rate of thromboembolism was low and there were few incidences of infection at any site. There were minimal changes in end organ function as measured by creatinine, blood urea nitrogen and total bilirubin. There were no incidences of mechanical failure. Specific analyses related to device performance indicated that the device performed as intended in the test animals. Results are summarized below in Table 4 through Table 9.

Table 4: Six – Hour Acute In Vivo Study (N=6)

Title	Evaluation of the CentriMag Blood Pumping System for Cardiopulmonary Bypass Surgery (Animal Study 202)
Animal model (Sample Size)	Bovine (6)
Cannulation	External jugular vein and common carotid artery (non-CentriMag cannulae)

Duration	6 hours
Results	CentriMag Blood Pumping System performed safely and effectively in providing mechanical circulatory support during cardiopulmonary bypass. The device generated the intended flows (50 ml/kg) throughout support with minimal damage to the blood. No device malfunctions were observed, and the pumps were free of thrombus based on direct visual examination of the devices at study termination. No infarcts or thrombus were observed in the heart or kidneys at necropsy.

Table 5: 28-Day Veno-Venous Study (N=7)

Title: Description	Veno-venous 28-day Study: Assessment of hemocompatibility independent of comorbidities associated with open chest implantation.
Animal model (Sample Size)	Bovine (7)
Cannulation	Right and left jugular veins (non-CentriMag cannulae)
Duration	3 – 28 days
Results	A pump flow of 50 ml/kg was targeted throughout support. The animals had normal laboratory findings throughout support, including end organ function. No remarkable findings were observed at pump retrieval or at necropsy. The pump performed well throughout support with no malfunctions or failures.

Table 6: Acute LVAD Study (N=3)

Title: Description	Acute LVAS Study: Feasibility study for use of the CentriMag system as a ventricular assist system. (Study Number 2002-06)
Animal model (Sample Size)	Bovine (3)
Cannulation	Left atrium & descending aorta, LV apex & descending aorta (non-CentriMag cannulae)
Duration	<24 hours
Results	This study verified that the system operates as designed for the intended indication for use as a ventricular assist system.

Table 7: Chronic 28-Day LVAD Study (N=5)

Title: Description	Chronic 28-Day LVAS Study: Validation of CentriMag as a ventricular assist system
Animal model (Sample Size)	Bovine (5)
Cannulation	LV apex and descending aorta (non-CentriMag cannulae)
Duration	29 - 30 days
Results	The system performed as anticipated. No device-related adverse events occurred during this study. There was no evidence of compromised hemocompatibility, biocompatibility, or hepatic function.

Table 8: Acute BVAD Study (N=2)

Title: Description	Acute BiVAD Study: Feasibility evaluation of CentriMag system for use as a biventricular assist device.
Animal model (Sample Size)	Bovine (2)
Cannulation	LV apex and descending aorta, Right atrial appendage and pulmonary artery (non-CentriMag cannulae)
Duration	< 24 hours
Results	The CentriMag system demonstrated satisfactory cannulation, hemodynamic support and biocompatibility when operated in the BiVAD configuration.

Table 9: In Vivo Evalaution of CentriMag Cannulae (N=6)

Title: Description	*In Vivo* Evaluation of the CentriMag Cannulae (Report PR-0091)
Animal model (Sample Size)	Ovine (6)
Cannulation	34Fr CentriMag Drainage cannula: Left ventricular apex 24Fr CentriMag Return cannula: aorta
Duration	0 – 33 days
Results	Four animals survived to 30 days; two animals were terminated at the time of implant due to surgical complications unrelated to device function. Adequate hemodynamic support was achieved with the cannulae. No cannula-related adverse effects. Thrombus observed on outer surface of two drainage cannulae but appeared to have originated at LV apex and to be independent of cannula type.

C. Additional Studies

1. In Vitro Device Performance

Table 10 below summarizes performance and functional bench testing of the CentriMag System.

Table 10: Device Performance Testing

Test	Purpose	Acceptance Criteria	Results
CentriMag System			
Hydro-dynamic (HQ) Performance of the CentriMag VAS Circuit	Assess the hydrodynamic ("HQ") characteristics of the CentriMag System (blood pump, cannulae and tubing). Verification of flow rate, pressure and correlation of flow with motor speed (rpm).	1. At lower pressures, the system is capable of pumping at a flow rate of at least 10 LPM. 2. The system can generate pressure of at least 600 mmHg. 3. The system is capable of pumping at a flow rate of at least 8 LPM at a pressure across the pump of at least 500 mmHg	Pass
Rough Handling – Drop Resistance, Shock Resistance and Vibration	Verify the ability of the Console and the Mag Monitor to withstand specified severities of shock (IEC 60068-2-27), vibration (IEC 60068-2-6), and drop from a specified height (IEC 60601-1) that might be encountered during ground (road or rail) transport of a patient supported by the CentriMag system.	1. Device free from damage (i.e. cracked display, cracked or broken ports on the back-panel, chipped corners) post rough handling testing. 2. The device remains fully operational during and after rough handling testing.	Pass
CentriMag Blood Pump			
Chemical Resistance	Evaluate the CentriMag Blood Pump's resistance to common cleaning fluids and chemicals present in the hospital environment.	• Visual - Contact with tested chemicals should not cause stress cracking, swelling of the plastic parts or the adhesive bond, or result in gumminess of the adhesive bond • Pump Leak Test - All test samples must pass the 2-bar leak check of blood pump assembly. • Functional - All devices must pass Final Functional Testing (rotor levitation / rotation test).	Pass

Test	Purpose	Acceptance Criteria	Results
In Vitro Hemolysis Platelet and WBC Testing	Compare the level of Hemolysis, Platelet Count, White Blood Cell Count, Red Blood Cell Count, and Hematocrit in test circuits containing CentriMag centrifugal blood pumps to another marketed blood pump.	Equivalent results (or better) for: • Hemolysis • Platelet count • White blood count • Hematocrit • Red cell count • Thrombus generation	Pass
Blood Pump Air Handling	Compare the air handling performance (micro bubbles and macro bubbles) of the CentriMag Blood Pump to another marketed blood pump.	CentriMag blood pump air handling performance is equivalent to the comparison device regarding: • the amount of air needed to de-prime pump, • the amount of air which escapes from the device during simulated use.	Pass
CentriMag Motor			
Fluids Ingress Protection Level	Verify the degree of protection from fluid ingress for the CentriMag Motor	IEC 60529 IPX4 (Protection against water sprayed from any direction)	Pass
CentriMag 2nd Generation Console and Mag Monitor			
Console Battery Run Time	Verify the run time of the internal, rechargeable Li-Ion Battery Pack	1. A new, fully charged battery pack lasts at least 120 minutes with a pump running at nominal load (3500 RPM, 5.5 LPM, blood analog) 2. The battery recharge time in a console running on full load (5000 RPM, 9 LPM, blood analog) should be: • less equal 4 hrs. to charge the battery to 90% of the capacity • less equal 5 hrs. to charge the battery to 100% of the capacity	Pass
Console Battery Recharge Cycles	Verify cycle life of the internal, rechargeable Li-ion Battery Pack	The battery must provide for a minimum of 100 full or partial charge/discharge cycles and remain capable of meeting battery use requirements.	Pass
Fluids Ingress Protection Level	Verify the degree of protection (IP code) from fluid ingress for the console and monitor.	IEC 60529 IPX1 (Protection against vertically falling drops of water (e.g. condensation)).	Pass
Surface Cleaning	Demonstrate the Console and Monitor can withstand repeated exposure to cleaning agents and standard germicidal agents commonly used in the hospital environment.	No stress cracking, swelling or discoloration.	Pass
CentriMag Drainage (Venous) and Return (Arterial) Cannula			
Pressure Drop Performance	Assess the pressure drop characteristics with blood analog solution on straight, bent and partially occluded CentriMag Cannulae.	• Return Cannula: ≤150 mmHg @ 6 LPM • Drainage Cannula: ≤100 mmHg @ 6 LPM	Pass
In Vitro Hemolysis Testing of CentriMag Cannulae	Compare the level of hemolysis resulting from the operation of the CentriMag Cannulae as compared to other commercially available cannulae.	Hemolysis level is equivalent or better than similar marketed cannulae.	Pass

