CardioMEMS™ HF System

Model CM3000

SYSTEM GUIDE

ST. JUDE MEDICAL™

Do not attempt to use the device before reading and fully understanding the User's Manual and the System Guide.

Carefully inspect all product packaging for damage or defects prior to use.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

Contents

Description

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

The system includes the following components:

- Implantable wireless sensor with delivery catheter
- Patient or Hospital Electronics System
- Patient database

The wireless sensor is designed for permanent implantation into the distal pulmonary artery. Once implanted, the CardioMEMS PA Sensor provides non-invasive hemodynamic data that is collected in the physician's office, clinic, hospital, or patient's home. The data provided by the system includes:

- PA pressure waveform
- Systolic, Diastolic, and Mean PA pressure
- Heart Rate

This hemodynamic data is transmitted to a secure website that serves as the patient database so that PA monitoring information is available at all times through the internet. Changes in PA pressure can be used in conjunction with heart failure signs and symptoms to guide adjustments to medications.

For information on the use of the sensor, please refer to the User's Manual. For information on the operation of the patient database, please refer to the Merlin.net™ Patient Care Network Heart Failure Management Application Help Manual. For clinical study information, please refer to the Clinical Study Information section.

Indications

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

Contraindications

The CardioMEMS HF System is contraindicated for patients with an inability to take dual antiplatelet or anticoagulants for one month post implant.

Warnings

Before use of the system, read this guide.

- Only trained personnel should use this product.
- Avoid excessive or damaging force when using the Hospital Electronics System (Model # CM3000).
- Do not change the system configuration without authorization from the manufacturer.
- If two electronic units are proximate to each other and are used at the same time, pressure measurements may be affected due to interference between the two systems. In such isolated cases, it is recommended that operation of each electronics unit occur at separate times.
- Two hospital electronics systems may interfere with each other. Only operate one electronics unit at a time in the same general vicinity.
- The CM3000 requires special precautions regarding electromagnetic compatibility (EMC) and needs to be placed into service according to the EMC information provided. If interference is noted, remove or stop using the interfering equipment.
- The use of accessories, transducers and cables other than those specified, with the exception of transducers and cables sold by the manufacturer of the CM3000 as replacement parts for internal components, may result in increased emissions or decreased immunity of the CM3000. The use of other attachable parts other than the parts provided may result in inaccurate readings, damage to the system, or injury to the user.
- The CM3000 should not be used adjacent to or stacked with other equipment. If it is necessary to operate adjacent or stacked with other equipment, observe the CM3000 to verify normal operation in the configuration in which it will be used.
- Other equipment may interfere with the CM3000 operation, even if the other equipment complies with CISPR emission requirements. Refer to the EMI/EMC and Troubleshoot Procedure sections for guidance.
- There are minimum amplitudes for the CM3000 to measure physiological signals. Operation of the equipment below the minimum amplitudes may cause inaccurate results.
- Do not attempt to connect the Hospital Electronics System to any network or data coupling equipment in the hospital other than those specified.
- Follow instructions on shutting down equipment. Failure to do so may cause file corruption.
- While in use, ensure that the power supply is easily accessible since unplugging the device from the outlet is the only means of completely isolating from mains.
- Ingestion of any part of the system may cause injury.
- Care should be taken to keep all cables away from the neck and face to prevent airway blockage.
- Patients should be advised that if they develop redness of the skin or a change in skin sensitivity occurs, they should discontinue use of this product immediately and contact their physician.

- All sensors have a unique calibration. Ensure readings are only taken using the correct calibration information from the sensor. Use of the incorrect calibration information may result in an inaccurate reading.
- All right heart catheterizations must be performed under fluoroscopic guidance to prevent sensor dislodgement.
- The sensor is visible under plain film X-ray and fluoroscopy. Under CT imaging, there may be localized beam hardening artifact around sensor implant.
- This product is not made with natural rubber latex.

Precautions

- Store the CM3000 in a temperature controlled, clean and dry area.
- Use the CM3000 at temperatures between 5º to 40º C (41º to 104º F) and 15% to 93% humidity. Store the system between -25 to 70º C (-13º to 158º F), 15% to 93% humidity.
- All electronic devices with the Hospital and Patient Electronics Systems, including components and accessories, are to be used only with the sensor and not with other products, appliances or devices. If there is evidence of a change in performance, please contact Technical Support to obtain more information.
- Avoid excessive or damaging force when using the AC adapter.
- Exposure to excess lint or dust may cause the system to malfunction.
- The system consists of an electronics unit and an antenna. If any of the following occurs, immediately unplug the electronics unit and contact Technical Support:
  - Any cords are noticeably frayed or damaged
  - Liquid has spilled onto the monitor, or it has been exposed to rain
  - The system has been dropped or the enclosure has been damaged
- If you lose the power cord, replace it with an identical cord. Contact Technical Support to obtain a new one.
- Only an authorized technician should remove the cover or attempt to service the device. The warranty may be voided otherwise.
- Do not place the system near a window. Exposing the LCD screen to rain, water, moisture or sunlight may severely damage it.
- Do not apply excessive pressure to the LCD screen. Excessive pressure may cause damage to the display.
- Portable and mobile RF communications equipment can affect medical electrical equipment and may cause a malfunction of the system.
- All new or refurbished equipment should be obtained from the manufacturer.
- The CM3000 may require secure data transfer through the use of the internet or networks. Portions of this internet or network pathway may become unavailable for periods of time for a variety of reasons including but not limited to: internet connectivity outage, hardware failure, power outage, or general infrastructure failures. Readings and data that are unable to transmit are stored and will transmit when connectivity is available.
- The mean pressure measurement accuracy of the system may be affected by various factors. Mean pressure measurement error has been observed when the sensor was deployed in a vessel which had an inner diameter of less than 7 mm, and in cases where there was an acute bend in the vessel of >30 degrees at the location of the sensor. Signs of mean pressure measurement error include the following:
  - Gradual mean pressure changes without a corresponding proportional change in the pulse pressure (systolic-diastolic pressure)
  - Negative mean pressures

  If either feature is observed, temporarily suspend use of the pressure information for management of the patient and contact Technical Support for further assistance. A right heart catheterization may be needed to recalibrate the Baseline (mean pressure) in order to continue use of the system.
- The touchscreen display on the handheld unit can be sensitive to electrostatic discharge (ESD) at high levels. To reduce the potential for ESD discharge to the touchscreen, remove and hold the plastic handle of the handheld prior to contact with the touchscreen.
  If the touchscreen becomes damaged due to ESD, the screen will be discolored or may be unresponsive. Contact Technical Support for replacement of the handheld unit.
  Please note that high levels of ESD are more likely in situations where the relative humidity is very low, such as inside a heated building during the winter in areas where it is cold outside. In order to reduce the potential for ESD levels, there are common situations which create static electricity that can be avoided prior to use, for example, putting on and removing clothes, dragging your feet across a carpet or rug, vacuuming, or removing clothes from a dryer.
- The system is not intended to be used in a severe electromagnetic radiation environment or an industrial environment.
- The system should not be used in conjunction or in association with Magnetic Resonance Imaging (MRI), computerized axial tomography (CT), diathermy, Radio Frequency Identification (RFID), and electromagnetic security systems such as metal detectors.

Package Contents

The system package contains:
- Hospital Electronics System
- Product documentation

Sterilization

The Hospital Electronics System is provided non-sterile.

Components and Setup

Connect the System Cables

1. Align the keyed antenna at an approximately 30 degree angle and twist on the locking connector.

Figure 1. Connecting the antenna
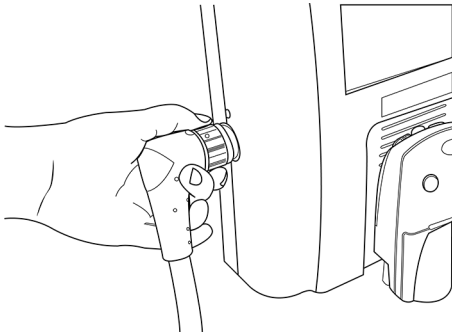
2. Attach the connectors as shown in the figure below.

    Connectors:
    -   Power supply connector (5 pin DIN)
    -   Printer serial communication cable (9 pin D-SUB)
    -   Printer power cable

    Note: A VGA cable can be connected to the auxiliary VGA connector.

Figure 2. The connectors
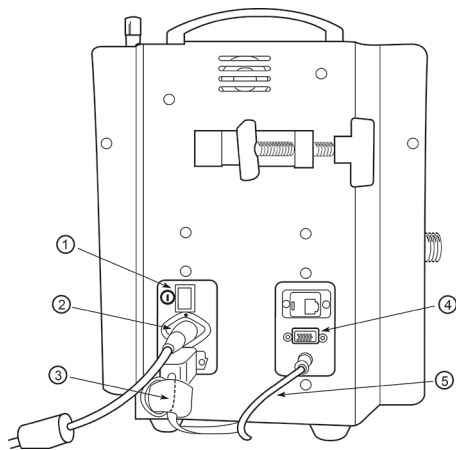
1. Power switch
2. Power cable
3. Printer serial cable
4. VGA connection
5. Printer power cable

3. Plug the power cord into the power supply and plug the power cord into the wall.

Printer

The printer clips into the mount on the front of the electronics unit. The cables for the printer run under the electronics unit. Disconnect them if necessary.

Figure 3. The printer mount
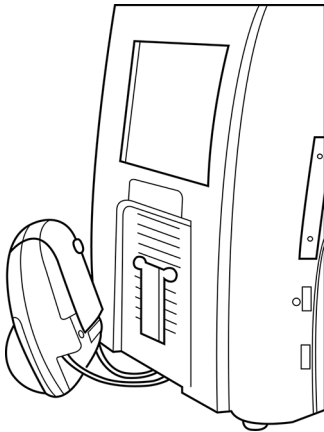
The Pole Attachment

1. To mount the electronics unit to a pole, use the pole clamp.

2. Ensure that the pole is sturdy and can remain stable when at an incline of 10 degrees. Recommended pole: Pryor Products, Inc. #135.

3. Ensure that the pole has locking wheels such that it can remain stationary on a 10 degree angle.

4. If the pole is on an incline, it may experience an initial settling movement prior to establishing a stable fix location, ensure that control of the pole is maintained until stable.

5. If the pole has the ability to extend, do not extend the height of the pole. Keep the pole at its lowest height setting.

Figure 4. The pole clamp
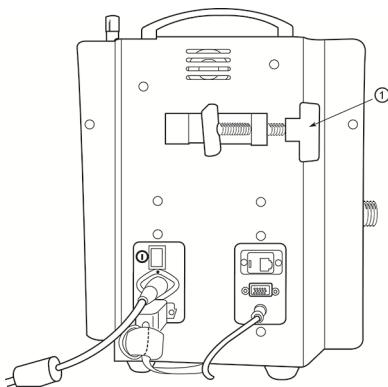
1. Pole clamp

Hospital Electronics System Password Access

By default, new Hospital Electronics Systems require you to enter a Merlin.net PCN username and password before you can use the system. This protects the privacy of patient information. If the system is in a secure area, and you are a Merlin.net PCN administrator, you can disable the Password Entry screen from the Settings screen.

If you are unable to gain access with the password, you can obtain a temporary password on the My Account page on the Merlin.net Patient Care Network Heart Failure Management Application. To access the system after you obtain a temporary password:

1. Enter your username and password on the User Log On screen.

2. Select the OK button.

    The system attempts to connect to the network.

3. Select the Cancel button.

    The system logs you in.

If you are unable to log in, contact Technical Support for additional assistance.

Patient and Hospital Electronics Systems

The CardioMEMS PA Sensor is implanted into a distal branch of the descending PA. Following implantation, patients are instructed to take pressure readings from home as directed by their physician. The information transmitted to the database is immediately available to clinicians for review. The information consists of pressure trend information and individual PA pressure waveforms.

The Patient and Hospital Electronics Systems have been designed to obtain information from the sensor. The functional components of the hardware include an electronics unit and an antenna. The antenna simultaneously sends a Radio Frequency (RF) signal to energize the sensor and measures the RF signal returned by the sensor. This returning signal is processed and stored in the electronics unit.

There are two types of electronics systems: the Patient Electronics System and the Hospital Electronics System. The Patient Electronics System is the primary means of monitoring. It is used at home by the patient to take regular measurements. The Hospital Electronics System is used during sensor implant and when the patient needs measurements taken in a clinical setting.

The Hospital Electronics System should be mounted on a portable pole stand with wheels and stored in the Catheterization Lab area or Heart Failure Clinic as needed by clinicians.

Figure 5. The Hospital Electronics System

1. Thermal printer
2. Touchscreen
3. USB ports
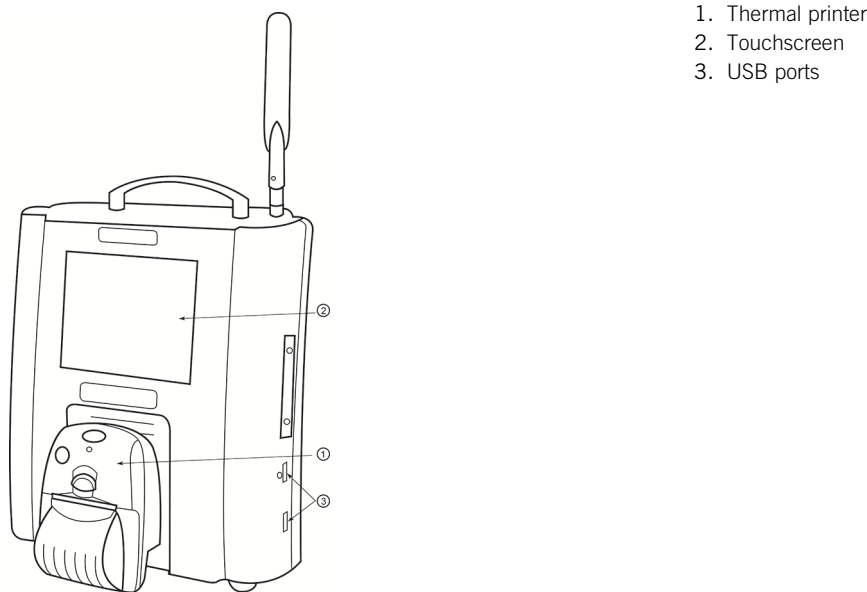
Antenna

The antenna attached to the Hospital Electronics System is designed for ease of use during implant and for follow-up measurements in the hospital or clinic. The antenna is the means of coupling to the sensor and is connected to the electronics unit by a custom cable with a locking connector. During a measurement, the antenna is placed near the sensor. The antenna uses RF energy to power the sensor. When the sensor is energized, it returns an RF signal. The antenna receives the signal and sends it to the electronics system for processing into a pressure waveform.

The arrows on the antenna control the Search pressure, and the green square lets you take a reading.

Due to the design of the system, you can leave the antenna attached to the electronics unit at all times if desired.

NOTE: The serial number on the antenna and on the electronics unit must match.

Figure 6. Antenna
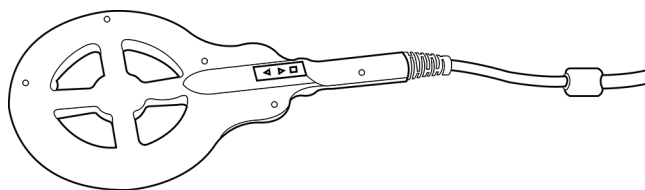
Overview

Implant Procedure Overview

Step 1:	Enter Info	• Patient information and sensor characteristics
Step 2:	Acquire Signal	• Position antenna to obtain the sensor signal
Step 3:	Set Baseline	• Correlate the sensor readings with reference pressures
Step 4:	Take Reading	• Collect data
Step 5:	Transfer Data	• Upload sensor and patient data

For detailed instructions, refer to the following sections:
- New Sensor Implant - Wireless Connection Available
- New Sensor Implant - No Wireless Connection Available

New Sensor Implant - Wireless Connection Available

This section presents using the Hospital Electronics System to perform a sensor implant when a wireless connection is available for communication with the Merlin.net Patient Care Network Heart Failure Management Application.

Before the Hospital Electronics can be used to measure a newly implanted sensor, the electronics must be set up with the following information:
- Patient Information
- Sensor Characteristics

Step 1: Enter Information

All Hospital Electronics Systems are equipped with cellular antennas. WiFi is an available accessory. The workflow presented in this section is recommended based on simplicity. These instructions expect that the conditions in your institution permit the use of wireless connectivity. If this is not possible in your institution see the section New Sensor Implant – No Wireless Connection Available below.

1. Patient Information: Prior to the first sensor implant of the day, use the Merlin.net Patient Care Network Heart Failure Management Application to enter the patient information for all of the patients expected to receive a CardioMEMS HF sensor in the cardiac catheterization lab that day. Please refer to the Merlin.net Patient Care Network Heart Failure Management Application Help Manual for details.

   Sensor Information: Each sensor has unique characteristics which must be loaded into the Hospital Electronics System. The sensor information is stored on a USB flash drive inside the sensor box. It is important that the sensor information loaded into the Hospital Electronics System matches the sensor implanted.

   Wait until the time of sensor delivery and then follow the instructions below on the Hospital Electronics System for each new sensor:

2. Insert USB flash drive from sensor package into the USB port.

3. Select New Implant button.

4. You will be presented with the list of patients that you entered into the Merlin.net Patient Care Network Heart Failure Management Application.

5. Select the desired patient from the list.

6. If prompted, insert the USB flash drive from the sensor package into the USB port. (System will only prompt if USB flash drive was not already inserted.)

7. After the sensor information is loaded, it will be displayed along with the patient information. Verify that Sensor Serial displayed matches the Serial Number printed on the sensor box.

The screens for these steps are shown in the following sequence.

Figure 7. Main screen, select New Implant.
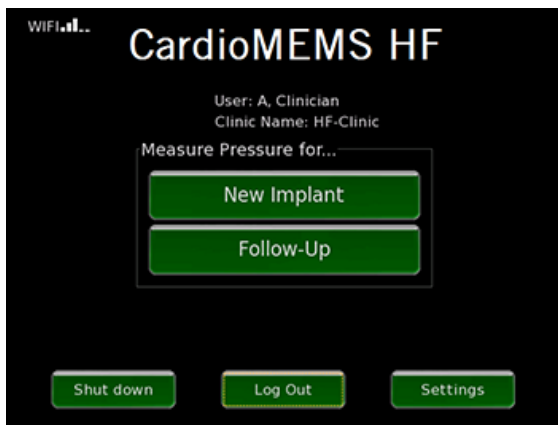
Figure 8. Select patient from list downloaded from Merlin.net Patient Care Network Heart Failure Management Application.

NOTE: All screenshots are simulations and do not represent actual patients or actual patient data.

Figure 9. Insert USB drive if prompted. This screen will not appear if USB drive was already inserted.

Figure 10. Verify patient and sensor information.
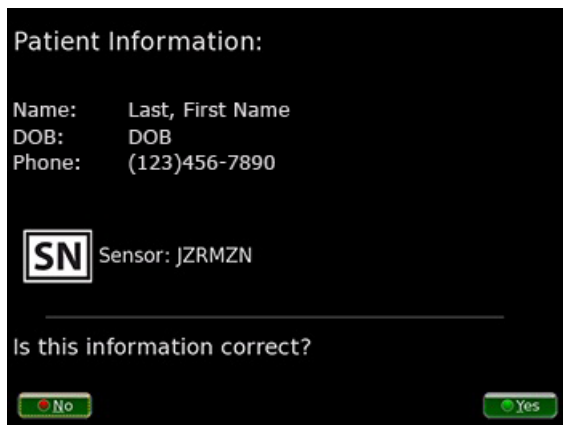
Step 2: Acquire Signal

Once you have loaded the patient and sensor information into the Hospital Electronics System and then implanted the sensor, the steps below describe how to set the pulmonary artery (PA) pressure baseline.

1. Place the antenna under the patient's back, approaching from the side where the sensor was placed. Antenna is not sterile. Sliding the antenna between the sheet and the table works well. Position the center of the antenna under the tip of the patient's shoulder blade on the side of the torso where the sensor is located.

2. The signal strength (SS) bar indicates the robustness with which the Hospital Electronics System is measuring the implanted sensor. If the signal strength bar is optimal (>70% and a green color, see figure below), go to the next step. If not, go to the section Optimize Signal Strength.

Step 3: Set Baseline

1. A pulmonary artery or Swan-Ganz[1] catheter is used to set the baseline pressure for the sensor. For an accurate sensor measurement, it is important to set up the pulmonary artery or Swan-Ganz catheter properly. See Pulmonary Artery Catheter Setup section.