Test	Purpose	Acceptance Criteria	Results
Computational Fluid Dynamics (CFD) Analysis – Drainage Cannula	Identification of areas of low blood flow and potential blood stasis in the CentriMag Drainage Cannula design	No areas of stasis at blood flow rate of 1 LPM.	Pass
Tip Radiopacity – Drainage Cannula	Verify the visibility of the tantalum disk embedded in the distal tip of the CentriMag Drainage Cannula	The radiopaque indicator in the proximal tip of the CentriMag Drainage Cannula is visible under "still x-ray" and continuous fluoroscopy.	Pass
Flex Life Testing	Demonstrate reliability of CentriMag Drainage and Return cannulae over intended use period of 30 days.	12 test units of each type of cannulae underwent accelerated flex testing (16,243 cycles of 360º rotation with 60º deflection) without failure. Estimated reliability is 95% with 95% confidence for a 30-day mission life.	Pass
Chemical Resistance	Verify the CentriMag Cannula are not adversely affected by exposure to common chemicals present in the hospital environment	1. Contact with test chemicals does not cause stress cracking or swelling of the plastic parts. 2. Cannula ink markings are not smeared/smudged and remain legible. 3. Maintains a static pressure of 6 psi for 5 minutes	Pass
Tensile Testing	Demonstrate the strength of the CentriMag Cannulae and connector engagement under tensile loading.	Drainage and Return Cannula: • Material must maintain 50 lb. tensile strength post pre-conditioning Drainage (barbed connector to cannula interface) and Return (interface with barbed connector) Cannula • 5 lbs. minimum hold strength for 1 minute Drainage Cannula Cap – Interface with Barbed Connector • 5 lbs. minimum hold for 1 minute Return Cannula – Introducer hub integrity • 5 lbs. minimum hold strength	Pass

2. Other testing

Table 11 below summarizes other non-clinical testing of the CentriMag System, including electrical safety, electromagnetic compatibility, reliability and packaging, software and sterilization valdiation.

Table 11: Additional Non-Clinical Testing Conducted with CentriMag SystemComponent

	Applicable Standards or Acceptance Criteria	Results
Electrical Safety & EMC Testing		
CentriMag System (motor, pump, console, monitor, flow probe, DTX pressure transducer)	IEC 60601-1:2005/A1:2012 (ed. 3.1)	Pass
	IEC 60601-1-6:2010/A1:2013	Pass
	IEC 60601-1-8:2006/A1:2012	Pass
	IEC 60601-1-2:2007/AC:2010	Pass
CentriMag System (motor, pump, console, flow probe, DTX pressure transducer)	RTCA/DO-160G (Sec's. 20, 21)	Pass
Mechanical strength in fixed and rotary wing aircraft		

	Applicable Standards or Acceptance Criteria	Results
CentriMag System (free fall testing)	Free fall testing has been completed in accordance with IEC 60068-2-31:2008 and the system demonstrated compliance with IEC 60601-1-12:2014.	Pass
CentriMag System (shock)	Shock testing was performed to demonstrate compliance to IEC 60068-2-27:2008, Environmental Testing – Part 2-27: Tests – Test Ea and Guidance: Shock, at 30 g (peak). This testing is equivalent for showing compliance to IEC 60601-1-12:2014 clause 10.1.4, since the test conditions and criteria are equivalent or exceeded by IEC 60068-2-27:2008.	Pass
CentriMag System (vibration)	For use of the system in the EMS environment, vibration testing was performed in accordance with IEC 60068-2-6:2007 Environmental testing – Parts 2-6: Tests – Test Fc: Vibration (sinusoidal).	Pass
In Vitro 30-Day Reliability		
CentriMag Pump & Motor (Performance)	CentriMag Blood Pumps and Motors (n=12) must each pass 1440 hours (60-days) of testing with zero failures to achieve 90% reliability with 90% confidence [for 30-day mission life].	Pass
2nd Generation CentriMag Console and Monitor Reliability (Performance)	CentriMag Consoles (n=12) and Monitors (n=6) must be operational for 60 days without failure. Estimated reliability is 90% with 90% confidence [for a 30-day mission life].	Pass
CentriMag Pump (Visual)	• No visual leakage of fluid on the outside of the pump. • No ingress of fluid into the impeller. • No cessation of pumping. • Flow rate must be maintained within 15% of the desired rate. • No evidence of visual damage to the impeller. • No naked-eye evidence of damage to internal pump housing, including scraping, abrasion, fractures or particles. • No evidence of pump material fatigue, such as cracking or excessive abrasion.	Pass
Sterilization		
CentriMag Pump	90% EtO/10% CO_2 sterilization process is used. The process has been validated to achieve a minimum sterility assurance level (SAL) of 10^{-6} using the three half-cycle overkill approach described in the ANSI/AAMI/ISO 11135:2014, Sterilization of health care products - Ethylene oxide - Requirements for development, validation and routine control of a sterilization process for medical devices. A validated post-sterilization aeration process assures that residual levels of EO and ECH (ethylene chlorohydrin) are within acceptable limits specified by ANSI/AAMI/ISO 10993-7:2008.	Pass
Cannulae	100% EtO sterilization process is used. The process has been validated to achieve a minimum sterility assurance level (SAL) of 10^{-6} using the three half-cycle overkill approach described in the ANSI/AAMI/ISO 11135:2014, Sterilization of health care products - Ethylene oxide - Requirements for development, validation and routine control of a sterilization process for medical devices. A validated post-sterilization aeration process assures that residual levels of EO and ECH (ethylene chlorohydrin) are	Pass

	Applicable Standards or Acceptance Criteria	Results
	within acceptable limits specified by ANSI/AAMI/ISO 10993-7:2008.	
Packaging and Shelf Life		
CentriMag System	Comprehensive transit and shelf life studies were conducted on the components of the CentriMag System in accordance with ASTM D4169:2009 and ANSI ISO 11607-1:2006. Shelf life of the sterile components (blood pump and cannulae) has been established as three (3) years from the date of manufacture.	Pass
Software Validation		
2nd Generation CentriMag Console and Mag Monitor	All software development processes comply with IEC 62304:2015, Medical Device Software - Software Life-Cycle Processes. The CentriMag software are components of a Programmable Electrical Medical System (PEMS) and as such, the software development process meets the requirements of Clause 14, Programmable Electrical Medical Systems, of IEC 60601-1:2012 – Ed. 3.1: Medical electrical equipment - Part 1: General requirements for basic safety and essential performance.	Pass