2. Initially, you will observe that the pressure values on the right of the waveform are dashed out. This indicates that the PA pressure baseline has not been set.

Figure 11. Initial Pressure Waveform.
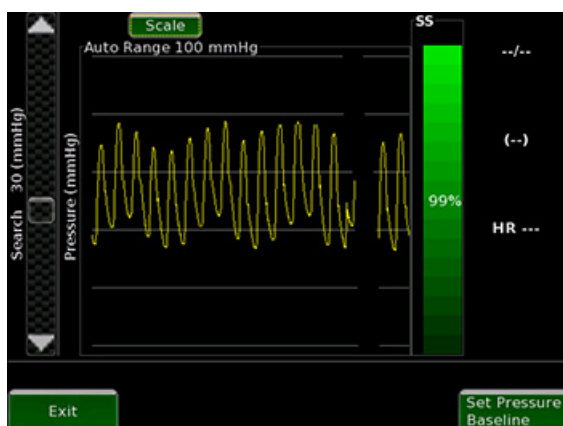
3. To Set the PA Pressure Baseline, wait for the screen to fill with a stable pressure waveform and then select the Set Pressure Baseline button.

4. Enter the mean pressure from the pulmonary artery catheter measurement and select the OK button.

---

[1] Swanz-Ganz is a registered trademark of Edwards Lifesciences Corporation.

Figure 12. Setting PA Pressure Baseline.
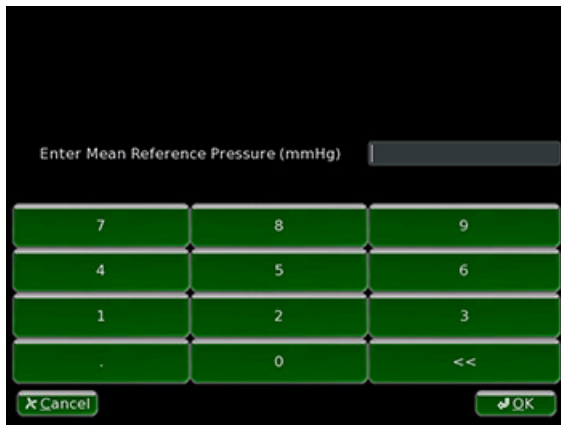
5. Wait for the screen to re-fill with a stable pressure waveform and then confirm that the sensor mean pressure matches the catheter PA mean pressure within +/- 1mm Hg. Repeat the PA Baseline step as necessary to achieve a good match between measurements.

Figure 13. System after PA Pressure Baseline has been set.
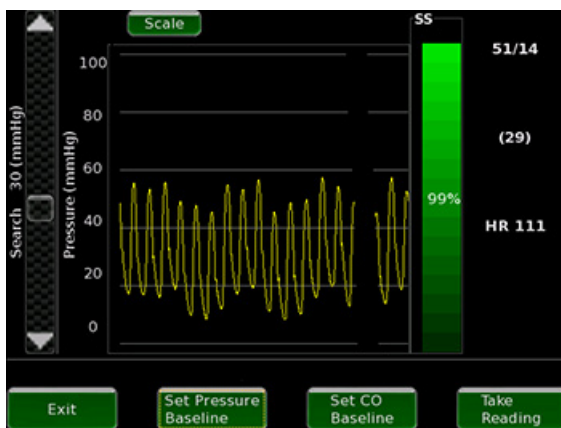
6. Confirm that the height of the sensor pressure signal (i.e., pulse pressure (systolic – diastolic)) is within +/- 25% of the catheter pulse pressure. See Pulmonary Artery Catheter Setup section. Set the PA Pressure Baseline again, if necessary.

7. Setting the cardiac output baseline is an optional step.

8. To set the cardiac output (CO) baseline, you will need a reference value for cardiac output. This can be either thermodilution or modified Fick.

9. Select the button Set CO Baseline. The Hospital Electronics System will indicate that the baseline data is being collected and will prompt for the reference cardiac output once finished.

Figure 14. Enter Reference Cardiac Output to Set Baseline.

10. Enter the reference cardiac output value and select OK.

Step 4: Take Reading

Once you are satisfied with the PA pressure baseline, take as many pressure readings as desired. Establishing accurate baseline PA pressure at the time of implant is important to ensure accurate PA pressure readings from home.

1. Select the Take Reading button to capture pressure measurements.

2. The system will then prompt you to enter the comparative pulmonary artery catheter pressure values for reference. Enter the catheter values and select the OK button. The comparative pulmonary artery catheter pressure values are optional. They are used to visually check that the PA pressure values have the proper baseline and amplitude.

Figure 15. Enter Pulmonary Artery Catheter Pressure Values.

3. The captured reading is displayed graphically for confirmation. The colored horizontal lines indicate the catheter pressure values entered as reference. The green line indicates systolic pressure, blue indicates mean pressure, and red indicates diastolic pressure.

Figure 16. Pulmonary Artery Catheter Pressure Reading
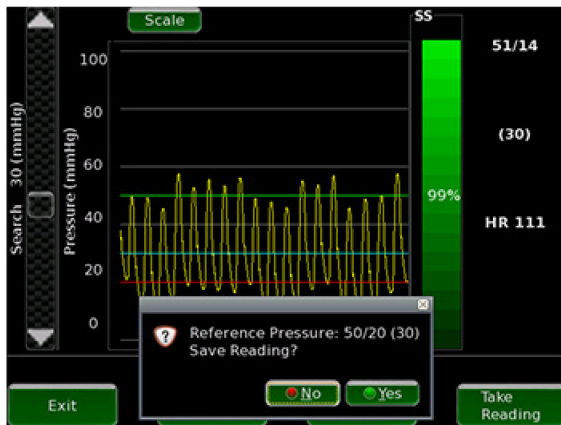
4. If the reading is acceptable, select the Yes button to save the reading. If the reading is unacceptable, select the No button and repeat the reading.

5. Re-confirm that the sensor mean pressure matches the catheter PA mean pressure within +/- 1mm Hg. Check the setup and if necessary, set the PA Pressure Baseline again to achieve a good match between measurements.

6. Re-confirm that the height of the sensor pressure signal (i.e., pulse pressure (systolic – diastolic)) is within +/- 25% of the catheter pulse pressure. Check the setup and if necessary, set the PA Pressure Baseline again to achieve a good match between measurements.

Step 5: Transfer Data

Once the readings are complete, the Merlin.net Patient Care Network Heart Failure Management Application must be updated with the information. In the case a wireless data connection is available, this happens automatically.After the data is transferred, the system checks for software updates. Refer to the Software Update section for more information.

1. Select Exit from the data acquisition screen. If the user selects to print, the readings will print.

2. The baselines and readings will be automatically transmitted to the Merlin.net Patient Care Network Heart Failure Management Application.

Step 6: Shutting Down the System

To shut down the system:

1. Navigate to the Main screen.

2. Select Shut Down on the Main screen.

Figure 17. Main screen, Select Shut Down
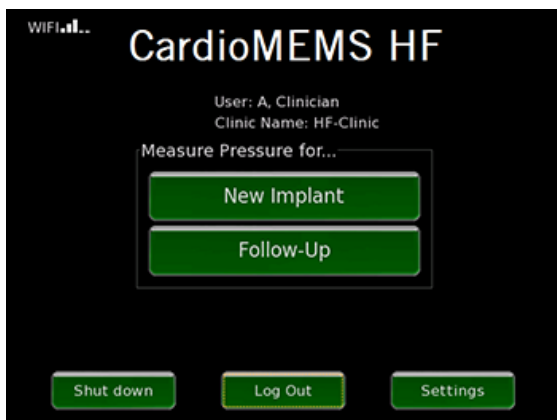
3. Allow the system to complete the shut-down sequence prior to disconnecting power from the system.

CAUTION: Disconnecting power before the shut-down sequence is completed may cause file corruption.

New Sensor Implant – No Wireless Connection Available

This section presents the use of the Hospital Electronics System to perform a sensor implant when a wireless connection is not available for communication with the Merlin.net Patient Care Network Heart Failure Management Application. The patient information is entered manually on the Hospital Electronics System.

Before the Hospital Electronics can be used to measure a newly implanted sensor, the electronics must be set up with the following information:

- Patient Information
- Sensor Characteristics

Step 1: Enter Information

Each sensor has unique characteristics which must be loaded into the Hospital Electronics System. The sensor information is stored on a USB flash drive inside the sensor box. It is important that the sensor information loaded into the Hospital Electronics System matches the sensor implanted.

Wait until the time of sensor delivery and then follow the instructions below on the Hospital Electronics System for each new patient:

1. Insert USB flash drive from sensor package into the USB port.

2. Select New Implant.

3. Patient Information: Enter the patient information using the touch screen keyboard. To modify a field such as first name, simply touch it and the touch keyboard will appear. It is necessary to fill out the first and last name fields and the birthdate. The phone number field is optional. All of this information will appear on the website once implant is complete.

4. Sensor Information: Each sensor has unique characteristics which must be loaded into the Hospital Electronics System. The sensor information is stored on a USB flash drive inside the sensor box. It is important that the sensor information loaded into the Hospital Electronics System matches the sensor implanted.

5. If prompted, insert the USB flash drive from the sensor package into the USB port. (The system will only prompt if USB flash drive was not already inserted.)

6. After the sensor information is loaded, it will be displayed along with the patient information. Verify that Sensor Serial displayed matches the Serial Number printed on the sensor box.

The screens for these steps are shown in the following sequence.

Figure 18. Main screen, select New Implant.
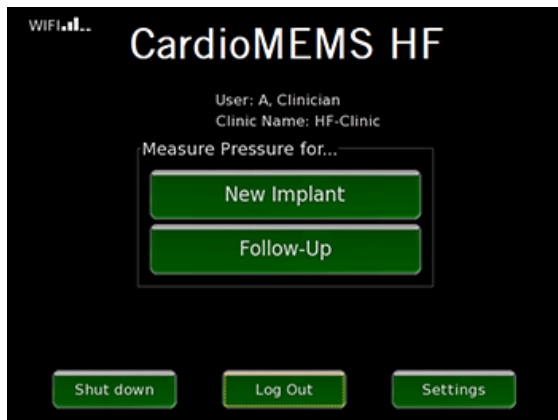
Figure 19. Enter patient demographic information.

Figure 20. Enter patient information using touch keyboard.

Figure 21. Insert USB drive if prompted. This screen will not be shown if the USB drive was already inserted.

Figure 22. Verify patient and sensor information.

Step 2: Acquire Signal

Once you have loaded the patient and sensor information into the Hospital Electronics System and then implanted the sensor, the steps below describe how to set the pulmonary artery (PA) pressure baseline.

1. Place the antenna under the patient's back, approaching from the side where the sensor was placed. Position the center of the antenna under the tip of the patient's shoulder blade on the side of the torso where the sensor is located.

2. The signal strength (SS) bar indicates the robustness with which the Hospital Electronics System is measuring the implanted sensor. If the signal strength bar is optimal (>70% and a green color), go to the next step. If not, go to the Optimize Signal Strength section.

Step 3: Set Baseline

1. A pulmonary artery catheter is used to set the baseline for the sensor. For an accurate sensor measurement, it is important to set up the catheter properly. See Pulmonary Artery Catheter Setup section.

2. Initially, you will observe that the pressure values on the right of the waveform are dashed out. This indicates that the PA pressure baseline has not been set.

Figure 23. Initial Pressure Waveform.
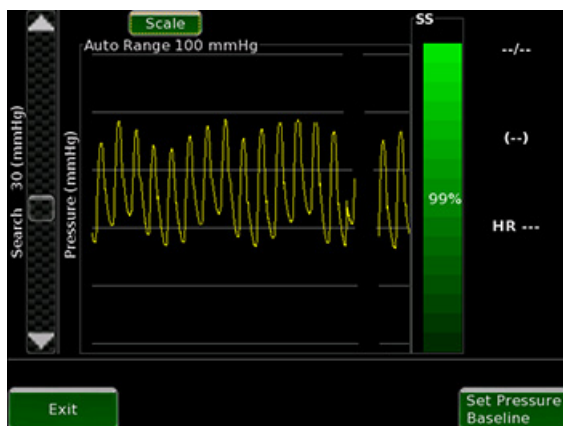
3. To Set the PA Pressure Baseline, wait for the screen to fill with a stable pressure waveform and then select the Set Pressure Baseline button.

4. Enter the mean pressure from the pulmonary artery catheter measurement and select the OK button.

Figure 24. Setting PA Pressure Baseline.
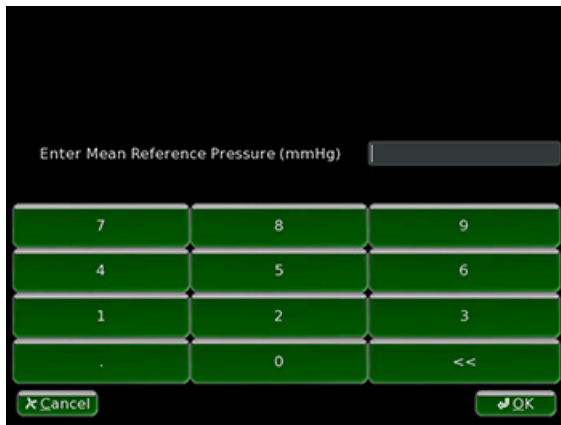
5.   Wait for the screen to re-fill with a stable pressure waveform and then confirm that the sensor mean pressure matches the catheter PA mean pressure within +/- 1mm Hg. Set the PA Pressure Baseline step again as necessary to achieve a good match between measurements.

Figure 25. System after PA Pressure Baseline has been set.
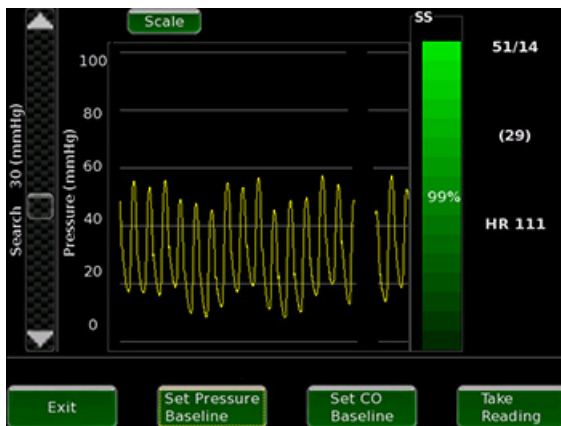
6.   Confirm that the height of the sensor pressure signal (i.e., pulse pressure (systolic – diastolic)) is within +/- 25% of the catheter pulse pressure. See Pulmonary Artery Catheter Setup section. Set the PA Pressure Baseline again, if necessary.

7.   Setting the cardiac output baseline is an optional step.

8.   To set the cardiac output (CO) baseline, you will need a reference value for cardiac output. This can be either thermodilution or modified Fick.

9.   Select the button Set CO Baseline. The Hospital Electronics System will indicate that the baseline data is being collected and will prompt for the reference cardiac output once finished.

Figure 26. Enter Reference Cardiac Output to Set Baseline.

10.   Enter the reference cardiac output value and select OK.

Step 4: Take Reading

Once you are satisfied with the PA pressure baseline, take as many pressure measurements as desired. Establishing accurate baseline PA pressure at the time of implant is important to ensure accurate PA pressure readings from home

1.   Select the Take Reading button to capture pressure measurements.

2.   The system will then prompt you to enter the comparative catheter pressure values for reference. Enter the catheter values and select the OK button. The comparative pulmonary artery catheter pressure values are optional. They are used to visually check that the PA pressure values have the proper baseline and amplitude.

Figure 27. Enter Pulmonary Artery Catheter Pressure Values.
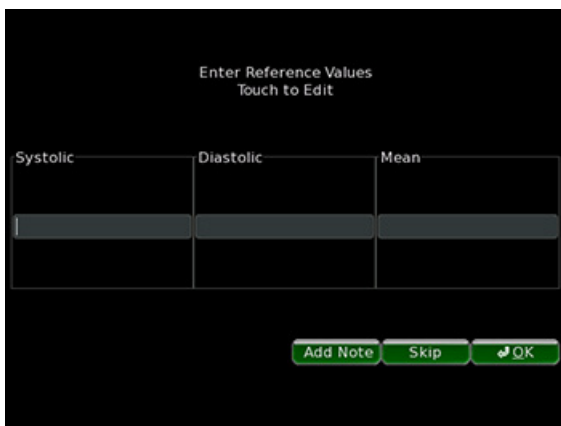
3.   The captured reading is displayed graphically for confirmation. The colored horizontal lines indicate the entered catheter pressure values entered as reference. The green line indicates systolic pressure, blue indicates mean pressure, and red indicates diastolic pressure.

Figure 28. Pulmonary Artery Catheter Pressure Reading.

4. If the reading is acceptable, select the Yes button to save the reading. If the reading is unacceptable, select the No button and repeat the reading.

5. As was discussed in the Step 2: Acquire Signal section above, re-confirm that the sensor mean pressure matches the catheter PA mean pressure within +/- 1mm Hg. Check the setup and if necessary, set the PA Pressure Baseline again to achieve a good match between measurements.

6. As was also discussed in the Step 2: Acquire Signal section above, re-confirm that the height of the sensor pressure signal (i.e., pulse pressure (systolic – diastolic)) is within +/- 25% of the catheter pulse pressure. Check the setup and if necessary, set the PA Pressure Baseline again to achieve a good match between measurements.

Step 5: Transfer Data

Once the readings are complete, the Merlin.net Patient Care Network Heart Failure Management Application must be updated with the information. A USB flash drive is used to accomplish this.

1. Select Exit from the data acquisition screen. If the user selects to print, the readings will print.

2. You will be prompted to save the information to a USB flash drive.

   NOTE: A USB flash drive is provided in the sensor box with each sensor, but you can use any USB flash drive. Most commercial USB flash drives will be compatible with both the electronics system and the computer used to access the Merlin.net Patient Care Network Heart Failure Management Application.

Figure 29. Save Implant Data to the USB Flash Drive.
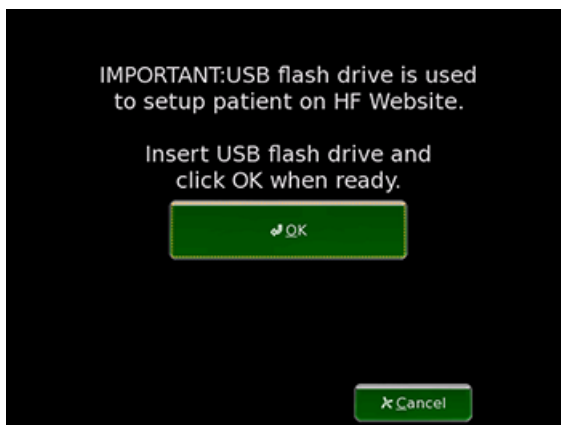
Step 6: Shutting Down the System

To shut down the system:

1. Navigate to the Main screen.

2. Select Shut Down on the Main screen.

Figure 30. Main screen, Select Shut Down
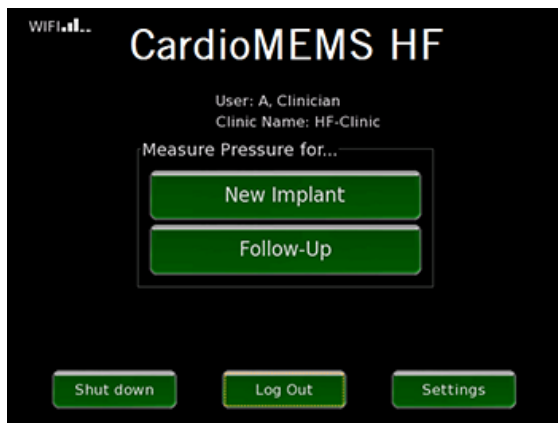
3. Allow the system to complete the shut-down sequence prior to disconnecting power from the system.

   CAUTION: Disconnecting power before the shut-down sequence is completed may cause file corruption.

Merlin.net Patient Care Network Heart Failure Management Application Setup

The Merlin.net Patient Care Network Heart Failure Management Application is the central window from which to view the status of your patient. After the implant you need to confirm the proper setup of your patient on the website.

The following important information is updated on the website after implant:

- The link between your medical institution and the patient. Patient data is only visible to users associated with your medical institution.
- The baselines and readings from the implant procedure. This allows accurate trending once your patient begins to take readings at home.

Refer to the Merlin.net Patient Care Network Heart Failure Management Application Help Manual for specific website setup instructions.

You will not be able to set up the Patient Electronics until the website has been set up with your patient's information.

Patient Electronics System Setup

After the website has been properly set up, the Patient Electronics must be set up before your patient can begin taking readings at home.

Figure 31. Patient Electronics System
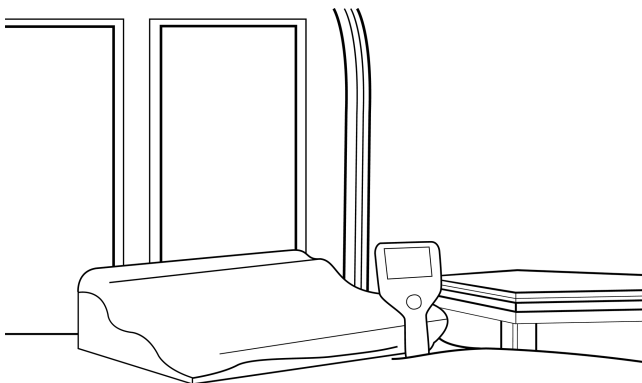
The Patient Electronics will be set up with the following:

- Patient Information
- Sensor Characteristics
- Baseline Information

There are two primary ways to set up the electronics with this information.

1. From the website using wireless connectivity

2. Locally on the electronics using the USB flash drive

A third option is available as a backup method in case the primary methods are unavailable See Manual Setup Instructions section. In this option, no USB flash drive is used and all of the information is entered via the touch screen.

Setup – Wireless Connection Available

Most Patient Electronics Systems will have cellular connections. Follow these steps if a cellular connection is available.

1. When the system starts, it will prompt for the language and country. To select the language and country, press the Next button until the desired language or country appears and then press the Select button.

2. To enter the sensor serial number, select the Enter button and then type in the serial number using the keyboard.

3. The Patient Electronics System will then download the necessary information for the patient from the Merlin.net Patient Care Network Heart Failure Management Application and then prompt you to confirm the information.

4. When the system is successfully setup the system will display the patient's name above the Start button.

5. To shut down the system, press the Options button on the Start screen and then press the Shut Down button. Allow the system to complete the shut-down sequence prior to removing power from the system. Failure to do so may cause file corruption.

The following screens illustrate the sequence.

Figure 32. Enter the language
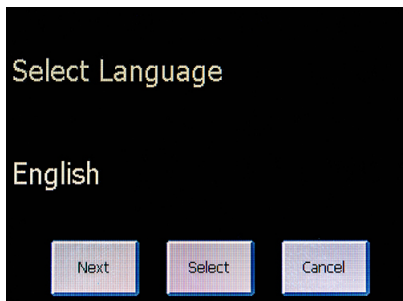
Figure 33. Enter the country
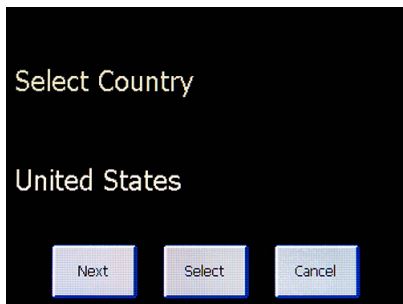
Figure 34. System prompts to enter sensor serial number
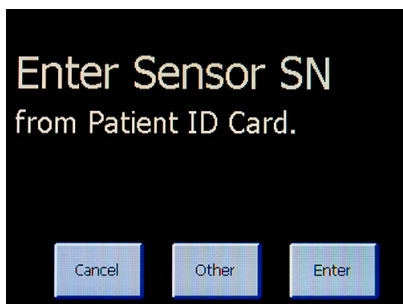
Figure 35. Confirm patient and sensor information
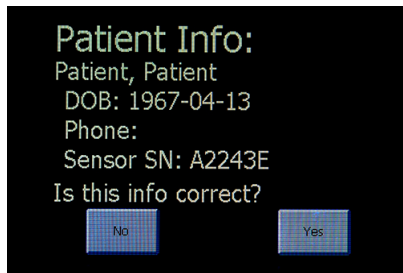
Figure 36. Patient name will be displayed on starting screen
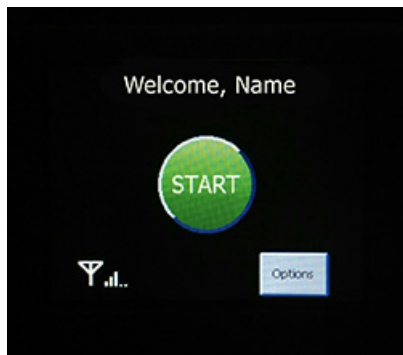
Setup - No Wireless Connection Available

When the system starts, wireless connectivity may be unavailable for the following reasons.

- The system has a dial up telephone modem.
- If the system has a cellular modem, but the cellular signal is weak, move the system to try to get a better signal. If successful, follow the wireless connection setup steps above. If not, follow the instructions below.

1. Insert a USB flash drive into the USB port of the computer.

2. On the Merlin.net Patient Care Network Heart Failure Management , use the Export feature beneath the More Actions link on the Patient Profile tab for your patient. For more information consult the Merlin.net Patient Care Network Heart Failure Management Application Help Manual.

3. On the Patient Electronics System, select the Other button.

4. Select the OK button on the Insert Website USB screen.

5. If there are multiple patient files found on the USB flash drive, you will be shown screens for each patient file on the USB flash drive. Select the Nxt Pat button to move to the next patient. Select the Load button to load the correct patient.

6. When prompted to confirm the information, review the information. Ensure the name and sensor serial number are correct.

7. When the system is successfully setup the electronics unit will display the patient's name above the Start button.

8. To shut down the system, press the Options button on the Start screen and then press the Shut Down button. Allow the system to complete the shut-down sequence prior to removing power from the system. Failure to do so may cause file corruption.

Figure 37. Select the Other button
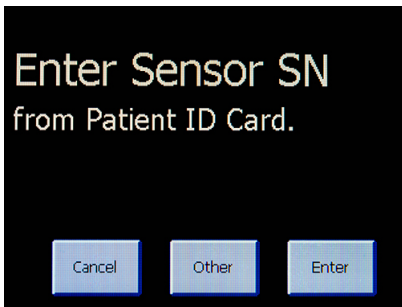
Figure 38. USB screen
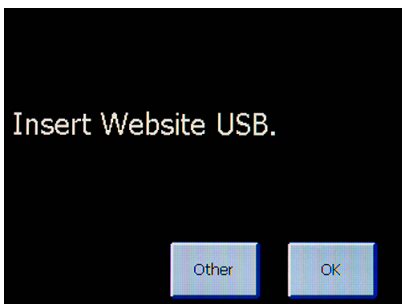
Figure 39. Confirm patient and sensor information.
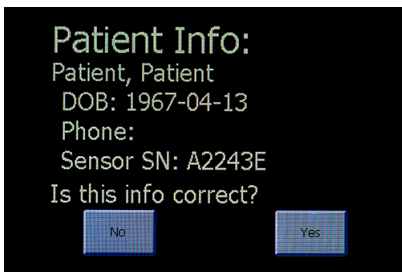
Figure 40. Patient name will be displayed on start screen
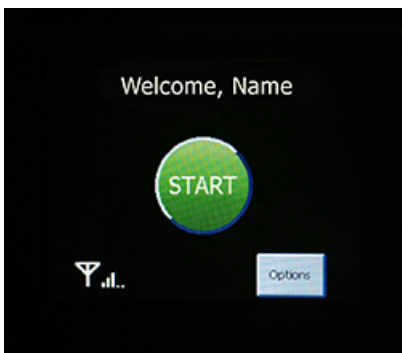
Patient Training

Discuss the information in the Patient Instructions and Patient System Guide with your patient before and after sensor implantation. For additional copies of the patient's guide, contact Technical Support. You should also explain the established benefits and risks of the CardioMEMS HF System with the patient. Discuss the home measurement schedule and the intended use of the system to assist their healthcare provider in the management of their heart failure. Refer to the Patient System Guide for details.

Train the patient how to set up and use their Patient Electronics System prior to their discharge from the hospital. Make sure that the patient is able to operate all of the connectors. For the best results have the patient or family member run through all the steps from start to finish.

1. Have the patient lie supine on the pillow.

    The patient should position their torso with the center of the pillow directly under the sensor. Typically this means that the tip of the shoulder blade nearest the sensor will be centered on the pillow. Use the same antenna position that gave the optimal signal during the implant procedure. The typical location for the sensor is on the left side. Check the patient's records to confirm actual location.

2. After the patient is in position, have the patient press either the Start button on the touchscreen or the round green button below the touchscreen.

    The system will guide the patient with voice prompts. The screen below appears while the system searches for a signal.

Figure 41. System prompts to change position.
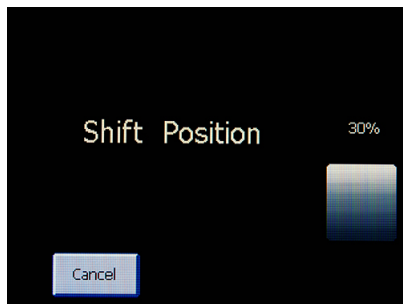
If the shift position screen appears, have the patient shift their position to find the best position. Once a good signal is available, the system will indicate with the voice prompt "Good Position on Pillow, Stay Still" and then begin to play music.

WARNING: Avoid placing the handheld unit directly on the pillow during a reading.

Figure 42. Reading in Progress.
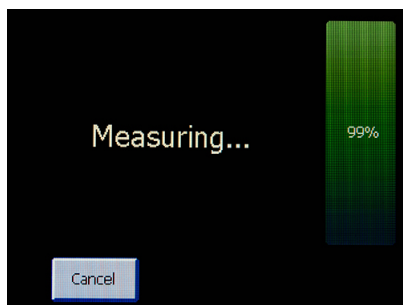
A reading takes approximately 18 seconds to complete. This allows the system to average multiple heart beats over several breaths. When the reading is complete, the system will attempt to send the reading.

Figure 43. Connection in Progress.
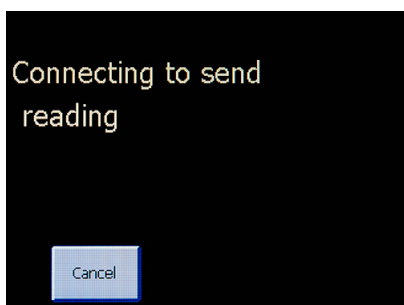
If cellular coverage is available, the system will send the data and shut down following transmission.

If wireless coverage is not available or if the system uses a dial-up connection, select Cancel to stop the system from continuing to attempt the connection. Explain to the patient that their system will automatically send the data from their home and automatically shut down afterwards. If the system is unable to transfer the readings to the website they will be stored for later transmission.

3. Once the system successfully sends the reading, it will automatically shut down. During training, if you do not wish the system to shut down, select 'Cancel' while it is sending. Allow the system to complete the shut-down sequence prior to disconnecting power from the system. Failure to do so may cause file corruption. If the automatic shut- down was cancelled, shut the system down by pressing the Options button on the Start screen, followed by Shut Down.

4. If the system has shut down, restart the system to take additional training readings.

Overview

Follow-up Reading Overview

For detailed instructions, refer to the following sections:
- Follow-Up Reading - Wireless Connection Available
- Follow-Up Reading - No Wireless Connection Available

Follow-Up Reading – Wireless Connection Available

When your patient returns to your institution for follow up visits, you will use the Hospital Electronics System to take follow-up pressure readings. If your Hospital Electronics System has wireless connectivity through WiFi or a cellular connection, all of the patients on the Merlin.net Patient Care Network Heart Failure Management Application will be available on the system.

Step 1: Retrieve Information

1. Select Follow-Up.

2. You will be presented with the list of patients that are available on this electronics unit.

3. Select the Check HF Website button to refresh the list from the Merlin.net Patient Care Network Heart Failure Management Application.

4. The list can be searched by entering information into the search box at the top.

5. Select the desired patient from the list.

6. Select OK.

Review the following sequence screens to perform these actions.

Figure 44. Select Follow-Up.
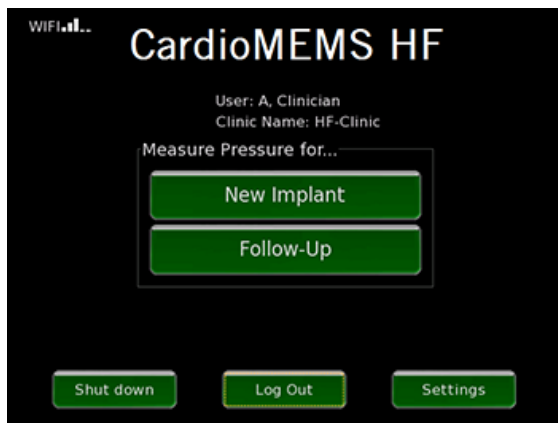
Figure 45. Select desired patient from the list.
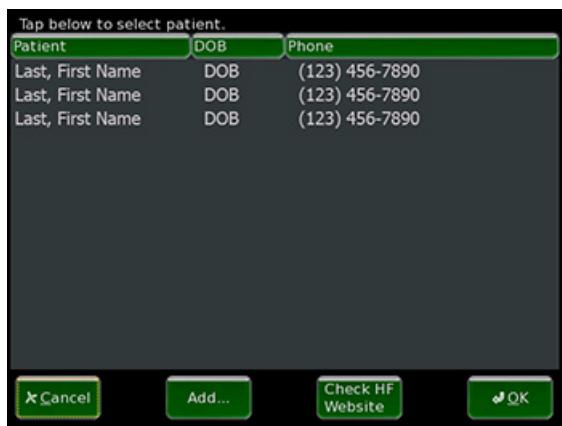
Step 2: Acquire Signal

1. Place the antenna under the patient's back, approaching from the side where the sensor was placed. Position the center of the antenna under the tip of the patient's shoulder blade on the side of the torso where the sensor is located. The preferred location for sensor placement is on the left side. Check your patient's chart to confirm.

2. The system will prompt if pulmonary artery catheter pressure readings are available. Select Yes or No. This allows the system to capture these values for reference if they are available.

3. The signal strength (SS) bar indicates the robustness with which the Hospital Electronics System is measuring the implanted sensor. If the signal strength bar is optimal (>70% and a green color), go to the next step. If not, go to the section Optimize Signal Strength.

Step 3: Take Reading

The system will allow you to take as many readings as needed.

1. Select the Take Reading button to capture pressure measurements.

2. If available, the system will then prompt you to enter the comparative catheter pressure values for reference. Enter the values and select the OK button.

Figure 46. Follow-up Pressure Reading.
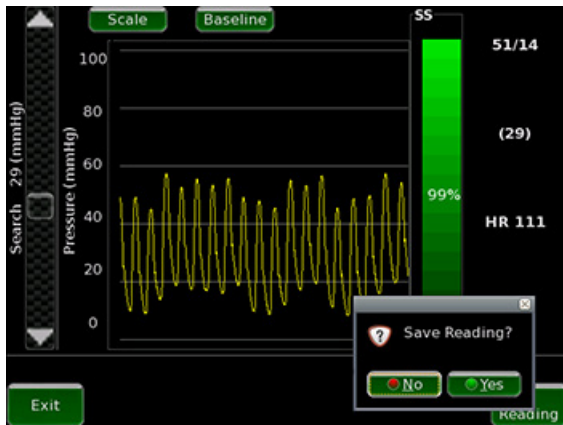
The captured reading is displayed for confirmation. The colored horizontal lines indicate the catheter pressure values entered as reference (if available). The green line indicates systolic pressure, blue indicates mean pressure, and red indicates diastolic pressure.

3. If the reading is acceptable, select the Yes button to save the reading. If the reading is unacceptable, select the No button and repeat the reading.

Step 4: Transfer Data

1. Select Exit from the data acquisition screen. If the user selects to print, the readings will print.

2. Since your system has a wireless connection, the baselines and readings will be transmitted to the Merlin.net Patient Care Network Heart Failure Management Application.

Step 5: Shutting Down the System

To shut down the system:

1. Navigate to the Main screen.

2. Select Shut Down on the Main screen.

Figure 47. Main screen, Select Shut Down
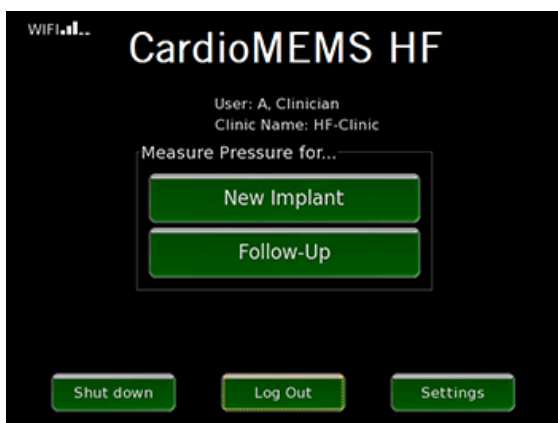
3. Allow the system to complete the shut-down sequence prior to disconnecting power from the system.

   CAUTION: Disconnecting power before the shut-down sequence is completed may cause file corruption.

Follow-Up Reading – No Wireless Connection Available

When your patient returns to your institution for follow up visits, you may use the Hospital Electronics System to take follow-up pressure readings. On the first follow-up visit, you will need to retrieve the information on your patient from the Merlin.net Patient Care Network Heart Failure Management Application. You will also need to retrieve the updated information on your patient if there have been any repeat right heart catheterizations where the baseline changed.

Step 1: Retrieve Patient Information [follow up no wireless]

1. Insert a USB flash drive into the USB port of the computer.

2. On the Merlin.net Patient Care Network Heart Failure Management Application, use the Export feature beneath the More Actions link on the Patient Profile tab for your patient. For more information consult the Merlin.net Patient Care Network Heart Failure Management Application Help Manual.

   NOTE: You can use any USB drive. Most commercial USB drives will be compatible with both the Hospital Electronics System and the computer used to access the Merlin.net Patient Care Network Heart Failure Management Application.

3. On the Hospital Electronics System, select Follow-Up.

4. You will be presented with the list of patients that are available on this electronics unit. Select the button 'Add…' below the list.

5. Insert the USB Drive when prompted.

6. Review and confirm the patient and sensor information.

7. Select OK.

The screens for this sequence are presented below.

Figure 48. Select Follow-Up.
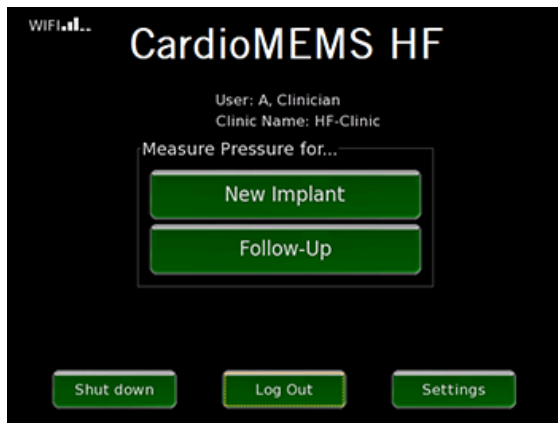
Figure 49. In this case, the patient is not available, select 'Add…' from below the list.

Figure 50. Insert USB Drive when prompted.

Figure 51. Confirm patient and sensor information.
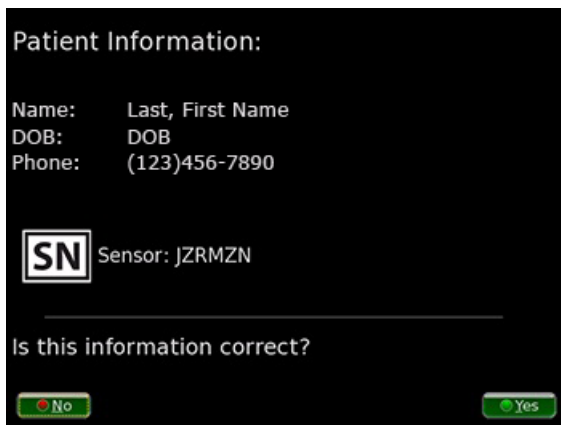
Step 2: Acquire Signal

1. Insert the antenna under the patient's back, approaching from the side where the sensor was placed. Position the center of the antenna under the tip of the patient's shoulder blade on the side of the torso where the sensor is located. The preferred location for sensor placement is on the left side. Check your patient's chart to confirm.

2. The system will prompt if pulmonary artery catheter pressure readings are available. Select Yes or No. This allows the system to capture these values for reference if they are available.