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed four (4) clinical studies to establish a reasonable assurance of safety and effectiveness of providing circulatory support for periods up to 30 days with the CentriMag Circulatory Support System for post-cardiotomy patients who fail to wean from cardiopulmonary bypass. The clinical studies were conducted in the United States under IDE numbers G030052, G030052/S21, G040029, and HDE H070004/S1. The pivotal study conducted under IDE G030052/S21 enrolled only post-cardiotomy patients who failed to wean (FTW) from cardiopulmonary bypass (CPB), the indication for use for this PMA, while the other three (3) studies included patients enrolled for other indications as well. Data from these clinical studies, together with the results of a comprehensive literature review and an analysis of global post market surveillance data were the basis for the PMA approval decision. Because the pivotal study (IDE G030052/S21) was the only study to strictly enroll and analyze outcomes for the study population reflected in the indication for use in this PMA, it was the only one used to assess effectiveness of the device for this PMA. However, because adverse events while patients are on the device and device malfunctions and failures are not indication-specific, data from patients enrolled in all four studies were used to assess the safety of the device. No formal statistical hypothesis testing was performed on any of the above studies, as no pre-specified statistical analysis plan that propertly considers operating characteristics (e.g. sample size, type I error, power, etc.) was available for any of them. A summary of the clinical studies is presented below.

A. Study Design

Patients were treated in four (4) clinical studies between May 2004 and December 2013 as shown in Table 12. The database for this PMA reflected data collected through September 2014 and included 95 patients. There were 14 unique investigational sites across the four (4) studies.

Table 11: All CentriMag Clinical Studies

Study	Cardiogenic Shock Trial	RVAS Trial	Failure to Wean From CPB Pivotal Trial	RVAS HDE Post Approval Study
FDA Ref. No.	G030052	G040029	G030052/S21	H070004/S1
Start Enrollment	May 2004	Oct 2004	Oct 2008	Feb 2010
End Enrollment	Dec 2007	Feb 2008	Mar 2013	Dec 2013
Investigational Sites*	6	2	8	7
Patients	26	12	32	25

*14 unique investigational sites; many sites participated in more than one study

The CentriMag studies were prospective, non-randomized, open-label, multicenter, unblinded, controlled clinical studies. Each patient was followed for 6 months post device removal in the three pre-market studies and for 30 days post device removal in the HDE post approval study.

The Failure to Wean from CPB pivotal trial (G030052/S21) utilized a Data Safety Monitoring Board (DSMB) and Clinical Events Committee (CEC). The CEC was responsible for adjudicating all adverse events occurring during the study. The DSMB was responsible for reviewing adverse events, data quality, endpoints, device efficacy data and overall study conduct to evaluate device safety.

Data were compared to outcomes of patients who failed to wean from cardiopulmonary bypass and who required mechanical circulatory support, as reported in peer-reviewed, published scientific literature.

The failure to wean (FTW) from cardiopulmonary bypass (CPB) population was defined as a subset of patients suffering from post-cardiotomy cardiogenic shock (PCCS) who were unable to be separated from CPB prior to leaving the operating room.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the studies was limited to patients at least 18 years of age for whom informed consent was given either by the patient or their legally authorized representative, and who met the following inclusion criteria. Inclusion and exclusion criteria by study are summarized in Table 13 and Table 14.

Table 12: All CentriMag Clinical Studies – Inclusion Criteria

Inclusion Criteria – Failure to Wean from Cardiopulmonary Bypass Pivotal Trial (G030052/S21)	
a) Cardiac dysfunction due to failure-to-wean from cardiopulmonary bypass.	
b) All potential subjects must meet the following hemodynamic criteria at the time of enrollment:	
i) Cardiac index ≤ 2.2 L/min/m^2.	
ii) For patients being evaluated for left-sided support (LVAD):	
Pulmonary Capillary Wedge Pressure (PCWP) ≥ 18 mmHg or	
Pulmonary Artery Diastolic Pressure (PADP) ≥ 18 mmHg or	
Left Atrial Pressure (LAP) ≥ 18 mmHg.	
iii) For patients being evaluated for Right or Biventricular support (BVAD):	
Central Venous Pressure (CVP) ≥ 15 mmHg or	
Right Atrial Pressure (RAP) ≥ 15 mmHg.	
Right Ventricular Stroke Work Index (RVSWI) ≤ 4.1 gm·m2/beat.	
iv) Enrollment without hemodynamic measurements due to frequent or unpredictable dysrhythmias, unacceptable cardiac function, or hemodynamic instability is allowed.	
c) Placement of an intra-aortic balloon pump has been attempted unless contraindicated.	
d) All possible measures have been attempted to correct low arterial pH, arterial blood gas abnormalities, electrolytes, hypovolemia, hypervolemia, inadequate cardiac rate, dysrhythmias and residual hypothermia.	
e) Cardiac resuscitation using pharmacologic agents, and epicardial pacing (if appropriate and possible) has been attempted.	
Inclusion Criteria – Other Premarket CentriMag Studies	
G030052	**G040029**
Cardiogenic Shock Trial	**CentriMag RVAS**
Potentially reversible cardiogenic shock with one of the following diagnoses:	Undergoing treatment with an LVAS as a bridge to transplant or for destination therapy
Post-cardiotomy cardiogenic shock	Not applied to this study
Post Acute Myocardial Infarction cardiogenic shock	
Potentially reversible cardiogenic shock following myocardial infarction (AMI) subjects must meet two of the following three criteria:	
History and physical consistent with acute myocardial infarction	
ECG changes consistent with AMI	
Serum cardiac protein or enzyme changes consistent with AMI	
Potentially reversible post-cardiotomy cardiogenic shock following a cardiac surgical procedure subjects must be within 6 hours of the surgical procedure.	Potentially reversible post-cardiotomy cardiogenic shock following implantation of an FDA cleared, commercially available LVAS. Enrollment must be within 24 hours of the surgical procedure to implant the LVAS

For patients considered for LVAS support:	Not applied to this study
PCWP ≤ 18 mm Hg or	
PAD ≤ 18 mm Hg or	
LAP ≤ 18 mm Hg	
With cardiac index ≤ 2.0 l/min/m^2	
Patients supported with a CentriMag LVAS, with a dilated right ventricle, and being considered for BVAS support must meet two of the following three criteria:	Patients being considered for RVAS support must meet two of the following three criteria:
CVP or RVP ≥ 15 mmHg	
Right Ventricular Stroke Work Index (RVSWI) ≤ 4.1 gm-m^2/beat.	
Decrease in mean PAP ≤ 10 mmHg following the initiation of LVAS support	
For patients unweanable from CPB:	For patients unweanable from CPB and being considered for BVAS support:
No hemodynamic inclusion criteria required for either LVAS or BVAS support	No hemodynamic inclusion criteria required for RVAS support
Patient is unable to maintain adequate hemodynamics due to dysrhythmias:	Not applied to this study
No hemodynamic inclusion criteria required for either LVAS or BVAS support	
All possible measures have been attempted to correct low arterial pH, arterial blood gas abnormalities, electrolytes, hypovolemia, hypervolemia, inadequate cardiac rate, dysrhythmias and residual hypothermia.	
Cardiac resuscitation using pharmacologic agents, and epicardial pacing (if appropriate and possible) has been attempted.	