3. The signal strength (SS) bar indicates the robustness with which the Hospital Electronics System is measuring the implanted sensor. If the signal strength bar is optimal (>70% and a green color), go to the next step. If not, go to the section Optimize Signal Strength.

Step 3: Take Reading

The system will allow you to take as many readings as needed.

1. Select the Take Reading button to capture pressure measurements.

2. If available, the system will then prompt you to enter the comparative catheter pressure values for reference. Enter the values and select the OK button.

Figure 52. Follow-up Pressure Reading.

The captured reading is displayed for confirmation. The colored horizontal lines indicate the catheter pressure values entered as reference (if available). The green line indicates systolic pressure, blue indicates mean pressure, and red indicates diastolic pressure.

3. If the reading is acceptable, select the Yes button to save the reading. If the reading is unacceptable, select the No button and repeat the reading.

Step 4: Transfer Data

For routine follow-ups, transferring the patient information and readings back to the Merlin.net Patient Care Network Heart Failure Management Application is an optional step. The advantage is that all follow-up readings will be visible on the website along with the home readings.

If there is any change to the baseline it is important to transfer the information back to the Merlin.net Patient Care Network Heart Failure Management Application so that the system in your patient's home uses the updated baseline.

1. Select Exit from the data acquisition screen. The readings will print.

2. You will be prompted to save the information to a USB flash drive.

3. Insert the USB flash drive and select OK.

4. Import the information into the Merlin.net Patient Care Network Heart Failure Management Application.

Step 5: Shutting Down the System

To shut down the system:

1. Navigate to the Main screen.

2. Select Shut Down on the Main screen.

Figure 53. Main screen, Select Shut Down
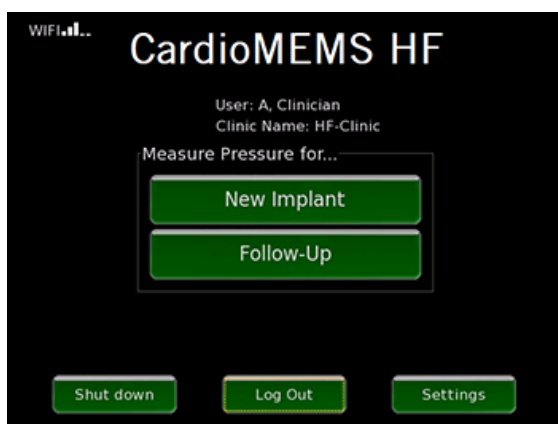
3. Allow the system to complete the shut-down sequence prior to disconnecting power from the system.

CAUTION: Disconnecting power before the shut-down sequence is completed may cause file corruption.

Locating Sensor Signal

This section outlines procedures to help locate the sensor signal.

A. Optimize Signal Strength

Follow this procedure if the signal strength is not optimal (<70% or not green). Use fluoroscopy to improve the position of the antenna relative to the implanted sensor.

1. Align the center of the antenna with the sensor and adjust the antenna to maximize the signal strength.

    If the signal strength is optimal (>70%), return to the section Acquire Sensor Signal and resume where you left off. If not, go to step 2 below.

    NOTE: The system reads the PA pressure by sending out RF signals to the sensor and then detecting a return signal from the sensor. These RF signals can reflect from the building structure and can cause the system to detect a strong signal level that is not the true sensor signal. These technically suspect readings do not have a pulse like the pulmonary artery pressure. The software aids the user in identifying whether or not a signal is pulsatile. If the system detects that the signal is pulsatile, the Signal Strength bar will turn green. If the system determines that the signal is not pulsatile, the Signal Strength bar will turn blue. It is possible that the system could identify an actual signal with extremely low pulse amplitude as non-pulsatile, so user-discretion is advised when using the colored pulsatility indication.

Figure 54. Pulsatile signal strength.

Figure 55. Non-pulsatile signal strength.

2. Adjust the pressure search scrollbar on the left side of the acquisition screen signal tuner up or down in small increments. Try to match the Search pressure value displayed next to the scrollbar to the mean pulmonary artery catheter pressure value.

    If the signal strength is optimal (>70%), return to the section Acquire Sensor Signal and resume where you left off. If the signal is not acquired after changes in the scrollbar position, return the slider bar to the original starting position and go to step 3 below.

3. Shift the antenna position.

    If the signal strength is optimal (>70%), return to the section Acquire Sensor Signal and resume where you left off. If not, go to step 4 below.

4. If the sensor orientation is fully lateral, lift the outer edge of the antenna into a partially tilted or lateral orientation from the side of the rib cage to detect the sensor.

B. Technically Suspect Readings

Technically suspect readings are readings which result from a signal other than the sensor.

If you receive technically suspect readings that have a high signal strength (> 70%) within the search range of the sensor:

- Be aware of the angulation of the sensor relative to the antenna and have the patient shift positions until the suspect reading minimizes.
- Place the antenna between the operator and the patient.
- Relocate to a different room.
- See section Solutions for Interference below.

Figure 56. Technically suspect reading with high signal strength. Pressure waveform is non-pulsatile with no inflection for the heart beat. Signal strength bar is blue.
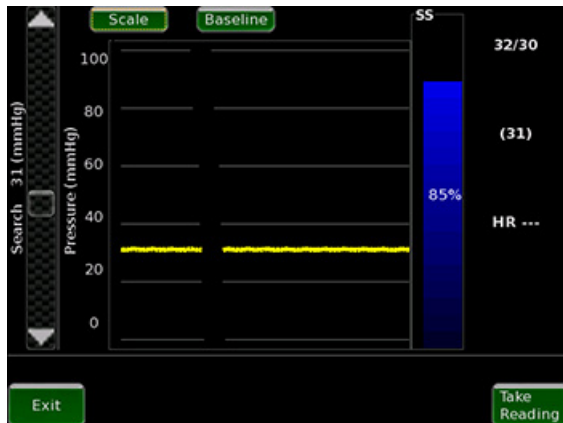
If the signal strength indicator is 0, the system is most likely measuring a technically suspect reading and the system is purposely forcing the signal strength to 0. To resolve this:

- Use the search scrollbar to move off this reading by repeatedly (and quickly) pressing the search scrollbar button several times.
- Move the search scrollbar in the direction that makes most sense according to physiological pressures.
- See section Solutions for Interference below.

Figure 57. Technically suspect reading with low signal strength. Signal is pulsatile with a heart beat but is at a high pressure that does not make sense for this patient.
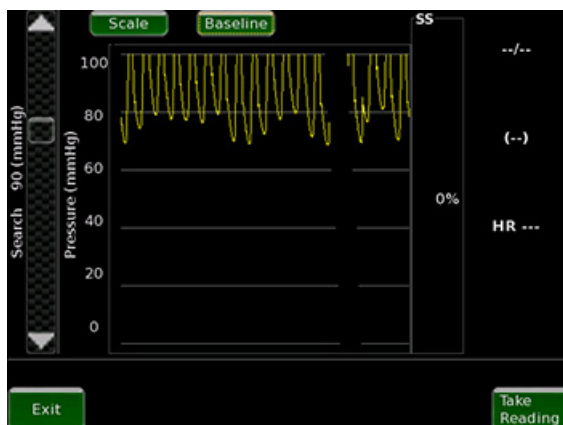
For either high or low signal strength technically suspect readings, if the reported mean pressure reads above or below the expected value from the pulmonary artery catheter:

- Increase the mean of the search scrollbar if it's too low
- Decrease the mean of the search scrollbar if it's too high

C. Distance

You can improve the signal if the sensor and antenna are located close together. To decrease the distance between the sensor and the antenna:

- Ask the patient to orient and locate the antenna over the position of the sensor.

- Ask the patient to press the antenna firmly into their back as much as is still comfortable.
- Ask the patient to remove all metallic objects.
- Have the patient shift into different positions.

D. Angulation

The signal strength is strongest when the antenna and sensor are parallel. Try these steps to change the angulation:

- Ask the patient to orient and locate the antenna over the position of the sensor.
- Adjust the search scrollbar until the mean pressure reads near the expected value.
- Ask the patient to press the antenna firmly into their back as much as is still comfortable.

E. Solutions for Interference

To reduce interference:

- Reduce the amount of metal in the vicinity of the sensor
- Reduce the number of electrical equipment and cables in the area
- Avoid the use of power strips and poorly grounded outlets when possible
- Move the C-arm away from the interrogation site
- Uncross guidewire
- Move or angle the antenna away from implantable devices
- Route ECG leads away from the area which the antenna will be located during a reading

Troubleshooting the Patient Electronics System

Table 1. Troubleshooting

Problem	Symptom	Solution
Cannot get a signal	Green bar never goes high Voice continues to indicate low signal Not able to complete a reading successfully	Check for any noticeable damage to the unit. Make sure there is no metal near the pillow. Make sure there is no electric blanket near the pillow. Reposition yourself on the pillow. Contact your clinic.
Reading completes but cannot send data to your doctor	Error message says to check connections Error message says reading cannot be sent	Check the USB cellular adapter, phone line or Wi-Fi adapter. Make sure the phone line is working or you are getting adequate signal strength on your wireless connection. Make sure the phone line is not busy. Make sure your Wi-Fi network name and password are correct. Make sure the electronics unit is calling the correct number. Contact your clinic.
Touchscreen does not respond	Buttons are not activated by repeated presses	Turn off the system by holding in the power button on the back of the electronics unit for greater than 5 seconds. Turn on the system and retry to use the touchscreen. If the problem is not resolved, contact your clinic.
Takes a long time to get a reading	Takes a long time (>30 seconds) to get a good signal Unit loses signal during reading and must re-start	Reposition yourself on the pillow until the green bar shows a higher signal strength. Make sure there are no electronics or metal in the vicinity of the measurement that may cause interference. Use the orientation ball to find the correct position. Contact your clinic.
Reading completes but is rejected by system	Error message says to repeat reading and reposition pillow away from any cords or metal objects	Remove any cords or metallic objects near the pillow or the pillow cable. Make sure there is no metal near the pillow. Make sure there is no electric blanket near the pillow. If you have a waterbed, take the measurements in another room. Contact your clinic.
Numeric error message	Error message with a number appears on the screen	Note the error. Click the OK button to acknowledge the error, wait for the error to transmit, and let the electronics unit shut down. Contact your clinic. You will not be able to take your reading.
	Error #0	There is a problem with the connections in the system such that important information cannot be sent.
	Error #1	The electronics system recorded an obviously incorrect value for the atmospheric pressure.
	Error #2	The two atmospheric pressure sensors in the electronics system do not agree.

Table 1. Troubleshooting

Problem	Symptom	Solution
	Error #3	Important data needed to make a measurement was not available.
	Error #4	The internal settings values needed to make a measurement were missing or damaged.
	Error #5	The atmospheric pressure sensor indicated an error in recording pressure or temperature.
	Error #6	An important part of the software was not able to run.
Numeric warning message	Warning message with a number appears on the screen	Note the warning. Retry the steps that caused the warning. If the warning appears a second time, contact your clinic. Continue to take your readings if possible.
Time of Day Clock is incorrect	Warning #5 message appears on the screen	Note the warning. Turn off the electronics unit from the Options menu. Restart the electronics unit. If the warning appears a second time,the time back-up battery may be dead. Continue to take readings until you are able to replace the battery. To replace the battery: 1. Use a screwdriver to remove the access door marked with a battery symbol on the back panel of the electronics. 2. Turn off and unplug the unit. 3. Remove the screws on the access door. Once the door is removed, note the "+" and "-" symbols which show the direction of the battery. 4. Replace the battery (type BR2032) and reinstall the access door. Contact your clinic if this does not resolve the issue.

Pulmonary Artery Catheter Setup

1. The pulmonary artery catheter is used to set the baseline for the sensor. For an accurate sensor measurement, it is important to set up the catheter properly. Ensure the transducer has been properly leveled and zeroed to atmospheric pressure. If there are any concerns, repeat the setup.

2. It is important to confirm that the pulmonary artery catheter PA pressure waveform appears to be valid with minimal waveform distortion due to measurement artifact.

   Potential forms of measurement artifact include catheter whip, air bubbles in the pressure line, or catheter tip wedging. If artifact is present, address the potential sources of this artifact per the standard procedures for fluid-filled catheter monitoring until the PA pressure waveform appears to be reliable with minimal waveform artifact.
   Confirm that the pulmonary artery catheter produces a steady mean pressure value.

3. Once the system is measuring the pressure, confirm that the height of the sensor pressure signal (i.e., pulse pressure (systolic – diastolic)) is within +/- 25% of the catheter pulse pressure.

   If not, confirm that any monitoring artifact has been sufficiently minimized. If changes are made to minimize pulse pressure measurement artifact result in a discrepancy between mean pressures, set the PA Pressure Baseline again after such changes are made. If the PA pressure waveform has artifact minimized and pulse pressures are not within +/- 25%, repeat the sensor signal acquisition steps until pulse pressures match within +/-25%.

Manual Setup Instructions

The instructions above for New Sensor Implant, Patient Electronics System Setup and Follow-up Readings will cover situations where wireless communication is available and/ or when USB flash drive transfer is available. As a backup, all information can be entered manually into the system.

New Sensor Implant

Each sensor has unique characteristics which must be loaded into the Hospital Electronics System. The sensor information for these steps is printed on the sensor box.
Wait until the time of sensor implant and then follow these instructions for each new sensor:

1. Select New Implant.

2. Enter the patient information using the touch screen keyboard. To modify a field such as first name, simply touch it and the keyboard will appear. It is necessary to fill out the first and last name fields and the birthdate. The phone number is optional. All of this information will appear on the website once implant is complete.

3.   When prompted for the USB flash drive from the sensor package, select 'Enter Manually'.

4.   Use the touch screen to enter the sensor serial number and calibration code using the label on the sensor package.

5.   After the sensor information is loaded, it will be displayed along with the patient information. Verify that Sensor Serial displayed matches the Serial Number printed on the sensor box.

The screens for these steps are shown in the following sequence.

Figure 58.   Starting screen, select New Implant.
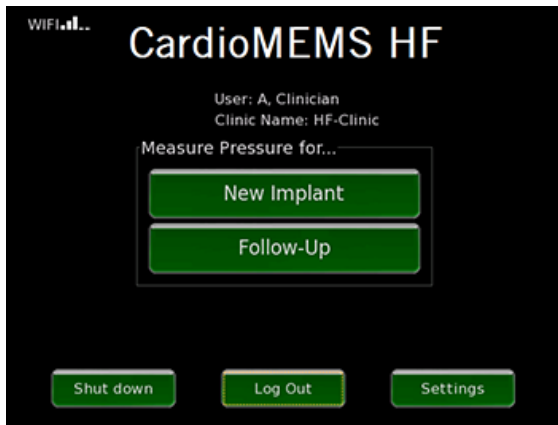
Figure 59.   Enter patient demographic information.
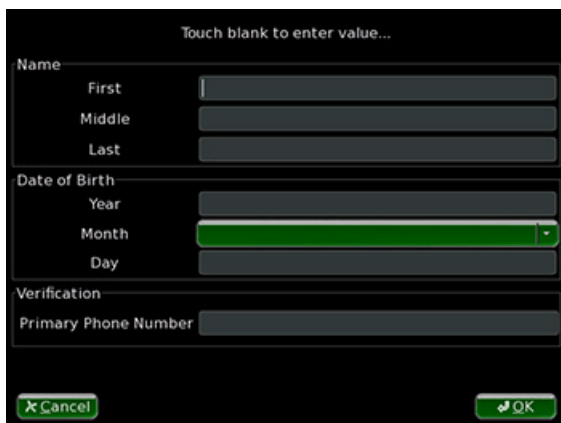
Figure 60.   Enter patient information using touch keyboard.
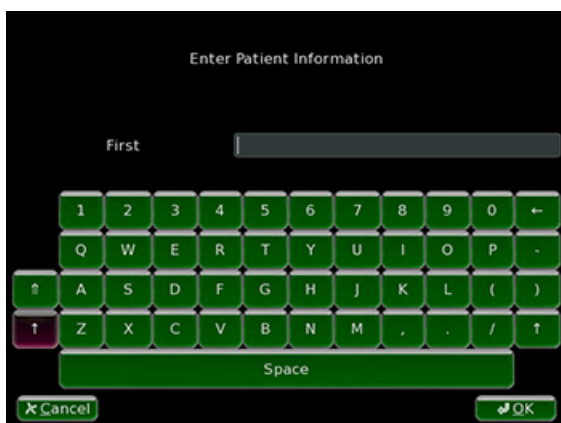
Figure 61. For manual entry of sensor information, touch 'Enter Manually'.
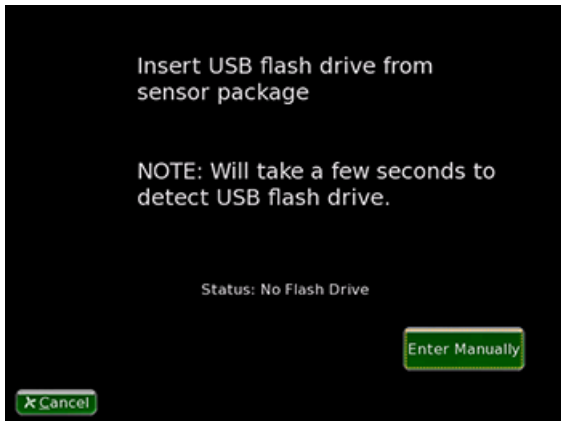
Figure 62. Enter sensor information from sensor package.
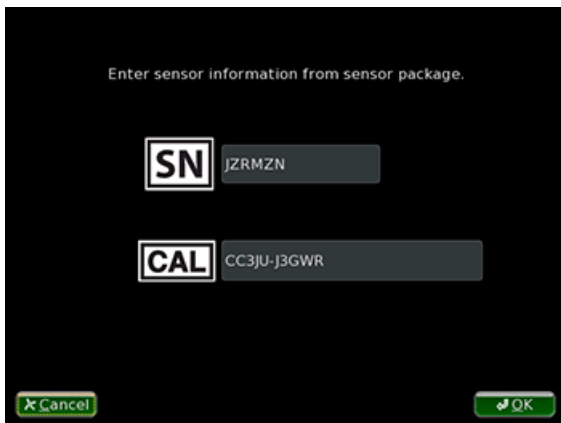
Figure 63. Verify patient and sensor information.
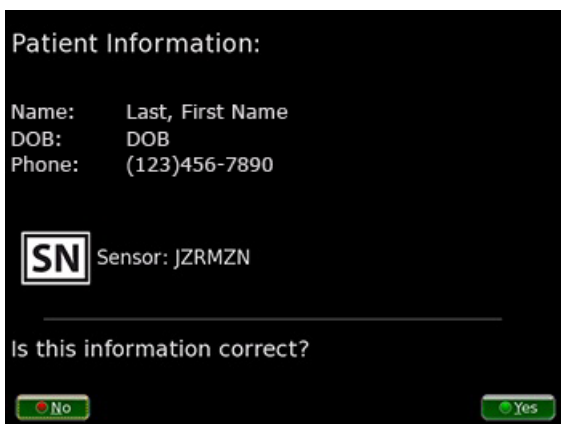
Patient Electronics System Setup

This is a backup option if the cellular connection is unavailable and you are unable to use a USB flash drive to retrieve the sensor information from the Merlin.net Patient Care Network Heart Failure Management Application.

1. These steps will require the patient information, the sensor characteristics and the baseline information be available. In addition, a 4 digit code is needed from the website. All of this information is available on the implant report which is printed from the Merlin.net Patient Care Network Heart Failure Management Application.

2. The Patient Electronics System powers up to an Enter Sensor SN screen. On this screen, select the Other button until you see the Enter Manually screen.

3. Select the OK button.

4. Enter the desired fields using the touch screen keyboard.

5. When prompted to confirm the information, review the information. Ensure the name and sensor serial number are correct.

6. If the information is incorrect, select the No button to repeat the process. You may need to return to the Merlin.net Patient Care Network Heart Failure Management Application to confirm that the information is correct.

7. When the system is successfully setup the electronics unit will display the patient's name above the Start button.

Figure 64. Select the Other button
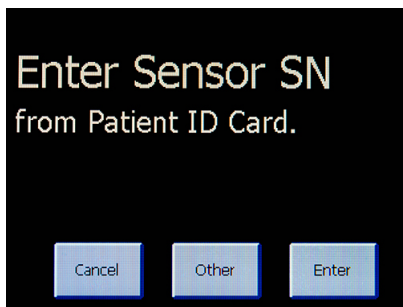
Figure 65. Enter Manually screen
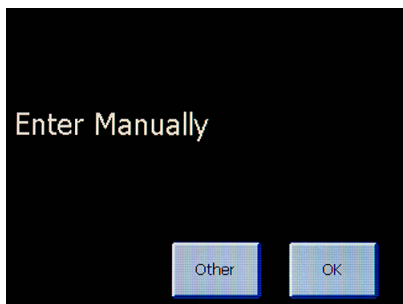
Figure 66. Enter the information from the implant report printed from the website.

Figure 67. Confirm patient and sensor information.
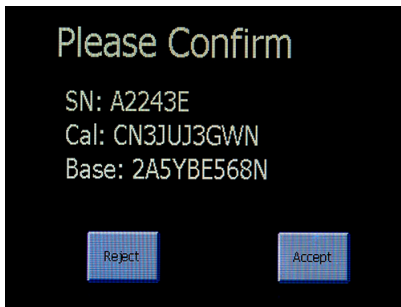
Figure 68. Patient name will be displayed on starting screen every time the system is started.
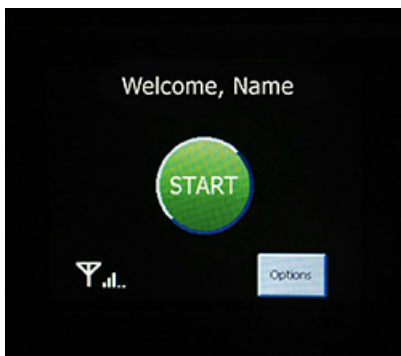
Follow-Up

1. Select Follow-Up.

2. You will be presented with the list of patients that are available on this electronics unit. Select the button 'Add…' below the list.

3. Select 'Enter Manually'.

4. Enter the information from the Implant Report using the touch screen keyboard.

5. Review and confirm the patient and sensor information.

6. Select OK.

For this sequence, review the screens below.

Figure 69. Select Follow-Up.
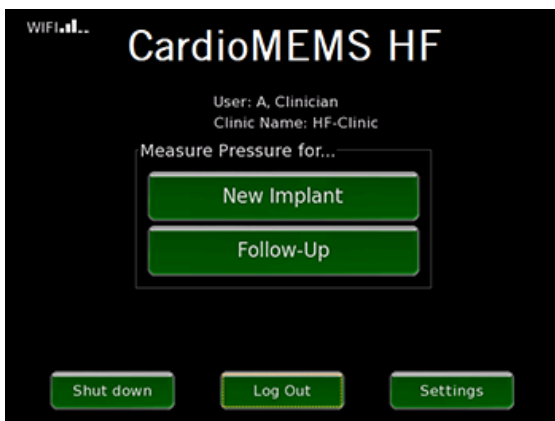
Figure 70. In this case, the patient is not available, select 'Add…' from below the list.
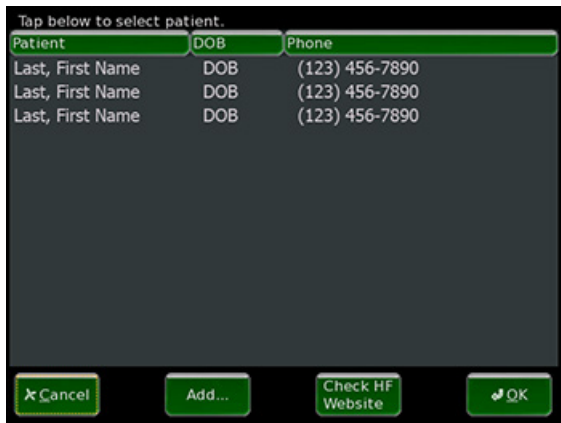
Figure 71. Select Manual Entry when prompted.
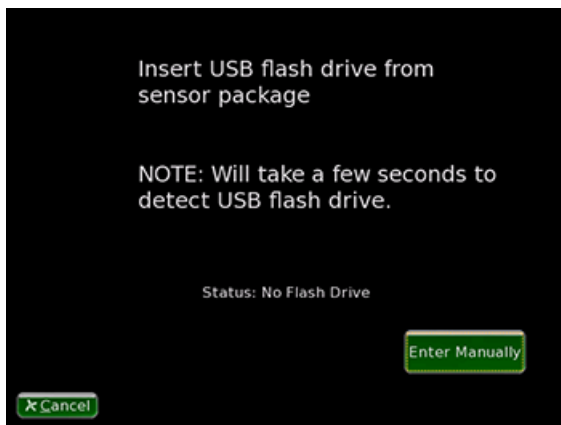
Figure 72. Enter the patient and sensor information.
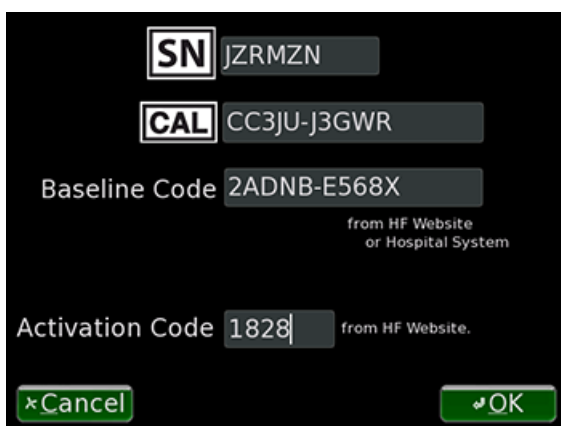
Figure 73. Confirm patient and sensor information.
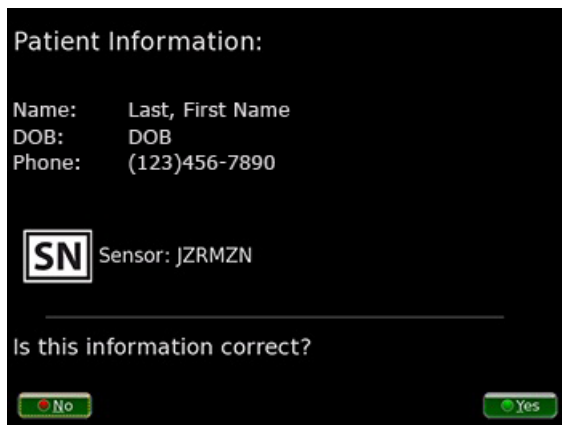
Additional Hospital Electronics System Functions

A. Wireless Connectivity Setup

The Hospital Electronics System can be configured to communicate with the Merlin.net Patient Care Network Heart Failure Management Application using local WiFi or cellular using the built-in GSM antenna.

WiFi is not installed by default. Contact Customer Service to obtain the compatible WiFi accessory.

Once you have obtained the WiFi accessory, contact the IT group at your facility for credentials to your WiFi network. Some important information to consider regarding the use of WiFi by the Hospital Electronics System.

- The system only uses the WiFi network at your facility as a means to gain access to the Merlin.net Patient Care Network Heart Failure Management Application which is available on the internet.
- The system does not communicate with any other devices within your facilities' network.
- All information passed between the system and the Merlin.net Patient Care Network Heart Failure Management Application is encrypted using secure sockets (SSL).
- The system will only operate on WiFi networks that are sufficiently encrypted (WPA2). It will not operate on unprotected or open networks.
- The credentials for the WiFi network are not sent to the Merlin.net Patient Care Network Heart Failure Management Application.

Using the screen below, enable the network and then enter the network name and password.

Figure 74. WiFi Setup

B. Setting Baseline in Follow-Up Reading

If the follow-up readings are being performed in the cardiac catheterization lab, you will be able to set the baseline to a new value.

1. Select the Baseline button at the top of the screen. This will enable the buttons used during implant to set the baselines.

Figure 75. Setting Baseline in Follow-Up

2. Select Set Pressure Baseline or Set CO Baseline to adjust baselines. Refer to the section Step 3: Set Baseline for instructions on properly setting the baseline.

If there is any change to the baseline it is important to transfer the information back to the Merlin.net Patient Care Network Heart Failure Management Application so that the system in your patient's home uses the updated baseline.

C. Settings Screen

Figure 76. Settings screen.

Patient Options…

Select the Patient Options Button to print any previously captured images, to export information from the USB flash drive for website upload, or to display baseline information for manual input into website.

Password

To change the system password or disable the password, use the Password button and follow the prompts.

Date & Time

Readings taken are identified with the Date and Time. Use this button to adjust the time on your system.

Touch

Use this option to align the touch screen.

WiFi

Select WiFi to set or update the WiFi wireless configuration. See Wireless Connectivity Setup section for details.

Service…

Provides access to service related functionality such as diagnostic test and system information.

D. The Admin Screen

The Admin screen is restricted to Merlin.net PCN administrators. If you are not a Merlin.net PCN administrator, contact your clinic administrator for help. To access the Admin screen:

1. Enter the username and password of a Merlin.net PCN administrator on the User Log On screen and then select the OK button.

2. Select the Settings button on the CardioMEMS HF screen.

   The Settings screen appears.

3. On the Settings screen, select the Service button.

4. On the Service screen, select the Admin button.

By default, new Hospital Electronics Systems require you to enter a Merlin.net PCN username and password to use the system. If your system does not require this, a Device Log On screen appears once you start the system.

If you are not a Merlin.net PCN administrator, contact your clinic administrator for help. To access the Admin screen:

1. Select the User Log On button on the Device Log On screen.

   The User Log On screen appears.

2. Enter the username and password of a Merlin.net PCN administrator and then select the OK button.

3. Select the Settings button on the CardioMEMS HF screen.

   The Settings screen appears.

4. On the Settings screen, select the Service button.

5. On the Service screen, select the Admin button.

If you are unable to gain access with the password, you can obtain a temporary password on the My Account page on the Merlin.net Patient Care Network Heart Failure Management Application. To access the system after you obtain a temporary password:

1. Enter your username and password on the User Log On Screen.

2. Select the OK button.

   The system attempts to connect to the network.

3. Select the Cancel button.

   The system logs you in.

If you are unable to log in, contact Technical Support for additional assistance.

Merlin Logon Mode

If you enable the Merlin Logon mode, users can log in to the Hospital Electronics System with their Merlin.net PCN username and password. This allows users from different clinics to share the same system.

You can only view the list of patients that are also available to your clinic on the Merlin.net Patient Care Network Heart Failure Management Application.

Remote Access

To troubleshoot an issue with your system, the Remote Access feature is available. A technician can log in to your system remotely when you enable this feature. For more information, contact Technical Support.

Software Update

Updates to the Hospital Electronics System software occur occasionally. If a network connection is available, the system automatically checks for an update after transferring the data from the first new implant or follow-up readings of the day.

If a software update is available, the system prompts you to install it:

▪ Select the Yes button to download and install the software.
   The update takes approximately 20 minutes depending on the network connection.

▪ Select the No button if you do not want to install the software.
   To update the software at any time, select the Patient Options button on the Settings screen and then select the Software Update button.

If your Hospital Electronics System does not have a network connection, software updates are installed with a USB flash drive by St. Jude Medical™.

Additional Patient Electronics System Functions

Patient Electronics System - Viewing Pressure Values During the Reading

In daily use, your patient will not see their pressure values. For clinicians only, during patient training, a special clinical mode may be enabled to show the reading values. To enable this mode perform the following steps.

1. From the main electronics screen, select the Options button until the Advanced Options screen appears and then select the SelectAdv button.

2. Enter the Advanced Options password. This is 'sensor'. This password is reserved for clinicians. Please do not share it with your patients. If the patient ever needs to enter this screen, they can be given a daily password that is only valid for one day.

3. Select the Toggle button.

Figure 77. Enable reading values.
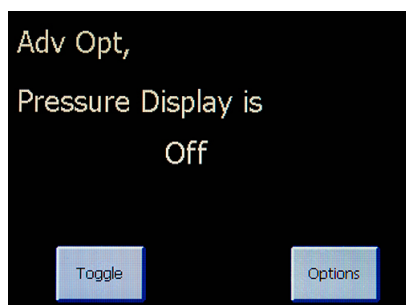
4. Press the round green button below the touchscreen on the handheld unit.

5. Have the patient get in position and then start the reading. During the reading, the screen will show the reading values as below.

Figure 78. Patient pressure reading with pressure values.
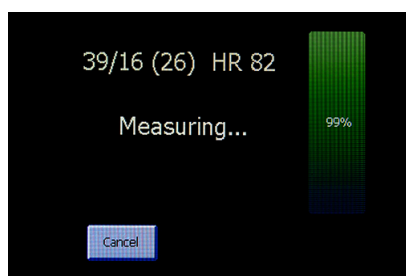
Guidelines for the Management of Hemodynamic Parameters

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

Pulmonary Artery Pressure Ranges

PA Systolic: 15 - 35 mmHg

PA Diastolic: 8 - 20 mmHg

PA Mean:10 - 25 mmHg

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

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

A decrease in the pulmonary pressures below the patient's pressure ranges should be considered a volume depletion event and managed according to the hypo-volemic guideline (see Low PA Pressures (Hypo-volemic) section) . Diuretic therapy should be held and the chronic dose should be lowered.

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

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

Elevated PA Pressures (Hyper-volemic)

Hyper-volemic Definitions

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

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

Low PA Pressures (Hypo-volemic)

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

Treatment Recommendations
- Lower or discontinue diuretic
  - If on a thiazide diuretic with loop diuretic, lower or discontinue the dose of thiazide (and adjust electrolyte replacement)
  - If on only loop diuretic, lower the dose or discontinue
  - Consider liberalization of oral fluid restriction and salt restriction
- If postural hypotension, hold or lower vasodilators and/or oral nitrates, especially if hypotensive when sitting or supine
- If worsening renal function, hold or lower ACE/ARB dose, especially if hypotensive
- If subject had signs and symptoms of poor perfusion (cold) in addition to being hypo-volemic:
  - Consider admission if clinical evidence suggests need for IV fluid repletion, telemetry monitoring or the use of IV therapeutic agents
  - Consider invasive hemodynamic monitoring for determination of Cardiac Output, if indicated

Recommended Frequency of CardioMEMS HF System Review

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

Clinical Study Information

Introduction

Heart failure (HF) is a major public health problem in the United States affecting over 5 million people with over 1 million HF hospitalizations per year. Elevated pulmonary artery (PA) pressures may occur prior to signs and symptoms of HF decompensation and can provide a sound physiologic basis for HF patient management.

The CardioMEMS HF System provides a novel method for measuring PA pressure using a wireless pressure sensor implanted into the PA, an external communication device, and a patient database. The CardioMEMS HF System provides physicians knowledge of

PA pressure while the patient is at home allowing them to manage patients proactively with the goal of reducing heart failure hospitalizations.

CHAMPION (CardioMEMS HF Sensor Allows Monitoring of Pressures to Improve Outcomes in NYHA Functional Class III Heart Failure Patients) was a prospective, multicenter, single-blind, randomized, clinical trial in 550 patients across 64 centers in the United States.

Purpose

The goal of CHAMPION was to determine if physicians could reduce HF hospitalizations by managing patient PA pressures using the CardioMEMS HF System.

Methods

Study Design

550 patients with NYHA Class III HF and a prior HF hospitalization within 12 months were randomized to standard of care plus the CardioMEMS HF System (Treatment group; 270 patients) or to standard of care only (Control group; 280 patients). All patients were implanted with the PA sensor and took daily readings from home. Patients were enrolled regardless of their baseline ejection fraction so that patients with both reduced and preserved systolic function were included. Physicians had access to PA pressure information for patients in the Treatment group but not for patients in the Control group.

Following the completion of Randomized Access, patients transitioned to a period of Open Access, during which PA pressures were provided to physicians for patients in both the Treatment and the Control groups. Specifically, physicians continued to have access to the Treatment group's PA pressures in an unchanged manner, whereas access to the Control group's PA pressure was provided for the first time.

Follow-Up Schedule

After RHC and sensor implantation, all patients had follow-up study visits at 1 month, 3 months, 6 months, and every 6 months thereafter until study termination.

Study Endpoints

The primary and secondary endpoints were evaluated after 6 months of patient follow-up. The primary safety endpoints were 1) Freedom from device / system-related complications (DSRC), and 2) Freedom from pressure sensor failures. The primary efficacy endpoint was the rate of HF hospitalizations. All hospitalizations were adjudicated by an independent Clinical Events Committee (CEC) who were blinded to treatment assignment. Secondary endpoints were tested in a hierarchical fashion and included changes in PA pressures, proportion of subjects hospitalized for HF, days alive outside of the hospital for HF, and quality of life. Because blinded follow-up continued until the last patient completed 6 months of follow-up, the average patient follow-up was much longer (17.6 months) and pre-specified supplementary analyses were conducted on the full duration of follow-up data (Randomized Access).

Patient Demographics and Disposition

575 patients were consented for trial enrollment and underwent right heart catheterization (RHC). Of these 575 patients, 25 (4.3%) underwent a RHC but did not receive an implant primarily because of anatomical/physiological conditions identified during the RHC. Of the 550 randomized patients, 270 were assigned to the Treatment group and 280 to the Control group. The two groups were similar with respect to baseline characteristics (see table below).

Table 2. Patient Demographics

Variables	Randomized Group		
	Treatment (N=270)	Control (N=280)	p-value[2]
Age (years)	61.3 ± 12.98 (270)	61.8 ± 12.73 (280)	0.5927
Male	194/270 (71.9%)	205/280 (73.2%)	0.7745
Race (White)	196/270 (72.6%)	205/280 (73.2%)	0.9236
Systolic BP (mmHg)	121.2 ± 22.52 (270)	123.2 ± 21.01 (280)	0.1286
Heart Rate (bpm)	72.4 ± 12.91 (269)	73.0 ± 12.14 (280)	0.4873
BMI	30.5 ± 6.50 (270)	30.9 ± 7.35 (280)	0.6228
BUN (mg/dL)	29.6 ± 17.99 (248)	28.1 ± 16.17 (267)	0.6325
Creatinine (mg/dL)	1.4 ± 0.47 (270)	1.4 ± 0.42 (280)	0.5560
GFR (mL/min/1.73m²)	60.4 ± 22.50 (270)	61.8 ± 23.20 (280)	0.5638
Ejection Fraction (EF>=40%)	62/270 (23.0%)	57/279 (20.4%)	0.5343
Cardiac Output (L/min)	4.5 ± 1.41 (270)	4.6 ± 1.54 (278)	0.5499
Cardiac Index (L/min/m²)	2.1 ± 0.59 (270)	2.2 ± 0.64 (278)	0.4405
PVR	2.9 ± 2.02 (270)	2.7 ± 1.82 (278)	0.4609
PA Wedge Pressure (mmHg)	17.5 ± 7.97 (270)	19.0 ± 8.12 (280)	0.0276
PA Mean Pressure (mmHg)	28.9 ± 9.92 (270)	29.9 ± 10.05 (280)	0.3021
CRT-D/ICD Implant	179/270 (66.3%)	197/280 (70.4%)	0.3145
Ischemic Cardiomyopathy	158/270 (58.5%)	174/280 (62.1%)	0.4327

[2] Wilcoxon Rank-Sum Test for continuous measures and Fisher's exact test for categorical measures.

Table 2. Patient Demographics

| Variables | Randomized Group | | |
	Treatment (N=270)	Control (N=280)	p-value[2]
Hypertension	207/270 (76.7%)	220/280 (78.6%)	0.6100
Hyperlipidemia	204/270 (75.6%)	218/280 (77.9%)	0.5458
Coronary Artery Disease	182/270 (67.4%)	202/280 (72.1%)	0.2290
History of MI	134/270 (49.6%)	137/280 (48.9%)	0.9320
Diabetes Mellitus	130/270 (48.1%)	139/280 (49.6%)	0.7337
AFIB	120/270 (44.4%)	135/280 (48.2%)	0.3932
COPD	76/270 (28.1%)	83/280 (29.6%)	0.7078
ACE/ARB use	205/270 (75.9%)	222/280 (79.3%)	0.3584
Beta Blocker use	243/270 (90.0%)	256/280 (91.4%)	0.6595

The mean follow-up during Randomized Access was 17.6 months for a total duration of approximately 800 patient years. During the course of Randomized Access, 93 patients in the Treatment group and 110 patients in the Control group exited the study with the primary reason being death.

A total of 347 patients (177 in the Treatment group and 170 in the Control group) completed Randomized Access and entered Open Access. The mean follow-up during Open Access was 13 months for a total duration of approximately 400 patient years. During the course of Open Access, 58 patients in the Treatment group and 43 patients in the Control group exited the study with the primary reason being death.