The post-approval study of the CentriMag RVAS HDE (H070004/S1) did not have any specific entry criteria beyond the provision of informed consent. The first 25 consecutive patients with acute right ventricular failure from any cause requiring use of the CentriMag RVAS to sustain life were enrolled into the study.

Patients were not permitted to enroll in the three (3) IDE premarket studies if they met any of the following exclusion criteria. No exclusion criteria were specified in the post-approval study protocol for the CentriMag RVAS HDE (H070004/S1).

Table 13: All CentriMag Clinical Studies – Exclusion Criteria

G030052/S21	**G030052**	**G040029**
FTW from CBP Pivotal Trial	**Cardiogenic Shock Trial**	**CentriMag RVAS**
BUN > 100 mg/dl. (Based on lab data from the 24 hours prior to enrollment).		
Creatinine > 5 mg/dl (Based on lab data from the 24 hours prior to enrollment).		
Presence of any investigational mechanical circulatory support device.		Presence of any ongoing mechanical circulatory support device, other than a commercially approved LVAS and an intra-aortic balloon pump.
Not applied to this study		On a Thoratec PVAD (LVAD) undergoing treatment for failure to wean from CPB.
Not applied to this study	Presence of any mechanical cardiac valve prosthesis	
Known history of liver cirrhosis or portal hypertension.		
Pulmonary infarction. Pulmonary angiograms with evidence of significant embolism within two weeks prior to consideration. A significant embolism is one that causes lung infarction in more than one lung segment proven by a V/Q scan or pulmonary angiogram.		

<table>
<tr><th>G030052/S21</th><th>G030052</th><th>G040029</th></tr>
<tr><th>FTW from CBP
Pivotal Trial</th><th>Cardiogenic Shock Trial</th><th>CentriMag RVAS</th></tr>
<tr><td>Not applied to this study</td><td colspan="2">Fixed pulmonary hypertension with a PVR > 8 Wood unit, unresponsive to pharmacologic intervention, O_2, NO, etc.</td></tr>
<tr><td colspan="3">Stroke, TIA or history of either condition within the last six months and/or any confirmed, existing neurologic deficits.</td></tr>
<tr><td colspan="3">Active systemic infection defined as positive blood cultures, core temperature >100.5°F, white blood count > 12,500, and treatment with antimicrobials.</td></tr>
<tr><td>Not applied to this study</td><td colspan="2">Prolonged (>15 min) or unsuccessful attempts at cardiopulmonary resuscitation prior to initiation of the surgical procedure, or prior to initiation of CPB.</td></tr>
<tr><td>Participation in a clinical trial with any experimental treatment within 30 days prior to screening or previous participation in the present study.</td><td colspan="2">Not applied to this study</td></tr>
<tr><td colspan="2">Not applied to this study</td><td>Severe blood dyscrasia as determined by INR >1.5, PT >16.0, PTT >45.0, and Platelet count <50,000 unresponsive to therapy.</td></tr>
<tr><td>Other serious disease(s) limiting life expectancy.</td><td colspan="2">Cancer – unresolved malignancy</td></tr>
</table>

2. Follow-up Schedule

All patients were followed throughout their course of treatment with the CentriMag Circulatory Support System. Patients were also assessed at the time of discharge from the hospital, and at 30 days and 6 months after removal of the device. Preoperatively, hemodynamic data (e.g. blood pressure, cardiac output, CVP, PAP, PCWP, LAP) and laboratory assessments (blood chemistry, coagulations studies, hematology) were collected for each patient.

Postoperatively, the objective parameters measured during the study included survival, hemodynamic data, laboratory assessments and adverse events.

Hemodynamic data and laboratory assessments were obtained at the following timepoints:

- Baseline (prior to initiation of CentriMag support)
- 4 hours after initiation of CentriMag support
- Daily during CentriMag support (except for invasive hemodynamic monitoring which was only required for the first two days of CentriMag support)
- Daily during the first two days after CentriMag removal
- Hospital discharge
- 30 days after CentriMag removal

Survival was assessed as a percentage of patients discharged alive from the hospital, and at 30 days and 6 months after CentriMag removal. Adverse events and complications were recorded throughout the duration of CentriMag support, through device removal and until the patient was discharged from the hospital.

3. Clinical Endpoints

With regards to safety, the frequency of major adverse events such as neurological dysfunction, bleeding, infection, and device failure was assessed.

Survival was the primary measure of effectiveness. Secondary measures of effectiveness included improvements in hemodynamics and key laboratory values as measures of end organ function.

Regarding success/failure criteria, patients were considered successes if they survived to hospital discharge or 30 days after device removal, whichever was longer. Patients were also considered successes if they survived on CentriMag support until induction of anesthesia for the purpose of cardiac transplantation or converting the patient to a longer-term mechanical circulatory support device. Overall, the Pivotal FTW study was considered a success if at least 27% of the patients survived to the longer of either hospital discharge or 30 days post device removal. This success criteria was based upon data from published clinical reports of FTW patient outcomes.

B. Accountability of FTW Study Cohorts

Ninety-five (95) patients were enrolled in the four (4) clinical studies supporting this PMA as shown Table 15. One (1) of the studies (IDE G030052/S21) enrolled only patients for the indication for use in this PMA, post-cardiotomy failure to wean from cardiopulmonary bypass, but the other three (3) enrolled patients for other indications as well. Data from patients enrolled for the other indications for use were used to assess safety of the device. All patients enrolled in the studies were evaluated. No patients withdrew from the studies or were lost to follow-up.

Table 14: All CentriMag Clinical Study Enrollment

Clinical Study	Indication for Use		Total Patients Enrolled
	Post-cardiotomy Failure to Wean From CPB	Other	
FTW from CPB Pivotal Trial (G030052/S21)	32	0	32
Cardiogenic Shock Trial (G030052)	10*	16	26
RVAS Trial (G040029)	11	1	12
RVAS Post-Approval Study (H070004/S1)	0	25	25
Total	**53**	**42**	**95**

*estimated number of FTW subjects (± 2-3) within total enrollment in Cardiogenic Shock Trial

C. Study Population Demographics and Baseline Parameters

The demographics of the study populations are typical for studies of mechanical circulatory support devices performed in the United States. Demographic information for the four (4) study populations is summarized in Table 16.

Table 15: Demographics – All CentriMag Clinical Studies

Clinical Study	FTW from CPB Pivotal Trial (G030052/S21) §	Cardiogenic Shock Trial (G030052) †	RVAS Trial (G040029) ‡	RVAS HDE Post Approval Study (H070004/S1) ¥
Patients (N)	32	26	12	25
Sex: Male Female	24 (75%) 8 (25%)	15 (58%) 11 (42%)	8 (67%) 4 (33%)	20 (80%) 5 (20%)
Race: White African Am. Other	24 (75%) 4 (13%) 4 (13%)	*	*	19 (76%) 4 (16%) 2 (8%)
Age: (mean years ± SD)	58 ± 13.8	59 ± 11.6	55 ± 14.3	53 ± 13.9
Hx of diabetes	12 (38%)	10 (39%)	2 (17%)	*
Hx of cardiovascular disease	29 (91%)	24 (92%)	12 (100%)	*

* Not collected per study protocol

§ Pivotal FTW Trial enrolled 100% (32/32) FTW subjects.