Primary and Secondary Endpoint Results

Primary Safety Endpoints

CHAMPION met the two primary safety endpoints: (1) Freedom from device/system related complications (DSRC) and (2) Freedom from sensor failure. The protocol pre-specified objective performance criteria (OPC) were that at least 80% of patients were to be free from DSRC and at least 90% were to be free from pressure sensor failure. Of the 575 patients in the safety population, 567 (98.6%) were free from DSRC at 6 months (lower confidence limit 97.3%, p<0.0001). This lower limit of 97.3% is greater than the pre-specified OPC of 80% (see tables below). There were no sensor explants or repeat implants and all sensors were operational at 6 months for a freedom from sensor failure of 100% (lower confidence limit 99.3%, p<0.0001). This lower limit of 99.3% is greater than the pre-specified OPC of 90% (see Primary Safety Endpoint – Freedom from Pressure Sensor Failures table).

Table 3. Primary Safety Endpoint – Freedom from Device/System Related Complications

Device/System Related Complications (n=575)		Lower 95.2%[3] Confidence Limit	Objective Performance Criterion (OPC)	p-value[4]
Yes	No			
8 (1.4%)[5]	567 (98.6%)	97.3%	80%	p<0.0001

Table 4. Primary Safety Endpoint – Description of Device/System Related Complications

Description	Number of Subjects with Device or System related complication (%) (N = 575)
Hemoptysis	1 (0.2%)
Sensor did not deploy	1 (0.2%)
Transient Ischemic Attack (TIA)	1 (0.2%)
Atypical chest pain	1 (0.2%)
Sepsis → death	1 (0.2%)
Atrial arrhythmia → death	1 (0.2%)
Arterial embolism (upper extremity)	1 (0.2%)
Pulmonary artery (in-situ) thrombus	1 (0.2%)
Total Subjects Experiencing a DSRC	**8 (1.4%[6], 95.2% LCB 97.3%)**

---

[3] Exact 95.2% Clopper-Pearson lower confidence limit
[4] p-value from exact test of binomial proportions compared to 80% for all patients
[5] DSRCs (8 total) by group: Consented but not randomized (2), Treatment (3), Control (3)
[6] Pressure sensor failure counts by group: Treatment (0), Control (0)

Table 5. Primary Safety Endpoint – Freedom from Pressure Sensor Failures

Pressure Sensor Failures (n=550)		Lower 95.2% Confidence Limit[7]	Objective Performance Criterion (OPC)	p-value[8]
Yes	No			
0 (0.0%)	550 (100%)1	99.3%	90%	p<0.0001

Primary Efficacy Endpoint

The primary efficacy endpoint of the CHAMPION trial was the rate of HF hospitalizations during the first 6 months of Randomized Access. There were 84 HF hospitalizations in the Treatment group compared with 120 HF hospitalizations in the Control group. This difference between the groups represented a 28% reduction in the 6-month rate of HF hospitalization in the Treatment group (0.32 hospitalizations per patient in the Treatment group vs. 0.44 hospitalizations per patient in the Control group, HR 0.72, 95% CI 0.60-0.85, p = 0.0002) (Primary Efficacy Endpoint – HF Hospitalization rates During First 6 months of Randomized Access table).

Table 6. Primary Efficacy Endpoint – HF Hospitalization rates During First 6 months of Randomized Access

	Number of HF Hospitalizations	6 Month HF Hospitalization Rate	Hazard Ratio (95% CI) [p-value][9]
Treatment Group (n=270)	84	0.32	0.72 (0.60-0.85)
Control Group (n=280)	120	0.44	p=0.0002

Secondary Endpoints

The four secondary efficacy endpoints were analyzed hierarchically at 6 months (table below). At baseline, both Treatment and Control patients had similar PA mean pressures. When compared with patients in the Control group, the patients in the Treatment group had greater reduction in mean PA pressure (p=0.0077); were less likely to be hospitalized for heart failure (p=0.0292); spent more days alive outside of the hospital for heart failure (p=0.0280); and reported a better quality of life (Minnesota Living with Heart Failure Questionnaire) (p=0.0236).

Table 7. Secondary Efficacy Endpoints at 6 Months

	Treatment	Control	p-value
Change from baseline in mean pulmonary artery pressure, area under the curve (mean mmHg-days)	-155.7 (n=265)	33.1 (n=272)	0.0077[10]
Proportion of patients hospitalized for heart failure (%)	55 (20.4%) (n=270)	80 (28.6%) (n=280)	0.0292[11]
Days alive outside the hospital for heart failure (mean)	174.4 (n=270)	172.1 (n=280)	0.0280[12]
Minnesota Living with Heart Failure Questionnaire (mean[median])	45.2 [45.0] (n=229)	50.6 [52.0] (n=236)	0.0236[13]

Medical Management

Physicians responded to Treatment patients' elevated PA pressures by making medication changes to lower PA pressures in an attempt to reduce the risk for HF hospitalization. Physicians documented all medication changes for all patients and indicated whether the change was made in response to PA pressures or standard of care information. During the 6-month follow-up period, physicians made 1113 HF medication changes in the Treatment group and 1061 HF medication changes in the Control group in response to standard of care information. In the Treatment group only, physicians made 1404 HF medication changes in response to PA pressures, primarily through diuretics and vasodilators. This incremental HF management in response to PA pressures using the CardioMEMS HF System led to a significant reduction in HF hospitalizations.

Results from the Entire Randomized Access Period

HF Hospitalizations

During the entire Randomized Access period, the rate of HF hospitalizations was 33% lower in the Treatment group than in the Control group (0.46 vs. 0.68 annualized HF hospitalization rates, HR 0.67, 95%CI 0.55-0.80) (table below). The magnitude of the

---

[7] Exact 95.2% Clopper-Pearson lower confidence limit
[8] p-value from exact test of binomial proportions compared to 90% for all patients
[9] p-value and hazard ratio from negative binomial regression model
[10] p-value from analysis of covariance with baseline pressure as the covariate
[11] p-value from Fisher's exact test
[12] p-value from Wilcoxon rank sum test after controlling for subject duration in study (i.e., days alive outside the hospital / subject duration x 180)
[13] p-value from two-group t-test

effect during the entire Randomized Access period was slightly larger than that seen during the 6-month primary endpoint period (33% vs. 28%), indicating durability of the treatment effect. The number needed to treat (NNT) per year to prevent one HF hospitalization was 4. For every 100 patients treated, 23 HF hospitalizations would be prevented per year.

Table 8. HF Hospitalization Rates During Randomized Access

	Number of HF Hospitalizations	Annualized HF Hospitalization Rate	Hazard Ratio[14] (95% CI)	NNT Per Year to Prevent One HF Hospitalization
Treatment Group (n=270)	182	0.46	0.67 (0.55-0.80)	4
Control Group (n=280)	279	0.68		

Mortality

The proportion of patients who died in the Treatment group (18.5%) was smaller than in the Control Group (22.9%) with a relative risk reduction of 20% (HR 0.80, 95% CI 0.55 – 1.15).

Freedom from Death or First HF Hospitalization

The proportion of patients who died or had at least one HF hospitalization in the Treatment group (44.8%) was smaller than in the Control Group (51.8%) with a relative risk reduction of 23% (HR 0.77, 95% CI 0.60 – 0.98).

All Cause Hospitalizations

All cause hospitalizations were reduced in the Treatment group (554 in the Treatment group vs. 672 in the Control group, HR 0.84, 95% CI 0.75 – 0.95). The NNT per year to prevent one all cause hospitalization was 4. For every 100 patients treated, 26 all cause hospitalizations would be prevented per year.

Death or All Cause Hospitalizations

Death or all cause hospitalizations were reduced in the Treatment group (604 in the Treatment group vs. 736 in the Control group, HR 0.84, 95% CI 0.76 – 0.94). The NNT per year to prevent one death or all cause hospitalization was 4. For every 100 patients treated, 29 deaths or all cause hospitalizations would be prevented per year.

Results from the Open Access Period (Longitudinal Analysis)

In the Open Access period, physicians were given access to PA pressures in the Control group for the first time while access to PA pressures for the Treatment group continued. In the Control group, new physician access to PA pressures resulted in a 48% reduction in HF hospitalization rates (0.36 vs. 0.68, HR 0.52, 95% CI 0.40-0.69, p<0.0001*). In the Treatment group, continued physician access to PA pressures resulted in the maintenance of low HF hospitalization rates (0.45 vs. 0.48, HR 0.93, 95% CI 0.70-1.22, p=0.5838*).

To account for potential longitudinal confounders, the change in HF hospitalization rates in the Control group as result of new access to PA pressures was compared to the change in HF hospitalization rates in the Treatment group. The change in HF hospitalization rates in the Control group was significantly greater than in the Treatment group (HR 0.56, 95% CI 0.38-0.83, p=0.0040*), indicating that the significant 48% reduction in HF hospitalization rates observed in the Control group was the result of physician access to PA pressure and not longitudinal effects.

(*P-values should be interpreted with caution because the analyses including Part 2 data were not specified before the onset of the study and there are various sources of confounding effects which cannot be separated from the treatment effect.)

Treatment Effects in Women

The CHAMPION study was not powered to show statistical significance for gender, thus a complete determination of the effect of the device in women cannot be made. At the request of FDA, a post-hoc gender analysis was conducted for the CHAMPION study, and the initial finding of a treatment-by-gender interaction for the effect of the CardioMEMS device on the HF hospitalization rate was related to (1) fewer women being in the study and the short duration of follow-up leading to a small number of events in women; and (2) the low HF hospitalization rate in Control women due to an early excess of deaths in women in the Control group, which acted as a competing risk to censor the occurrence of hospitalizations for heart failure.

A further analysis of the treatment-by- gender interaction was performed over the full period of Randomized Access and by incorporating death in the Cox Proportional Hazards. When these limitations and confounding issues were evaluated over the full period, there was neither a qualitative nor quantitative treatment-by-gender interaction and the treatment effect remained positive, independent of gender. However, the analyses conducted do not alleviate the possibility of a diminished treatment effect in women. Given the small number of women enrolled and small number of events observed in women, the true treatment effect in this group remains uncertain. In order to further complement and evaluate the results obtained during the CHAMPION study, the effect of the device in women is being studied as part of the post approval study.

The figures below depict the Freedom from HF Hospitalization and Freedom from Death for Men and Women over the Full Randomized Period (Part 1). Figure 79 below depicts the composite endpoint of Freedom from HF Hospitalization or Death for Men and Women over the Full Randomized Period (Part 1). They illustrate the apparent difference in treatment effect by gender. As seen in Figure 77, for HF hospitalizations alone, treatment and control women have similar outcomes. However, as seen in Figure 78, control women had an increased early mortality creating a competing risk for HF hospitalizations i.e., fewer control women were alive

---

[14] Hazard ratio from Andersen-Gill model

to have HF hospitalizations. Figure 79 examines Freedom from HF Hospitalization or Death and indicates a non-significant trend favoring women in the treatment group.

Figure 79. Freedom from HF Hospitalization over the Full Randomized Period (Part 1).
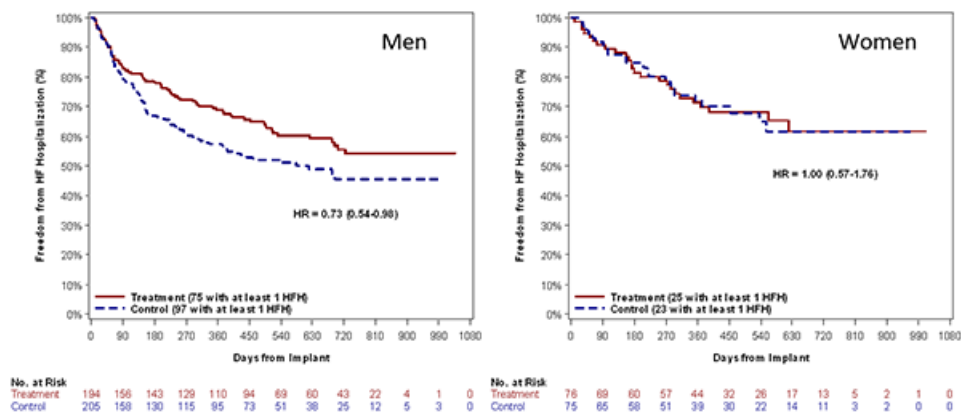
Figure 80. Freedom from Death over the Full Randomized Period (Part 1).
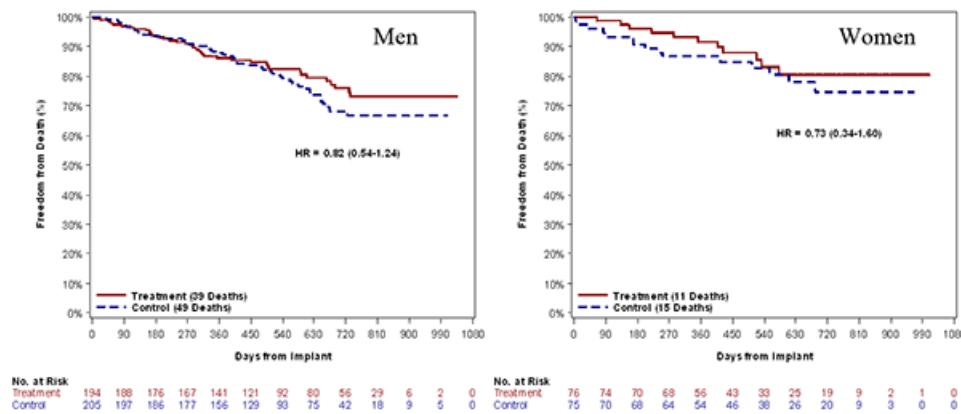
Figure 81. Freedom from HF Hospitalization or Death over the Full Randomized Period (Part 1).
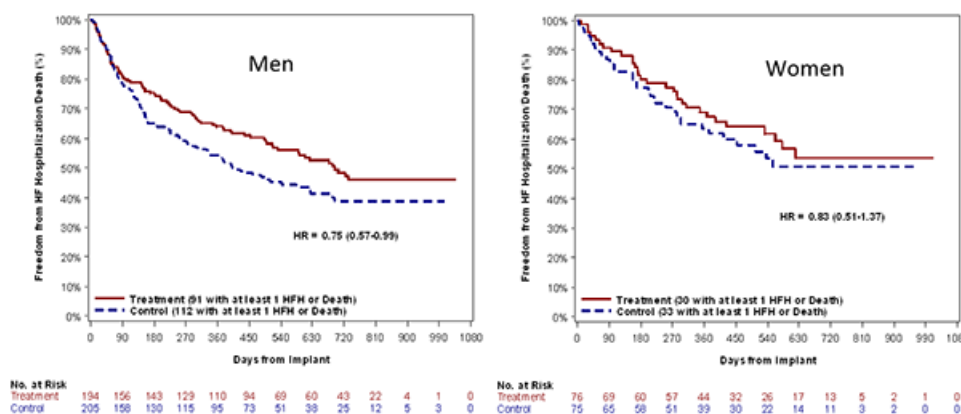
Also performed were an Anderson-Gill Model with Frailty, Anderson Gill Model with Robust Sandwich Estimates (RSE) and Negative Binomial Regression using an endpoint of time to HF hospitalization or death in Part 1 and Part 1 + Part 2. As seen in the gray rows in the tables below, all the competing risk analyses taking death into account as a competing risk show that there was no evidence of a treatment-by-gender interaction if a p-value of 0.05 is used. However, when analyses for interaction by gender are conducted, a p-

value of 0.15 is typically used because the analysis is typically not powered appropriately. When considering a p-value of 0.15, there was some evidence of treatment-by-gender interaction in the competing risk analyses under the following models:

- AG Model with Frailty for Part 1
- NB Regression for Part 1
- AG Model with Robust Sandwich Estimate for Part 1 + Part 2
- GEE NB Regression for Part 1 + Part 2

Table 9. Results of treatment by gender interaction using different statistical models

Models	Estimate	SE	p-value
Part 1			
Cox Model: Endpoint of first HFR hospitalization or Death	-0.113	0.289	0.6968
Cox Model: Endpoint of first HFR hospitalization	-0.330	0.327	0.3131
AG Model with Frailty: Endpoint of HFR hospitalization or Death	-0.373	0.239	0.1211
AG Model with Frailty: Endpoint of HFR hospitalization	-0.531	0.262	0.0459
AG Model with RSE: Endpoint of HFR hospitalization or Death	-0.433	0.316	0.1712
AG Model with RSE: Endpoint of HFR hospitalization	-0.577	0.360	0.1094
NB Regression: Endpoint of HFR hospitalization or Death	-0.412	0.242	0.0896
NB Regression: Endpoint of HFR hospitalization	-0.573	0.191	0.0027
Part 1 + Part 2			
Cox Model: Endpoint of first HFR hospitalization or Death	-0.204	0.249	0.4121*
Cox Model: Endpoint of first HFR hospitalization	-0.427	0.284	0.1331*
AG Model with Frailty: Endpoint of HFR hospitalization or Death	-0.376	0.274	0.1697*
AG Model with Frailty: Endpoint of HFR hospitalization	-0.588	0.271	0.0301*
AG Model with RSE: Endpoint of HFR hospitalization or Death	-0.477	0.274	0.0816*
AG Model with RSE: Endpoint of HFR hospitalization	-0.642	0.313	0.0399*
GEE NB Regression: Endpoint of HFR hospitalization or Death	-0.488	0.283	0.0841*
GEE NB Regression: Endpoint of HFR hospitalization	-0.761	0.319	0.0172*

Table 10. The Treatment vs. Control effects by Gender over Part 1 and over Part 1+ Part 2 under different models

Males	Hazard Ratio	p-value
Part 1 (Treatment vs. Control)		
AG Model with Frailty: Endpoint of HFR hospitalization or Death	0.67	0.0007
AG Model with Frailty: Endpoint of HFR hospitalization	0.64	0.0004
Part 1 + Part 2 (Former Control vs. Control)		
AG Model with Frailty: Endpoint of HFR hospitalization or Death	0.70	0.0176*
AG Model with Frailty: Endpoint of HFR hospitalization	0.53	<0.0001*
Females	Hazard Ratio	p-value
Part 1 (Treatment vs. Control)		
AG Model with Frailty: Endpoint of HFR hospitalization or Death	0.99	0.9440
AG Model with Frailty: Endpoint of HFR hospitalization	1.07	0.7584
Part 1 + Part 2 (Former Control vs. Control)		
AG Model with Frailty: Endpoint of HFR hospitalization or Death	0.80	0.4512*
AG Model with Frailty: Endpoint of HFR hospitalization	0.61	0.1482*

(*P-values should be interpreted with caution because the analyses including Part 2 data were not specified before the onset of the study and there are various sources of confounding effects which cannot be separated from the treatment effect.)

Non-Serious Adverse Device Events

There were 17 non-serious adverse device events that occurred over Part 1. There were no additional non-serious adverse device events over Part 2 of the clinical trial. These events were rare and are well known adverse events that occur during right heart catheterization procedures (table below).

Table 11. Non-serious Adverse Device Events Over Part 1 and Part 2

	Part 1						Part 2	
	TREATMENT (270)		CONTROL (280)		ALL PATIENTS (550)			
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
All Patients with an Event	5 (1.9%)	6	7 (2.5%)	11	12 (2.2%)	17	0 (0%)	0

Table 11. Non-serious Adverse Device Events Over Part 1 and Part 2

| | Part 1 | | | | | | Part 2 | |
| | TREATMENT (270) | | CONTROL (280) | | ALL PATIENTS (550) | | | |
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
General disorders and administration site conditions	1 (0.4%)	1 (16.7%)	4 (1.4%)	6 (54.5%)	5 (0.9%)	7 (41.2%)	0 (0%)	0 (0%)
Catheter site bleeding	0	0	1	1	1	1	0	0
Catheter site ecchymosis	0	0	1	1	1	1	0	0
Catheter site hematoma	0	0	1	1	1	1	0	0
Chest discomfort	0	0	1	1	1	1	0	0
Chest pain	0	0	1	1	1	1	0	0
Non-cardiac chest pain	1	1	0	0	1	1	0	0
Vessel puncture site pain	0	0	1	1	1	1	0	0
Investigations	2 (0.7%)	2 (33.3%)	1 (0.4%)	1 (9.1%)	3 (0.5%)	3 (17.6%)	0 (0%)	0 (0%)
Cardiac monitoring abnormal	1	1	0	0	1	1	0	0
Heart rate irregular	0	0	1	1	1	1	0	0
Serum creatinine increased	1	1	0	0	1	1	0	0
Respiratory, thoracic and mediastinal disorders	2 (0.7%)	2 (33.3%)	1 (0.4%)	1 (9.1%)	3 (0.5%)	3 (17.6%)	0 (0%)	0 (0%)
Hemoptysis	1	1	1	1	2	2	0	0
Dyspnea	1	1	0	0	1	1	0	0
Cardiac disorders	1 (0.4%)	1 (16.7%)	1 (0.4%)	1 (9.1%)	2 (0.4%)	2 (11.8%)	0 (0%)	0 (0%)
Congestive heart failure	1	1	0	0	1	1	0	0
Ventricular tachycardia	0	0	1	1	1	1	0	0
Nervous system disorders	0 (0.0%)	0 (0.0%)	1 (0.4%)	1 (9.1%)	1 (0.2%)	1 (5.9%)	0 (0%)	0 (0%)
Dizziness	0	0	1	1	1	1	0	0
Vascular disorders	0 (0.0%)	0 (0.0%)	1 (0.4%)	1 (9.1%)	1 (0.2%)	1 (5.9%)	0 (0%)	0 (0%)
Vessel perforation	0	0	1	1	1	1	0	0

Non-Serious Adverse Events not related to the device

Table 12. Non-Serious Adverse Events not related to the device Over Part 1 and Part 2

| | Part 1 | | | | | | Part 2 | |
| | Treatment (270) | | Control (280) | | All Patients (550) | | All Patients (347) | |
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
All Patients with an Event	216 (80.0%)	1229	223 (79.6%)	1135	439 (79.8%)	2364	219 (63.1%)	787
Blood and lymphatic system disorders	27 (10.0%)	37	22 (7.9%)	28	49 (8.9%)	65	13 (3.7%)	16
Cardiac disorders	81 (30.0%)	140	69 (24.6%)	117	150 (27.3%)	257	49 (14.1%)	71
Congenital, familial and genetic disorders	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	3 (0.9%)	3
Ear and labyrinth disorders	6 (2.2%)	6	2 (0.7%)	2	8 (1.5%)	8	2 (0.6%)	2
Endocrine disorders	4 (1.5%)	4	9 (3.2%)	10	13 (2.4%)	14	7 (2.0%)	7
Eye disorders	12 (4.4%)	12	14 (5.0%)	16	26 (4.7%)	28	7 (2.0%)	8
Gastrointestinal disorders	64 (23.7%)	104	60 (21.4%)	96	124 (22.5%)	200	48 (13.8%)	70
General disorders and administration site conditions	64 (23.7%)	102	45 (16.1%)	80	109 (19.8%)	182	50 (14.4%)	62
Hepatobiliary disorders	1 (0.4%)	1	7 (2.5%)	10	8 (1.5%)	11	3 (0.9%)	3

Table 12. Non-Serious Adverse Events not related to the device Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Immune system disorders	4 (1.5%)	4	4 (1.4%)	4	8 (1.5%)	8	4 (1.2%)	4
Infections and infestations	76 (28.1%)	129	91 (32.5%)	150	167 (30.4%)	279	65 (18.7%)	99
Injury, poisoning and procedural complications	32 (11.9%)	44	32 (11.4%)	37	64 (11.6%)	81	32 (9.2%)	43
Investigations	32 (11.9%)	51	26 (9.3%)	40	58 (10.5%)	91	22 (6.3%)	25
Metabolism and nutrition disorders	66 (24.4%)	116	52 (18.6%)	88	118 (21.5%)	204	37 (10.7%)	53
Musculoskeletal and connective tissue disorders	49 (18.1%)	75	58 (20.7%)	73	107 (19.5%)	148	56 (16.1%)	70
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	6 (2.2%)	8	9 (3.2%)	9	15 (2.7%)	17	6 (1.7%)	7
Nervous system disorders	61 (22.6%)	86	50 (17.9%)	67	111 (20.2%)	153	47 (13.5%)	56
Psychiatric disorders	34 (12.6%)	46	29 (10.4%)	36	63 (11.5%)	82	25 (7.2%)	31
Renal and urinary disorders	33 (12.2%)	55	35 (12.5%)	45	68 (12.4%)	100	21 (6.1%)	21
Reproductive system and breast disorders	7 (2.6%)	8	16 (5.7%)	16	23 (4.2%)	24	11 (3.2%)	13
Respiratory, thoracic and mediastinal disorders	68 (25.2%)	97	70 (25.0%)	117	138 (25.1%)	214	47 (13.5%)	66
Skin and subcutaneous tissue disorders	23 (8.5%)	26	24 (8.6%)	28	47 (8.5%)	54	9 (2.6%)	9
Surgical and medical procedures	17 (6.3%)	21	16 (5.7%)	20	33 (6.0%)	41	16 (4.6%)	19
Vascular disorders	41 (15.2%)	57	39 (13.9%)	46	80 (14.5%)	103	27 (7.8%)	29

Serious Adverse Events Over Part 1 and Part 2

Table 13. Serious Adverse Events Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
All Patients with an Event	198 (73.3%)	797	217 (77.5%)	956	415 (75.5%)	1753	201 (57.9%)	647
Cardiac disorders	138 (51.1%)	333	151 (53.9%)	443	289 (52.5%)	776	119 (34.3%)	238
Congestive heart failure	99	204	121	274	220	478	80	140
Heart failure	10	15	13	22	23	37	10	12
Ventricular tachycardia	10	14	12	16	22	30	8	9
Myocardial infarction	7	7	14	14	21	21	9	9
Cardiac pain	13	19	7	22	20	41	0	0
Atrial fibrillation	3	5	10	11	13	16	4	4
Cardiomyopathy	5	6	8	11	13	17	6	7
Cardiopulmonary arrest	3	3	7	7	10	10	3	3
Unstable angina	4	4	5	5	9	9	4	6

Table 13. Serious Adverse Events Over Part 1 and Part 2

| | Part 1 | | | | | | Part 2 | |
| | Treatment (270) | | Control (280) | | All Patients (550) | | All Patients (347) | |
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Coronary artery disease	5	5	3	3	8	8	4	4
Ventricular arrhythmia	3	3	5	7	8	10	0	0
Ventricular fibrillation	5	6	2	2	7	8	2	2
Anginal discomfort	1	1	5	8	6	9	2	4
Cardiac arrest	2	2	4	4	6	6	6	6
Ischemic cardiomyopathy	3	4	3	3	6	7	6	7
Atrial flutter	2	2	3	3	5	5	3	3
Cardiogenic shock	2	2	3	3	5	5	3	3
Acute decompensated heart failure	2	2	1	1	3	3	0	0
ADHF	2	2	0	0	2	2	0	0
Acute coronary syndrome	1	2	1	1	2	3	1	1
Arrhythmia	1	1	1	1	2	2	1	1
Atrial arrhythmia	1	1	1	1	2	2	0	0
Cardiac failure	0	0	2	2	2	2	0	0
Heart disease, unspecified	1	1	1	1	2	2	1	1
Non-ischemic cardiomyopathy	1	1	1	1	2	2	0	0
Sick sinus syndrome	1	1	1	1	2	2	0	0
Angina unstable	0	0	1	1	1	1	0	0
Arrhythmia ventricular	1	1	0	0	1	1	0	0
Arrhythmia ventricular (NOS)	1	1	0	0	1	1	0	0
Atrial tachycardia	0	0	1	1	1	1	0	0
Bradycardia	0	0	1	1	1	1	2	2
Bradycardia-tachycardia syndrome	0	0	1	1	1	1	0	0
Cardiac arrhythmia	1	1	0	0	1	1	1	1
Cardiomegaly	0	0	1	1	1	1	0	0
Cardiorenal syndrome	1	1	0	0	1	1	1	2
Chronic heart failure	1	1	0	0	1	1	0	0
Congestive cardiac failure aggravated	0	0	1	1	1	1	0	0
Coronary artery disease progression	1	1	0	0	1	1	0	0
Coronary atherosclerosis	1	1	0	0	1	1	0	0
Coronary spasm	0	0	1	1	1	1	0	0
Decompensated heart failure	1	1	0	0	1	1	0	0
End stage cardiac failure	0	0	1	1	1	1	0	0
Heart failure, congestive	0	0	1	1	1	1	0	0
Heart valve incompetence	1	1	0	0	1	1	0	0
Intermediate coronary syndrome	0	0	1	1	1	1	0	0
Junctional tachycardia	0	0	1	1	1	1	0	0
Left ventricular dysfunction	1	1	0	0	1	1	0	0
Mitral valve incompetence	1	1	0	0	1	1	1	1
Multi-valvular regurgitation	0	0	1	1	1	1	0	0
Non ST segment elevation myocardial infarction	1	1	0	0	1	1	0	0
Non-sustained ventricular tachycardia	1	1	0	0	1	1	0	0
Pacemaker mediated tachycardia	1	1	0	0	1	1	0	0
Paroxysmal supraventricular tachycardia	1	1	0	0	1	1	0	0
Pericardial disease	1	1	0	0	1	1	0	0
Pericardial effusion	1	1	0	0	1	1	0	0
Pericarditis	0	0	1	1	1	1	1	1
Premature ventricular contractions	0	0	1	1	1	1	0	0
Supraventricular tachycardia	0	0	1	1	1	1	0	0
Sustained ventricular tachycardia	1	1	0	0	1	1	0	0
Tachycardia	0	0	1	1	1	1	0	0
Tricuspid insufficiency	0	0	1	1	1	1	0	0
Ventricular ectopic beats	1	1	0	0	1	1	0	0

Table 13. Serious Adverse Events Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Ventricular rhythm	0	0	1	1	1	1	0	0
Wide complex tachycardia	0	0	1	1	1	1	0	0
Wide complex ventricular tachycardia	1	1	0	0	1	1	0	0
Asystole	0	0	0	0	0	0	2	2
Congestive cardiomyopathy	0	0	0	0	0	0	1	1
End stage heart disease	0	0	0	0	0	0	1	1
Hemopericardium	0	0	0	0	0	0	1	1
Palpitation	0	0	0	0	0	0	1	1
Paroxysmal atrial fibrillation	0	0	0	0	0	0	1	1
Polymorphic ventricular tachycardia	0	0	0	0	0	0	1	1
Tachycardia supraventricular	0	0	0	0	0	0	1	1
Infections and infestations	45 (16.7%)	62	61 (21.8%)	90	106 (19.3%)	152	52 (15.0%)	76
Pneumonia	11	11	15	16	26	27	17	19
Urinary tract infection	5	7	5	6	10	13	5	5
Bronchitis	3	3	5	6	8	9	3	3
Cellulitis	1	1	6	7	7	8	1	1
Sepsis	3	4	4	4	7	8	7	9
Acute bronchitis	1	1	4	4	5	5	2	2
Bacteremia	1	1	3	5	4	6	2	2
Upper respiratory infection	2	2	2	2	4	4	1	1
Influenza	3	3	0	0	3	3	0	0
Cellulitis of leg	0	0	2	2	2	2	0	0
Cellulitis of legs	0	0	2	2	2	2	0	0
Central line infection	0	0	2	2	2	2	2	2
Endocarditis	0	0	2	2	2	2	0	0
Foot infection	2	3	0	0	2	3	0	0
Gastroenteritis	2	3	0	0	2	3	3	3
Incision site infection	1	3	1	4	2	7	1	1
Infection	0	0	2	2	2	2	1	1
Osteomyelitis	1	1	1	1	2	2	1	1
Pyelonephritis	1	1	1	1	2	2	0	0
Respiratory infection	1	1	1	1	2	2	0	0
Viral gastroenteritis	1	1	1	1	2	2	0	0
Abscess	1	1	0	0	1	1	0	0
Acute diverticulitis	1	1	0	0	1	1	0	0
Acute pyelonephritis	0	0	1	1	1	1	0	0
Bacterial endocarditis	0	0	1	1	1	1	0	0
Bacterial infection	1	1	0	0	1	1	0	0
C.difficile colitis	1	1	0	0	1	1	0	0
Catheter site infection	0	0	1	1	1	1	0	0
Cellulitis of arm	0	0	1	1	1	1	0	0
Cellulitis of hand	1	1	0	0	1	1	0	0
Clostridium difficile infection	1	1	0	0	1	1	0	0
Community acquired pneumonia	0	0	1	1	1	1	1	1
Diverticulitis	1	1	0	0	1	1	2	2
Gastritis viral	0	0	1	1	1	1	0	0
Gastroenteritis adenovirus	1	1	0	0	1	1	0	0
Groin abscess	1	1	0	0	1	1	0	0
HIV-related dementia	0	0	1	1	1	1	0	0
Infection MRSA	0	0	1	1	1	1	0	0
Infection NOS	0	0	1	1	1	1	1	1
Klebsiella bacteremia	1	1	0	0	1	1	0	0
Maxillary sinusitis	1	1	0	0	1	1	0	0

Table 13. Serious Adverse Events Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Methicillin-resistant staphylococcal aureus sepsis	0	0	1	1	1	1	0	0
Obstructive pneumonia	1	1	0	0	1	1	0	0
Otitis media	0	0	1	1	1	1	0	0
Pneumonia MRSA	1	1	0	0	1	1	0	0
Prostatitis Escherichia coli	0	0	1	1	1	1	0	0
Purulent bronchitis	0	0	1	1	1	1	0	0
Salmonella infection, unspecified	0	0	1	1	1	1	0	0
Sepsis MRSA	0	0	1	1	1	1	1	2
Septic shock	0	0	1	1	1	1	3	3
Septicemia	0	0	1	1	1	1	0	0
Septicemia staphylococcal	0	0	1	1	1	1	0	0
Serratia infection	0	0	1	1	1	1	0	0
Sinusitis	0	0	1	1	1	1	1	1
Staphylococcal infection	1	1	0	0	1	1	0	0
Urosepsis	1	1	0	0	1	1	0	0
Viral infection	1	1	0	0	1	1	1	1
Viremia	0	0	1	1	1	1	0	0
Wound infection	0	0	1	1	1	1	0	0
Arthritis infective	0	0	0	0	0	0	1	1
Bronchopneumonia	0	0	0	0	0	0	1	1
Clostridium difficile colitis	0	0	0	0	0	0	3	3
Cytomegalovirus viremia	0	0	0	0	0	0	1	1
Febrile cold (excl flu like illness)	0	0	0	0	0	0	1	1
Febrile infection	0	0	0	0	0	0	1	1
GI infection	0	0	0	0	0	0	1	1
Infection pseudomonas aeruginosa	0	0	0	0	0	0	1	1
MRSA colonization	0	0	0	0	0	0	1	1
MRSA wound infection	0	0	0	0	0	0	1	1
Pneumonia aspergillus	0	0	0	0	0	0	1	1
Septic joint	0	0	0	0	0	0	1	1
Suppurative peritonitis, other	0	0	0	0	0	0	1	1
Respiratory, thoracic and mediastinal disorders	44 (16.3%)	58	52 (18.6%)	85	96 (17.5%)	143	32 (9.2%)	40
Dyspnea	16	23	19	24	35	47	10	10
Respiratory failure	6	6	11	11	17	17	2	2
COPD exacerbation	4	4	11	20	15	24	5	5
Pleural effusion	3	3	3	4	6	7	3	3
Shortness of breath	4	4	2	3	6	7	0	0
Aspiration pneumonia	2	2	1	1	3	3	1	1
Epistaxis	0	0	3	3	3	3	2	2
Pulmonary hypertension	2	3	1	1	3	4	2	2
Respiratory distress	3	3	0	0	3	3	0	0
COPD	1	1	1	1	2	2	0	0
Dyspnea exertional	1	1	1	1	2	2	0	0
Hypoxemia	0	0	2	2	2	2	0	0
Pneumonitis	0	0	2	2	2	2	0	0
Pulmonary edema	0	0	2	2	2	2	1	1
Pulmonary infiltration	0	0	2	2	2	2	1	1
Pulmonary thromboembolism	2	2	0	0	2	2	0	0
Acute respiratory failure	0	0	1	1	1	1	0	0
Apnea	1	1	0	0	1	1	0	0
Asthma	1	1	0	0	1	1	0	0
Asthma aggravated	0	0	1	1	1	1	0	0

Table 13. Serious Adverse Events Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Bronchitis asthmatic	0	0	1	1	1	1	0	0
Difficulty breathing	0	0	1	1	1	1	0	0
Dyspnea exacerbated	1	1	0	0	1	1	0	0
Exacerbation of asthma	0	0	1	1	1	1	0	0
Hemoptysis	0	0	1	1	1	1	1	3
Hypoxia	0	0	1	1	1	1	3	3
Productive cough	0	0	1	1	1	1	0	0
Pulmonary mass	1	1	0	0	1	1	0	0
Respiratory arrest	1	2	0	0	1	2	0	0
Chronic obstructive pulmonary disease	0	0	0	0	0	0	3	3
Cough	0	0	0	0	0	0	1	1
Hypoventilation	0	0	0	0	0	0	1	1
Pulmonary embolus	0	0	0	0	0	0	1	1
Tachypnea	0	0	0	0	0	0	1	1
General disorders and administration site conditions	35 (13.0%)	43	30 (10.7%)	40	65 (11.8%)	83	36 (10.4%)	46
Chest pain	16	20	10	11	26	31	17	26
Weakness	3	5	7	7	10	12	0	0
Chest pain (non-cardiac)	2	2	4	7	6	9	0	0
Fever	1	1	3	3	4	4	2	2
General malaise	3	3	0	0	3	3	1	1
Death	1	1	1	1	2	2	7	7
Pain	2	2	0	0	2	2	0	0
Sudden cardiac death	1	1	1	1	2	2	1	1
Anasarca	0	0	1	1	1	1	0	0
Central line complication	1	2	0	0	1	2	0	0
Chest discomfort	0	0	1	1	1	1	0	0
Chest pain aggravated	0	0	1	1	1	1	0	0
Chronic fatigue	0	0	1	1	1	1	0	0
Edema of lower extremities	1	2	0	0	1	2	2	2
Fatigue	1	1	0	0	1	1	0	0
Fatigue extreme	1	1	0	0	1	1	0	0
Febrile reaction	0	0	1	1	1	1	0	0
Fever of unknown origin	0	0	1	1	1	1	1	1
Infusion site bleeding	0	0	1	1	1	1	0	0
Multi-organ failure	0	0	1	1	1	1	0	0
Non-cardiac chest pain	0	0	1	1	1	1	1	1
Substernal chest pain	0	0	1	1	1	1	0	0
Sudden death	1	1	0	0	1	1	0	0
Swelling	1	1	0	0	1	1	0	0
Edema	0	0	0	0	0	0	1	1
Malaise	0	0	0	0	0	0	1	1
Organ failure	0	0	0	0	0	0	1	1
Thrombus in catheter	0	0	0	0	0	0	1	1
Ulcer	0	0	0	0	0	0	1	1
Vascular disorders	33 (12.2%)	42	27 (9.6%)	28	60 (10.9%)	70	15 (4.3%)	15
Hypotension	15	20	13	14	28	34	6	6
Hematoma	2	2	2	2	4	4	0	0
Orthostatic hypotension	2	2	2	2	4	4	0	0
Deep vein thrombosis leg	3	4	0	0	3	4	0	0
Low output state	3	3	0	0	3	3	0	0
Peripheral arterial disease	2	2	1	1	3	3	0	0
Claudication	2	2	0	0	2	2	1	1