† The Cardiogenic Shock Trial (G030052) enrolled a mixed cohort of patients in CS, at least 27% FTW subjects.

‡ The RVAS Trial (G040029) enrolled patients in post-cardiotomy cardiogenic shock following implantation of an LVAD, over 90% FTW subjects.

¥ The RVAS HDE Post Approval Study enrolled no identified FTW subjects.

Baseline hemodynamic and laboratory values for only the Pivotal FTW Study (n=32) of the post-cardiotomy failure to wean from CPB indication are summarized in Table 17 and Table 18, respectively.

Table 16: Baseline Hemodynamic Values – FTW from CPB (G030052/S21)

Variable	N	Mean	SD	Median	Min	Max
Systolic Blood Pressure (mmHg)	30	98.6	23.2	94.0	58.0	153.0
Diastolic Blood Pressure (mmHg)	30	54.2	12.7	52.5	22.0	79.0
Pulmonary Artery Systolic (mmHg)	22	37.3	14.0	36.0	13.0	58.0
Pulmonary Artery Diastolic (mmHg)	22	22.9	8.5	22.0	8.0	39.0
Central Venous Pressure (mmHg)	26	16.3	8.0	14.5	6.0	33.0
Cardiac Output (LPM)	11	3.9	1.3	3.7	2.6	7.2
Cardiac Index (L/min/m^2)	10	1.6	0.4	1.6	1.0	2.0

Table 17: Baseline Laboratory Values – FTW from CPB (G030052/S21)

Variable	n	Mean	SD	Median	Min	Max
Blood Urea Nitrogen (mg/dl)	32	39.1	21.3	32	12	94

Creatinine (mg/dl)	32	1.8	0.8	1.6	0.9	4
Total Bilirubin (mg/dl)	31	1.8	1.8	1.2	0.4	9.7
aPTT (sec)	29	81.4	60.7	49.8	23.4	200
PT (sec)	31	23.8	17.8	16.1	11.6	100
INR	31	2.3	2.3	1.3	0.9	12.8
Activated Clotting Time	21	294	182	174	117	640
Red Blood Cells ($x10^6$/ml)	32	4.6	5.2	3.5	2.4	32.6
White Blood Cells ($x10^3$/ml)	32	11.3	5.5	10.7	3	28.2
Platelets ($x10^6$/ml)	32	152	79.1	173	21	369
Hematocrit (%)	32	31.7	6.5	29.8	23	43.5
SGOT (U/L)	29	344	1071	48	16	5766
SGPT (U/L)	31	237	586	39	13	3125
LDH (U/L)	19	1203	1479	678	198	5404
Plasma Free Hemoglobin (mg/dl)	20	28.8	28.9	14.5	3.1	89

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on all 95 patients enrolled in the four clinical studies of the CentriMag Circulatory Support System described above, thereby providing a more conservative estimate of the safety profile inclusive of all study (mixed) cohorts, not just FTW subjects. Safety was evaluated based on adverse events and device malfunctions.

Adverse effects that occurred in all CentriMag clinical studies:

Adverse events observed during the four (4) studies are summarized in Table 19. The clinical studies were not powered for a specific analysis of adverse events. The adverse event rates observed during the clinical studies were not unexpected in this critically ill patient population, being typical for patients recovering from open heart surgery and supported by a mechanical circulatory support device, as reported in the literature. The risk of bleeding, infection and respiratory failure is high in this patient population, although the number of these events that were reported as directly attributable to the device was relatively low. There were no unanticipated adverse events reported in any of the four clinical studies. Adverse event definitions were similar but not identical across the studies so direct comparisons are not possible. However, Table 19 shows that general trends in types and incidence of adverse events were similar across all four (4) studies.

Table 18: Adverse effects that occurred in All CentriMag Clinical Studies

	IDE G030052 Pivotal FTW [§] (n=32)			IDE G030052 Pilot Cardiogenic Shock (BVAD) [†] (n=26)			IDE G040029 Pilot RVAD w/ LVAD [‡] (n=12)			RVAD HDE PAS RVAD w/HMII LVAD [¥] (n=25)			All CentriMag Clinical Patients (n=95)		
Adverse Event Type	**Total Number of Events**	**Number of Subjects with Event**		**Total Number of Events**	**Number of Subjects with Event**		**Total Number of Events**	**Number of Subjects with Event**		**Total Number of Events**	**Number of Subjects with Event**		**Total Number of Events**	**Number of Subjects with Event**	
Death [While on device support or < 30 days post explant]	10	10	31%	15	15	58%	5	5	42%	5	5	20%	35	35	37%
Infection	22	13	41%	39	13	50%	17	4	33%	25	15	60%	103	45	47%
Bleeding	74	27	84%	34	20	77%	29	11	92%	51	20	80%	188	78	82%
Respiratory Failure	14	14	44%	20	20	77%	9	8	67%	20	16	64%	63	58	61%
Arrhythmias	14	12	38%	14	9	35%	14	4	33%	17	16	64%	59	41	43%
Hypertension	1	1	3%	0	0	0%	0	0	0%	9	5	20%	10	6	6%
Hypotension	1	1	3%	5	5	19%	2	2	17%	0	0	0%	8	8	8%
Hepatic Dysfunction	1	1	3%	8	7	27%	3	2	17%	0	0	0%	12	10	11%
Renal Failure/ Dysfunction	8	8	25%	3	3	12%	1	1	8%	12	12	48%	24	24	25%
Neurologic Dysfunction	0	0	0%	8	8	31%	2	2	17%	4	4	16%	14	14	15%
Venous Thromboembolism	2	2	6%	0	0	0%	3	3	25%	1	1	4%	6	6	6%
Pericardial Fluid Collection	0	0	0%	0	0	0%	0	0	0%	5	4	16%	5	4	4%
Right Heart Failure	2	2	6%	14	14	54%	1	1	8%	7	6	24%	24	23	24%
Hemolysis	4	4	13%	7	4	15%	1	1	8%	2	2	8%	14	11	12%
Myocardial Infarction	0	0	0%	0	0	0%	0	0	0%	1	1	4%	1	1	1%
Psychiatric episode	2	2	6%	0	0	0%	0	0	0%	3	3	12%	5	5	5%
Arterial non-CNS thromboembolism	1	1	3%	0	0	0%	0	0	0%	1	1	4%	2	2	2%
Wound Dehiscence	1	1	3%	0	0	0%	0	0	0%	0	0	0%	1	1	1%

	IDE G030052 Pivotal FTW [§] (n=32)			IDE G030052 Pilot Cardiogenic Shock (BVAD) [†] (n=26)			IDE G040029 Pilot RVAD w/ LVAD [‡] (n=12)			RVAD HDE PAS RVAD w/HMII LVAD [¥] (n=25)			All CentriMag Clinical Patients (n=95)		
Adverse Event Type	**Total Number of Events**	**Number of Subjects with Event**		**Total Number of Events**	**Number of Subjects with Event**		**Total Number of Events**	**Number of Subjects with Event**		**Total Number of Events**	**Number of Subjects with Event**		**Total Number of Events**	**Number of Subjects with Event**	
Cardiac Tamponade	0	0	0%	3	3	12%	2	2	17%	0	0	0%	5	5	5%
Limb Ischemia	0	0	0%	0	0	0%	2	2	17%	0	0	0%	2	2	2%
Aneurysm	0	0	0%	0	0	0%	1	1	8%	0	0	0%	1	1	1%
Device Failure	0	0	0%	0	0	0%	0	0	0%	0	0	0%	0	0	0%
Device Malfunction	1	1	3%	2	2	8%	1	1	8%	0	0	0%	4	4	4%
Other	12[1]	9	28%	0	0	0%	0	0	0%	21[2]	10	40%	33	19	20%

§ Pivotal FTW Trial enrolled 100% (32/32) FTW subjects.
† The Cardiogenic Shock Trial (G030052) enrolled a mixed cohort of patients in CS, at least 27% FTW subjects.
‡ The RVAS Trial (G040029) enrolled patients in post-cardiotomy cardiogenic shock following implantation of an LVAD, over 90% FTW subjects.
¥ The RVAS HDE Post Approval Study enrolled no identified FTW subjects.

[1] Right arm compartment syndrome, bronchorrhea and desaturation, cardiogenic shock with suspected platelet dysfunction, tear in ventricular tissue near durable LVAD sewing ring, bilateral lower extremity ischemia with gangrene, coagulopathy, pressure ulcer, right abdominal wall hematoma, critical illness myopathy, septic shock, pleural effusion (x2)

[2] Pressure ulcer; ischemic bowel, mediastinal washout/wound management (x7), device thrombosis, thrombus in tubing RVAD circuit (x2), thrombocytopenia (x2), microcytic hypochromic anemia (x2), thrombus on pump impeller, leukocytosis, pleural effusion, pneumothorax, thrombus

Device Malfunctions/Failures

As shown in Table 19, four device malfunctions and no device failures were reported in the clinical studies. The one report of device malfunction during the Pivotal FTW study involved a blood pump stoppage that occurred due to thrombosis in the outflow cannula during the patient weaning process rendering lowered pump flow settings and pharmacological anticoagulation. In each of the pilot studies, a malfunction involved the motor was making noises; in each case, the motor and console were switched out with the back-up units, resolving the issue. The final reported device malfunction occurred in the Cardiogenic Shock Pilot Trial, in which a stopcock on the outflow circuit of the right side pump in a BiVAD patient popped off. The circuit was temporarily clamped off and the stopcock was replaced.

Because data on device malfunctions and failures in the clinical studies were limited due to the size of the studies, post-market safety data for the CentriMag System were also used to evaluate the safety of the device. These data were obtained by analyzing adverse events associated with marketed CentriMag Systems which were reported to Abbott between June 1, 2014, and June 30, 2019. The results from these Medical Device Reports (MDRs) are summarized in Table 20.

Post-market data is trended monthly and when trends are identified, they are investigated and assessed for risk as appropriate. If risk analysis determines that there is an unacceptable risk; or an acceptable risk trending to unacceptable, a CAPA request is generated to determine the need for corrective action. Based on the CAPA investigation, a Health Hazard Evaluation may be performed to determine if a field action is appropriate. Abbott has identified three (3) issues over the past five years that resulted in corrective action:

(1) Cannula blood leaks related to failure of a solvent bond between the body of the cannula and the integral barbed connector used to join the cannulae to the circuit tubing. The designs of the arterial and venous cannulae were changed to incorporate a non-integrated barbed connector to join the cannulae to the circuit tubing. This design change was cleared under 510(k)s K152161 and K152190.

(2) The motor cable break was the subject of a Class II recall (Z-0103-2019) initiated in September 2018 and impacted all motors. Labeling changes were initiated in September 2018 and the cable redesign was cleared under 510(k) K191557 and HDE approved under H070004/S021. All previously reported complaints with this failure mode were reanalyzed for reportability, resulting in an increase in reportable events related to motor cable break failure.

The CentriMag System was the subject of a Class I recall (Z-0221-2020) initiated in August 2019 involving reports of motor and pump issues resulting in system/alarm(s)/faults from electromagnetic interference (EMI). Root cause was determined to be associated with the calibration of the motors manufactured from August 8, 2017 to July 22, 2019. The production test tool software was fixed. All affected CentriMag motors are to be returned to an Abbott facility for inspection and recalibration and subsequently returned to the customer. Replacement units will be provided as appropriate. The “Motor cable break” (n=60) and “System Alarm(s)/Fault” (n=68) events comprise almost half (48%) of the reported adverse events for the five-year period.

The incidence of adverse events was calculated based on the distribution of over 32,000 CentriMag pumps during the analysis period, a reasonable estimate of the number of times that the CentriMag system was used. The rates observed for the CentriMag

Circulatory Support System are consistent with other short-term MCS devices as reported in the FDA Summary of Safety and Effectiveness (SSED) for the AbioMed BVS 5000 Bi-Ventricular Support System (P900023)(ref 1) and the Thoratec Ventricular Assist Device (VAD) System (P870072/S5).

Table 19: MDR Reports: CentriMag Circulatory Support System Adverse Events by Component (June 2014 – June 2019)

Component	Count
Motor	
Motor cable break	60
System stopped	25
Overheating	20
Abnormal sounds	12
Abnormal operation	4
Variable flow	1
Total	**122**
Console	
System Alarm(s)/Fault (console and/motor)	68
Abnormal operation	10
System stopped	4
Battery	2
Total	**84**
Pump (Adult and Pediatric)	
Thrombus	20
Variable flow	11
Damage	2
Blood leak	1
Death	1
Unknown/Other	1
Total	**36**
Cannula	
Blood leak (cannula connector)	8
Detachment (cannula color band)	4
Decannulation	1
Total	**13**
Multiple / Indeterminate Component(s)	
Stroke	7
Death	5
Unknown/Other	5
Physical damage	4
Infection	3
Air entrainment	3
Hemolysis	2
Bleeding	1
Total	**30**

Component	Count
Total Number of MDRs	**285**

2. Effectiveness Results

The primary analysis to assess effectiveness was based on the 32 evaluable Pivotal FTW Study patients at the 30-day post-device removal time point. The primary study endpoint of survival at 30 days post device removal or to hospital discharge in the pivotal trial for failure to wean from cardiopulmonary bypass (FTW from CPB) was 63%, far exceeding the typical rate of 27% reported in the literature. Key effectiveness outcomes are presented in Table 21 through Table 24.

Table 20: CentriMag Effectiveness in FTW Subjects from CPB Pivotal Study (G030052/S21) – Survival and Primary Endpoint

Clinical Study	N		Survival to 30 Days Post-device	Survival To Discharge	Primary Endpoint Success[1]
FTW from CPB Pivotal Trial (G030052/S21)	32		22/32 (69%)	20/32 (63%)	20/32 (63%)

[1] Success: Survival to 30 days post device removal or to hospital discharge, whichever is longer; or survival to induction to anesthesia for surgery for cardiac transplantation or conversion to other long-term mechanical circulatory support system.

The outcomes summarized in Table 21 were a function of use of the CentriMag Circulatory Support System for durations that ranged from a minimum duration of 1 day and up to maximum duration of 90days. The duration of support observed for the pivotal study is summarized below in Table 22.

Table 21: Duration of CentriMag Support in FTW Subjects from CPB Pivotal Study (G030052/S21)

Clinical Study	Indication For Use	N	Mean Duration Of Support (days)	Range (days)
FTW from CPB Pivotal Trial (IDE G030052)	FTW	32	12.7	1 - 90

Improvements in hemodynamics were evaluated as a secondary endpoint in the pivotal study for failure to wean from cardiopulmonary bypass. As shown in Table 23, Mean Arterial Pressure (MAP) increased and Central Venous Pressure (CVP) decreased during support with the CentriMag Circulatory System during the pivotal study for FTW from CPB, based on a comparison of paired values. No paired data points were available for analysis of Left Atrial Pressure or Cardiac Index because, given the hemodynamic instability of the patient population at baseline, data for these parameters were collected only at the discretion of the investigator.

Table 22: Hemodynamics - FTW from CPB Pivotal Study (G030052/S21)

Hemodynamic Parameter	Paired Values (n)	Baseline	Mean Value During CentriMag Support
CVP	5	19.2 mmHg	13.7 mmHg
MAP	23	67.6 mmHg	75.3 mmHg

Key indicators of end organ function (blood urea nitrogen [BUN], creatinine and bilirubin) were tracked during the Pivotal FTW study of the CentriMag

Circulatory Support System. Mean blood chemistry values during the first 14 days of support with the device during the pivotal study of failure to wean from cardiopulmonary bypass show decreasing trends for BUN and creatinine but increasing levels of bilirubin (Table 24).

Table 23: End Organ Function – FTW from CPB Pivotal Study

	Interval	n	Mean	Range
Blood Urea Nitrogen (BUN) (mg/dl)	Baseline	32	39	12 – 94
	Day 1	30	37	15 - 76
	Day 2	29	40	15 - 76
	Day 3	28	41	14 - 86
	Day 7	16	30	14 - 67
	Day 14	10	28	18 - 62
Creatinine (mg/dl)	Baseline	32	1.8	0.9 – 4.0
	Day 1	30	1.8	0.9 – 4.0
	Day 2	29	1.9	0.9 – 3.1
	Day 3	28	1.8	0.7 – 3.3
	Day 7	16	1.4	0.7 – 4.8
	Day 14	10	1.2	0.9 – 1.9
Total Bilirubin (mg/dl)	Baseline	31	1.8	0.4 – 9.7
	Day 1	26	3.8	0.7 – 8.7
	Day 2	26	5.0	0.5 – 14.5
	Day 3	27	5.9	0.8 – 13.2
	Day 7	15	5.0	0.5 – 16.0
	Day 14	10	5.7	0.5 – 28.1

Survival at six months after cessation of support with the CentriMag was also tracked as a secondary effectiveness endpoint in the pivotal study of the failure to wean from CPB indication for use. At six months after device removal, survival was 53%, compared to 69% at 30 days after device removal, showing that recovery from the initial hemodynamic instability that required use of the CentriMag for circulatory support was sustained over time.

A supplemental analysis of effectiveness at the 30-day post-device removal time point was conducted for the 38 evaluable patients that participated in the other premarket pilot studies. Each of these studies had mixed cohorts, with some percentage of FTW patients. These supplemental effectiveness outcomes are presented in Table 25 and Table 26.

Table 24: CentriMag Effectiveness in Two Pilot Studies – Survival and Primary Endpoint

Clinical Study	N	Survival to 30 Days Post-device	Survival To Discharge	Primary Endpoint Success
Cardiogenic Shock Trial (G030052) †	26	11/26 (42%)	---	Not Defined
RVAS Trial (G040029) ‡	12	7/12 (58%)	---	Not Defined

† The Cardiogenic Shock Trial (G030052) enrolled a mixed cohort of patients in CS, at least 27% FTW subjects.

‡ The RVAS Trial (G040029) enrolled patients in post-cardiotomy cardiogenic shock following implantation of an LVAD, over 90% FTW subjects.

Table 25: Duration of CentriMag Support in two Pilot Studies

Clinical Study	Indication For Use	N	Mean Duration Of Support (days)	Range (days)
RVAS Trial (IDE G040029)	PCCS after LVAD implantation, 90% FTW	12	15.3	1 - 29
Cardiogenic Shock Trial (IDE G030052)	CS (PCCS and /or post Myocardial Infarction); ≥27% FTW	26	12.8	1 - 60

3. Subgroup Analyses

Due to the small number of patients in the clinical studies, statistically meaningful evaluations of potential associations of preoperative characteristics with outcomes could not be performed.

For the Pivotal FTW Clinical Study, the primary effectiveness endpoint and survival to 6 months after cessation of CentriMag circulatory support were analyzed with respect to device configuration as shown in Table 27. Due to the small number of patients in each group no conclusions can be drawn from the analysis.

Table 26: Six Month Survival Post Device Removal for FTW from CPB Pivotal Study (G030052/S21)

Device Configuration	Number of Subjects	Primary Endpoint Success	Subjects Surviving to 6 Months
LVAD	7	4 (57%)	3 (43%)
BiVAD[1]	5	2 (40%)	0 (0%)
RVAD	3	1 (33%)	1 (33%)

RVAD with HM II[2]	17	13 (76%)	13 (76%)
All Configurations	32	20 (63%)	17 (53%)

[1] Two CentriMag pumps, one LVAD and one RVAD
[2] CentriMag RVAD used in conjunction with HeartMate II LVAD (Thoratec, PMA P060040).

4. Pediatric Extrapolation

In this premarket application, existing clinical data were not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. This marketing application was supported by three clinical studies conducted under two IDEs and one HDE post-approval study protocol. The numbers of investigators and sites that enrolled patients for each study are listed in Table 28.

Table 27: Number of Study Sites and Investigators

Study	IDE #G030052	IDE #G040029	HDE H070004/S1
Investigational Sites	11*	2	7
Investigators	43	7	17

*A total of six (6) sites enrolled patients in the Cardiogenic Shock Pilot Study (N=26). Three of those sites and an additional five (5) sites, enrolled patients in the Pivotal FTW Study (N=32).

None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

In support of this market application, a comprehensive literature search was conducted covering the period since commercial release of the first CentriMag product in 2003 to July 2016. This literature search was conducted under a formal protocol, in which peer-reviewed journals (via PubMed Medline database) were searched for reports pertaining to CentriMag systems using pre-defined criteria. The search identified 28 reports summarizing an estimated 413 patients outside of clinical trials sponsored by the applicant who were implanted with the CentriMag Circulatory Support System as a salvage procedure when the patient failed to wean (FTW) from cardiopulmonary bypass.

Of this FTW literature cohort, an estimated 370 of the 413 patients were supported with the CentriMag system as a ventricular assist device, either as a left ventricular assist device [LVAD – 14%], a right ventricular assist device alone [RVAD – 17%], supporting both sides of the heart [BiVAD – 30%], or supporting the right ventricle in patients supported by a durable LVAD [RVAD with LVAD, 39%]. The remaining 167 FTW patients were

supported by the CentriMag System in conjunction with an extracorporeal membrane oxygenator device in a cardiopulmonary mechanical support circuit using either peripheral or central cannulation.

Duration of support ranged from <1 to 146 days in the FTW literature pool, with an overall pooled mean of 12.5 days. This compares to the CentriMag Pivotal Trial mean duration of support of 12.7 days and the CentriMag Pilot Trials mean durations of support of 12.8 days for cardiogenic shock (including PCCS FTW[1] cases) and 15.3 days for RVAD support with a durable implanted LVAD.

Estimated survival to discharge in the FTW literature pool was 52% (95% confidence interval of 47%-57%),. This is greater than the reported 27% benchmark established from prior literature for alternate devices, and is comparable to current state of the art summaries of all post cardiotomy cardiogenic shock mechanical support (inclusive of failure-to-wean patients, who are anticipated to have a lower survival rate than the PCCS population as a whole).

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

For the 32 patients enrolled in the CentriMag Pivotal Trial for Failure to Wean from cardiopulmonary bypass, recovery, defined as survival to discharge (or 30 days, whichever was longer), was 63%. This recovery rate exceeds the benchmark historical rate of 27% baste on reports in literature for patients who failed to wean from cardiopulmonary bypass and were treated with other mechanical circulatory support devices. The results of the Pivotal Trial were corroborated by results of the Sponsor's other clinical studies of the CentriMag System and by a literature review of CentriMag use, both of which also demonstrated survival rates numerically higher than the historical rate of 27%. No formal statistical hypothesis testing was performed on any of the above studies, as no pre-specified statistical analysis plan that propertly considers operating characteristics (e.g. sample size, type I error, power, etc.) was available for any of them.

B. Safety Conclusions

[1] PCCS FTW: post-cardiotomy cardiogenic shock failure to wean from cardiopulmonary bypass

The risks of the device are based on nonclinical bench testing, animal studies and data collected in clinical studies conducted to support PMA approval as described above. Since the device has been in commercial distribution for other indications for use both in the United States and elsewhere, the clinical experience in commercial use was also assessed for risks. By definition, post-cardiotomy patients who fail to wean from cardiopulmonary bypass require continued mechanical circulatory support for survival. This critically ill patient population typically has numerous comorbidities at the time that support with the CentriMag System is initiated, resulting in a high rate of adverse events. Adverse events that occurred in more than 10% of the patients enrolled across the four clinical studies included; death (37%), bleeding (82%), respiratory failure (61%), infection (47%), arrhythmias (43%), right heart failure (24%), renal dysfunction (25%), hemolysis (12%) and hepatic dysfunction (11%). The rates of these adverse events are not unanticipated, being typical for patients recovering from open heart surgery and receiving mechanical circulatory support, as reported in the literature. The number of adverse events judged to be caused by the CentriMag system were relatively small.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in clinical studies conducted to support PMA approval as described above. Although adverse event rates were high in the clinical studies, they were not unexpected, and the CentriMag system provided a significant survival benefit (63%) in a patient population with an expected mortality of nearly 100%.

The probable risks of the device are also based on data collected in clinical studies conducted to support PMA approval as described above. There is a probability that every CentriMag patient will experience at least one harmful event. The incidence rate for the five most frequently occurring adverse events in the CentriMag clinical patients were:

- Bleeding: 82%
- Infection: 47%
- Respiratory Failure: 61%
- Arrhythmias: 43%
- Death: 37%

The following device-related non-serious adverse events have been observed for this device:

- Psychiatric Episode
- Wound Dehiscence

CentriMag patients are subject to all the potential complications associated with general anesthesia, cardiopulmonary bypass and open-heart surgery; e.g. bleeding, cardiac arrhythmias, neurological insults, infection, etc.

Additional factors to be considered in determining probable risks and benefits for the CentriMag Circulatory Support System included: consistency of results across all four clinical studies and literature review, the nearly 100% expected mortality in the indicated patient population, and the limited number of treatment options.

1. Patient Perspectives

   This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that the probable benefits of providing mechanical circulatory support with the CentriMag Circulatory Support System for up to 30 days outweighs the probable risks for post-cardiotomy patients who fail to wean from cardiopulmonary bypass.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the CentriMag Circulatory Support System when used to provide mechanical circulatory support for up to 30 days for post-cardiotomy patients who fail to wean from cardiopulmonary bypass (PCCS).

XIV. CDRH DECISION

CDRH issued an approval order on [date of approval order]. The final conditions of approval cited in the approval order are described below.

The applicant has agreed to provide the following non-clinical information in reports, which may be followed by a PMA supplement where applicable.

1. Cybersecurity: FDA has noted that the applicant performed some verification testing on the CentriMag Mag Monitor Version 2 to support the implemented cybersecurity controls and is aware that the applicant is performing a Security Evaluation and Analysis and project to have testing completed by November 15, 2019. In order to guarantee that the implemented controls are sufficient to ensure the device remains safe and effective for use, the applicant must perform the following:

a. Complete the Security Evaluation and Analysis Results and Assessment inclusive of vulnerability scanning on Mag Monitor Version 2 for Software Versions 3.00 and 3.01.
b. Submit the results to FDA by January 6, 2020.
c. For any uncontrolled risks are identified in accordance with the FDA Guidance "Postmarket Management of Cybersecurity in Medical Devices," issued December 2016:
   i. Provide an assessment of whether any uncontrolled risks require disclosure to FDA no later than January 6, 2020,

ii. Any patches for the uncontrolled risks should be available and submitted to FDA no later than May 15, 2020.

The applicant has also agreed to provide the following data in post approval study (PAS) reports:

1. ***CentriMag FTW PAS***: This study will be conducted per the study synopsis submitted in P170038. This PAS will be an observational hypothesis-driven clinical investigation whose purpose is to confirm the safety and effectiveness of the CentriMag Circulatory Support System for patients who fail to wean from cardiopulmonary bypass. A minimum of 31 consecutive consented subjects receiving the CentriMag device for the failure to wean indication will be enrolled at 5 to 15 US sites, followed, and evaluated to assess the rates of survival (primary endpoint) and the rates and descriptions of all adverse events and device malfunctions (secondary endpoints) at discharge or up to 30 days after device explant, whichever is longer. For patients who do not recover and are bridged to a heart transplant or a longer-term circulatory support device, the endpoints will be determined through the time of induction of anesthesia for the surgery. The expected duration of follow-up is a minimum of 30 days after device explant and the follow-on assessments should be performed per standard of care. This sample size was determined to have 80% power to demonstrate non-inferiority for the primary endpoint hypothesis test. The hypothesis will test that the proportion of subjects meeting the primary endpoint is non-inferior to the historical proportion from the CentriMag Pivotal Study of 63%, with a margin of 20%. If the lower bound of the one-sided 95% confidence limit for the primary endpoint is greater than 44%, non-inferiority will be demonstrated. Results from interim descriptive analyses of secondary endpoints, the number of investigational sites participating, and enrollment progress will be reported to the FDA in each PAS Progress Report and posted annually by the FDA. The FDA will post the primary endpoint results when they are evaluable. Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

1. AbioMed BVS 5000 Bi-Ventricular Support System, Summary of Safety And Effectiveness (SSED), approved by FDA on 20 November 1992.
2. Thoratec Vemtricular Assist Device (VAD) System, PMA P870072/S5, Summary of Safety and Effecitveness (SSED), approved by FDA on 21 May 1998 (https://www.accessdata.fda.gov/cdrh_docs/pdf/P870072S005B.pdf)