Table 13. Serious Adverse Events Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
DVT of legs	2	2	0	0	2	2	0	0
Aortic stenosis	0	0	1	1	1	1	0	0
Arterial thrombosis (limbs)	1	1	0	0	1	1	0	0
DVT	0	0	1	1	1	1	1	1
Deep vein thrombosis	0	0	1	1	1	1	0	0
Extremity necrosis	0	0	1	1	1	1	0	0
Hemorrhage, unspecified	1	1	0	0	1	1	0	0
Hemorrhagic shock	1	1	0	0	1	1	0	0
Hypertension	0	0	1	1	1	1	1	1
Hypovolemic shock	1	1	0	0	1	1	2	2
Labile blood pressure	0	0	1	1	1	1	0	0
Peripheral vascular disease	0	0	1	1	1	1	0	0
Shock hemorrhagic	0	0	1	1	1	1	0	0
Subclavian artery thrombosis	1	1	0	0	1	1	0	0
Thromboembolic event	0	0	1	1	1	1	0	0
Bleeding	0	0	0	0	0	0	1	1
Cardiovascular collapse	0	0	0	0	0	0	1	1
Hypertensive emergency	0	0	0	0	0	0	1	1
Ischemia	0	0	0	0	0	0	1	1
Nervous system disorders	29 (10.7%)	37	28 (10.0%)	38	57 (10.4%)	75	27 (7.8%)	32
Syncope	12	15	7	8	19	23	9	13
CVA	2	2	4	4	6	6	2	2
Stroke	3	3	2	2	5	5	3	3
Presyncope	0	0	3	3	3	3	2	2
Carotid artery stenosis	1	1	1	1	2	2	0	0
Dizziness	1	1	1	1	2	2	1	1
Embolic stroke	1	1	1	1	2	2	0	0
Subarachnoid hemorrhage	1	1	1	1	2	2	0	0
Anoxic encephalopathy	0	0	1	1	1	1	0	0
Ataxia	1	1	0	0	1	1	0	0
Cerebellar infarction	1	1	0	0	1	1	0	0
Cerebral degeneration	1	1	0	0	1	1	0	0
Cerebral infarct	0	0	1	1	1	1	0	0
Cerebrovascular accident	1	1	0	0	1	1	0	0
Disorder brain (chronic)	1	1	0	0	1	1	0	0
Embolic cerebral infarction	0	0	1	1	1	1	0	0
Encephalopathy	0	0	1	1	1	1	1	1
Headache	0	0	1	1	1	1	0	0
Hemorrhagic stroke	0	0	1	1	1	1	0	0
Hepatic encephalopathy	1	1	0	0	1	1	0	0
Hypertensive encephalopathy	0	0	1	1	1	1	0	0
Intracranial hemorrhage	1	1	0	0	1	1	0	0
Ischemic stroke	0	0	1	1	1	1	0	0
Loss of consciousness	1	2	0	0	1	2	1	1
Numbness	0	0	1	2	1	2	0	0
Ophthalmoplegic migraine	0	0	1	1	1	1	0	0
Paresthesia	0	0	1	1	1	1	0	0
Sciatica	1	1	0	0	1	1	0	0
Seizure	1	1	0	0	1	1	0	0
Slurred speech	0	0	1	1	1	1	0	0
Somnolence	1	1	0	0	1	1	0	0
Syncope convulsive	1	1	0	0	1	1	0	0
TIA	0	0	1	1	1	1	2	2

Table 13. Serious Adverse Events Over Part 1 and Part 2

| | Part 1 | | | | | | Part 2 | |
| | Treatment (270) | | Control (280) | | All Patients (550) | | All Patients (347) | |
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Unresponsive to stimuli	0	0	1	1	1	1	1	1
Vasovagal symptoms	0	0	1	1	1	1	0	0
Weakness left or right side	0	0	1	1	1	1	0	0
Brain injury	0	0	0	0	0	0	1	1
Restless leg syndrome	0	0	0	0	0	0	1	1
Todd's paralysis	0	0	0	0	0	0	1	1
Transient ischemic attacks	0	0	0	0	0	0	2	2
Vocal cord paralysis	0	0	0	0	0	0	1	1
Renal and urinary disorders	33 (12.2%)	41	24 (8.6%)	34	57 (10.4%)	75	20 (5.8%)	22
Acute on chronic renal failure	11	12	9	10	20	22	1	1
Acute renal failure	9	10	7	9	16	19	8	9
Renal insufficiency	9	11	3	4	12	15	5	5
Acute renal insufficiency	0	0	2	2	2	2	0	0
Azotemia	1	1	1	1	2	2	0	0
Chronic kidney disease	1	1	1	1	2	2	0	0
Renal failure	1	1	1	1	2	2	1	1
Acute tubular necrosis	0	0	1	1	1	1	0	0
Chronic renal failure worsened	0	0	1	1	1	1	0	0
End stage renal failure	0	0	1	1	1	1	0	0
Hematuria	1	1	0	0	1	1	0	0
Kidney failure	1	1	0	0	1	1	0	0
Lupus nephritis	0	0	1	1	1	1	0	0
Nephrolithiasis	1	1	0	0	1	1	0	0
Renal artery stenosis	1	1	0	0	1	1	0	0
Renal function abnormal	1	1	0	0	1	1	0	0
Uremia	0	0	1	1	1	1	0	0
Urinary retention	0	0	1	1	1	1	2	2
Chronic renal failure	0	0	0	0	0	0	1	1
Kidney disorder	0	0	0	0	0	0	1	1
Renal disease	0	0	0	0	0	0	1	1
Renal failure acute on chronic	0	0	0	0	0	0	1	1
Gastrointestinal disorders	24 (8.9%)	35	31 (11.1%)	49	55 (10.0%)	84	36 (10.4%)	53
GI bleed	6	7	7	7	13	14	9	10
Abdominal pain	3	3	5	6	8	9	2	2
Diarrhea	4	4	1	1	5	5	2	2
Nausea	4	4	1	1	5	5	0	0
Gastritis	3	3	1	1	4	4	1	1
Gastrointestinal bleed	0	0	4	6	4	6	6	8
Vomiting	2	2	2	4	4	6	1	1
Constipation	0	0	3	3	3	3	1	1
Pancreatitis	2	2	1	1	3	3	1	1
Ascites	2	2	0	0	2	2	0	0
Dysphagia	1	1	1	1	2	2	2	2
Emesis	2	2	0	0	2	2	0	0
Esophagitis	0	0	2	2	2	2	0	0
Gastroparesis	0	0	2	2	2	2	1	2
Abdominal bloating	1	1	0	0	1	1	0	0
Abdominal wall hematoma	0	0	1	1	1	1	0	0
Chronic epigastric pain	0	0	1	1	1	1	0	0
Dental caries	0	0	1	1	1	1	0	0
Esophageal spasm	1	1	0	0	1	1	0	0
Esophagitis ulcerative	1	1	0	0	1	1	0	0

Table 13. Serious Adverse Events Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Gastric polyps	0	0	1	1	1	1	0	0
Gastritis erosive	0	0	1	1	1	1	0	0
Ileus	0	0	1	1	1	1	0	0
Incarcerated umbilical hernia	0	0	1	1	1	1	0	0
Ischemic colitis	0	0	1	1	1	1	1	2
Melena	1	1	0	0	1	1	0	0
Odynophagia	0	0	1	1	1	1	0	0
Rectal bleeding	0	0	1	3	1	3	1	1
Rectal fistula	0	0	1	1	1	1	0	0
Rectal prolapse	0	0	1	1	1	1	0	0
Ventral hernia	1	1	0	0	1	1	2	4
Decay dental	0	0	0	0	0	0	1	1
Duodenitis	0	0	0	0	0	0	1	1
Fecal impaction (causing obstruction)	0	0	0	0	0	0	1	1
Gastric ulcer	0	0	0	0	0	0	1	1
Gastric ulcer haemorrhage	0	0	0	0	0	0	1	1
Gastro intestinal bleed	0	0	0	0	0	0	1	1
Gastrointestinal bleeding	0	0	0	0	0	0	2	2
Hematemesis	0	0	0	0	0	0	1	2
Hematochezia	0	0	0	0	0	0	2	2
Mesenteric ischemia	0	0	0	0	0	0	1	1
Reflux esophagitis	0	0	0	0	0	0	1	1
Right upper quadrant pain	0	0	0	0	0	0	1	1
Small bowel obstruction	0	0	0	0	0	0	1	1
Metabolism and nutrition disorders	26 (9.6%)	33	28 (10.0%)	38	54 (9.8%)	71	24 (6.9%)	30
Dehydration	7	9	5	5	12	14	8	8
Hyperglycemia	3	4	5	6	8	10	1	1
Hypoglycemia	4	4	2	2	6	6	2	2
Failure to thrive	2	2	3	4	5	6	1	1
Hypokalemia	2	2	3	3	5	5	3	3
Hypovolemia	2	2	3	3	5	5	0	0
Electrolyte imbalance	2	2	2	2	4	4	0	0
Hypervolemia	2	2	2	2	4	4	0	0
Hyponatremia	1	1	3	3	4	4	4	4
Diabetes	2	2	1	1	3	3	0	0
Hyperkalemia	1	1	2	2	3	3	1	1
Diabetes mellitus loss of control	1	1	1	1	2	2	0	0
Anorexia	0	0	1	1	1	1	0	0
Diabetes mellitus	1	1	0	0	1	1	0	0
Hypercalcemia	0	0	1	1	1	1	0	0
Ketoacidosis (diabetic)	0	0	1	1	1	1	0	0
Volume overload	0	0	1	1	1	1	0	0
Diabetes mellitus inadequate control	0	0	0	0	0	0	1	1
Diabetic ketoacidosis	0	0	0	0	0	0	1	1
Gout	0	0	0	0	0	0	1	1
Gout aggravated	0	0	0	0	0	0	2	2
Gout flare	0	0	0	0	0	0	2	3
Hyperosmolar state	0	0	0	0	0	0	1	1
Hypoglycemic attack	0	0	0	0	0	0	1	1
Surgical and medical procedures	24 (8.9%)	28	29 (10.4%)	34	53 (9.6%)	62	14 (4.0%)	15
Implantable cardioverter defibrillator insertion	4	4	2	2	6	6	0	0
Pacemaker battery replacement	1	1	5	5	6	6	3	3

Table 13. Serious Adverse Events Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Cardiac resynchronisation therapy	2	2	2	2	4	4	0	0
Heart transplant	1	1	3	3	4	4	2	2
Cardiac catheterization	3	5	0	0	3	5	0	0
Implantable defibrillator replacement	0	0	3	3	3	3	0	0
Amputation	0	0	2	2	2	2	0	0
Cardiac ablation	1	1	1	1	2	2	0	0
Cardiac resynchronization therapy	0	0	2	2	2	2	0	0
Cardioversion	1	1	1	1	2	2	0	0
Cholecystectomy	0	0	2	2	2	2	0	0
Foot surgery	1	1	1	1	2	2	1	1
Inguinal hernia repair	1	1	1	1	2	2	0	0
Abdominal hernia repair	1	1	0	0	1	1	0	0
Brachytherapy	1	1	0	0	1	1	0	0
Cardiac pacemaker revision	1	1	0	0	1	1	0	0
Central line placement	0	0	1	1	1	1	0	0
Colostomy closure	1	1	0	0	1	1	0	0
Epicardial lead placement	1	1	0	0	1	1	1	1
Gallbladder operation	0	0	1	1	1	1	0	0
Gastric bypass	0	0	1	1	1	1	0	0
Implantable defibrillator insertion	1	1	0	0	1	1	1	1
Incisional drainage	1	1	0	0	1	1	0	0
Knee total replacement	0	0	1	1	1	1	0	0
Mitral valve replacement	0	0	1	1	1	1	0	0
Neuroma removal	1	1	0	0	1	1	0	0
Parotidectomy	0	0	1	1	1	1	0	0
Polypectomy	1	1	0	0	1	1	0	0
Stent placement	1	1	0	0	1	1	0	0
Total hip replacement	1	1	0	0	1	1	0	0
Total knee replacement	0	0	1	2	1	2	0	0
Tricuspid valve repair	0	0	1	1	1	1	0	0
Arteriovenous graft	0	0	0	0	0	0	1	1
Catheterization cardiac	0	0	0	0	0	0	2	2
Hospitalization NOS	0	0	0	0	0	0	1	1
Knee surgery NOS	0	0	0	0	0	0	1	1
Left ventricular assist device insertion	0	0	0	0	0	0	1	1
Ventricular assist device insertion	0	0	0	0	0	0	1	1
Injury, poisoning and procedural complications	18 (6.7%)	21	16 (5.7%)	19	34 (6.2%)	40	15 (4.3%)	16
Lead dislodgement	2	2	2	2	4	4	0	0
Hip fracture	0	0	3	3	3	3	1	1
Bleeding postoperative	1	1	1	1	2	2	0	0
Device malfunction	0	0	2	2	2	2	0	0
Fall	2	2	0	0	2	2	2	2
Head injury	0	0	2	2	2	2	0	0
Lead conductor fracture	2	2	0	0	2	2	0	0
Subdural hematoma	2	2	0	0	2	2	2	2
Accidental overdose	1	1	0	0	1	1	0	0
Ankle fracture	1	1	0	0	1	1	0	0
Cardiac pacemaker malfunction	0	0	1	1	1	1	0	0
Compression fracture	0	0	1	1	1	1	0	0
Contusion	0	0	1	1	1	1	0	0
Device lead damage	0	0	1	1	1	1	0	0
Device lead issue	1	1	0	0	1	1	0	0
Digoxin toxicity	1	1	0	0	1	1	3	3

Table 13. Serious Adverse Events Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Femur fracture	0	0	1	1	1	1	0	0
Fracture rib	1	1	0	0	1	1	0	0
Fractured hip	1	1	0	0	1	1	0	0
Fractured nose	1	1	0	0	1	1	0	0
Fractured pelvis NOS	1	1	0	0	1	1	0	0
Hematoma traumatic	1	1	0	0	1	1	0	0
Humerus fracture	0	0	1	1	1	1	0	0
Medical device complication	0	0	1	1	1	1	0	0
Migration of implant	1	1	0	0	1	1	0	0
Motor vehicle accident	1	1	0	0	1	1	0	0
Pneumothorax traumatic	1	1	0	0	1	1	0	0
Skin avulsion injury	0	0	1	1	1	1	0	0
Subdural haemorrhage	0	0	1	1	1	1	0	0
Chemical pneumonitis	0	0	0	0	0	0	1	1
Device complication	0	0	0	0	0	0	5	5
Overdose accidental	0	0	0	0	0	0	1	1
Sciatic nerve injury	0	0	0	0	0	0	1	1
Musculoskeletal and connective tissue disorders	11 (4.1%)	14	13 (4.6%)	13	24 (4.4%)	27	16 (4.6%)	17
Back pain	0	0	2	2	2	2	1	1
Chest wall pain	1	1	1	1	2	2	0	0
Degenerative joint disease	1	1	1	1	2	2	1	1
Arthritis	1	1	0	0	1	1	1	1
Arthritis single joint	0	0	1	1	1	1	0	0
Back pain aggravated	1	2	0	0	1	2	0	0
Charcot's joint	0	0	1	1	1	1	0	0
Groin pain	0	0	1	1	1	1	0	0
Hemarthrosis involving lower leg	1	1	0	0	1	1	0	0
Lumbar spinal stenosis	0	0	1	1	1	1	0	0
Lupus erythematosus	0	0	1	1	1	1	1	2
Muscle necrosis	1	1	0	0	1	1	0	0
Musculoskeletal chest pain	1	1	0	0	1	1	0	0
Neck pain	1	1	0	0	1	1	1	1
Olecranon bursitis	0	0	1	1	1	1	0	0
Osteoarthritis knee	0	0	1	1	1	1	0	0
Polymyositis	1	1	0	0	1	1	0	0
Pseudogout	0	0	1	1	1	1	0	0
Rheumatoid arthritis	1	1	0	0	1	1	0	0
Rotator cuff tear	1	1	0	0	1	1	1	1
Scleroderma	0	0	1	1	1	1	0	0
Shoulder blade pain	1	1	0	0	1	1	0	0
Spinal column stenosis	1	1	0	0	1	1	0	0
Cervical spondylosis	0	0	0	0	0	0	1	1
Foot pain	0	0	0	0	0	0	1	1
Joint instability	0	0	0	0	0	0	1	1
Knee pain	0	0	0	0	0	0	1	1
Low back pain	0	0	0	0	0	0	1	1
Osteoarthritis knees	0	0	0	0	0	0	1	1
Pain in joint involving lower leg	0	0	0	0	0	0	1	1
Shoulder pain	0	0	0	0	0	0	1	1
Spinal stenosis NOS	0	0	0	0	0	0	1	1
Spondylolisthesis	0	0	0	0	0	0	1	1
Blood and lymphatic system disorders	13 (4.8%)	14	10 (3.6%)	13	23 (4.2%)	27	14 (4.0%)	20

Table 13. Serious Adverse Events Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Anemia	11	12	8	10	19	22	11	12
Thrombocytopenia	1	1	1	1	2	2	1	1
Anemia microcytic	1	1	0	0	1	1	0	0
Leukocytosis	0	0	1	1	1	1	0	0
Neutropenia	0	0	1	1	1	1	0	0
Anemia aggravated	0	0	0	0	0	0	1	1
Hemolysis	0	0	0	0	0	0	1	5
Neutropenic fever	0	0	0	0	0	0	1	1
Investigations	10 (3.7%)	10	5 (1.8%)	6	15 (2.7%)	16	3 (0.9%)	4
Serum creatinine increased	2	2	1	2	3	4	0	0
Transplant evaluation	2	2	0	0	2	2	0	0
Anticoagulation drug level above therapeutic	1	1	0	0	1	1	0	0
Blood culture positive	1	1	0	0	1	1	0	0
Blood glucose fluctuation	0	0	1	1	1	1	0	0
INR	0	0	1	1	1	1	0	0
INR increased	1	1	0	0	1	1	0	0
International normalized ratio decreased	0	0	1	1	1	1	0	0
Mediastinoscopy	1	1	0	0	1	1	0	0
Pulmonary arterial pressure increased	1	1	0	0	1	1	1	1
QT interval prolonged	1	1	0	0	1	1	0	0
Ventricular filling pressure increased	0	0	1	1	1	1	0	0
Blood sugar abnormal	0	0	0	0	0	0	1	1
INR decreased	0	0	0	0	0	0	1	1
Urinary output diminished	0	0	0	0	0	0	1	1
Psychiatric disorders	7 (2.6%)	7	7 (2.5%)	7	14 (2.5%)	14	6 (1.7%)	7
Acute mental status changes	3	3	7	7	10	10	4	4
Agitation	1	1	0	0	1	1	0	0
Delirium toxic	1	1	0	0	1	1	0	0
Panic attack	1	1	0	0	1	1	0	0
Suicidal ideation	1	1	0	0	1	1	0	0
Mental status changes	0	0	0	0	0	0	2	2
Withdrawal syndrome	0	0	0	0	0	0	1	1
Hepatobiliary disorders	6 (2.2%)	8	7 (2.5%)	8	13 (2.4%)	16	2 (0.6%)	3
Acute cholecystitis	4	4	0	0	4	4	0	0
Cholecystitis	1	1	3	3	4	4	0	0
Cholelithiasis	2	2	0	0	2	2	2	2
Gallstones	0	0	1	1	1	1	1	1
Hepatic fibrosis	0	0	1	2	1	2	0	0
Injury to liver	1	1	0	0	1	1	0	0
Liver disorder	0	0	1	1	1	1	0	0
Portal hypertension	0	0	1	1	1	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5 (1.9%)	7	4 (1.4%)	5	9 (1.6%)	12	5 (1.4%)	5
Lung cancer	2	2	1	1	3	3	1	1
Large cell lung cancer	0	0	1	1	1	1	0	0
Lung nodule	0	0	1	1	1	1	0	0
Lymphocytic leukemia	0	0	1	1	1	1	0	0
Myelodysplastic syndrome	1	1	0	0	1	1	0	0
Ovarian cancer	1	1	0	0	1	1	0	0
Prostate cancer metastatic	0	0	1	1	1	1	0	0
Skin cancer	1	1	0	0	1	1	0	0
Small cell carcinoma of the lung	1	2	0	0	1	2	0	0
Adenoma	0	0	0	0	0	0	1	1

Table 13. Serious Adverse Events Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Breast cancer	0	0	0	0	0	0	1	1
Esophageal cancer	0	0	0	0	0	0	1	1
Lymphoma	0	0	0	0	0	0	1	1
Endocrine disorders	2 (0.7%)	2	1 (0.4%)	1	3 (0.5%)	3	1 (0.3%)	1
Adrenal insufficiency	1	1	0	0	1	1	0	0
Hypothyroidism	1	1	0	0	1	1	1	1
Myxedema	0	0	1	1	1	1	0	0
Immune system disorders	2 (0.7%)	2	1 (0.4%)	1	3 (0.5%)	3	0 (0.0%)	0
Amyloidosis	1	1	0	0	1	1	0	0
Heart transplant rejection	0	0	1	1	1	1	0	0
Transplant rejection	1	1	0	0	1	1	0	0
Skin and subcutaneous tissue disorders	0 (0.0%)	0	3 (1.1%)	3	3 (0.5%)	3	3 (0.9%)	4
Diabetic ulcer	0	0	1	1	1	1	0	0
Foot ulcer	0	0	1	1	1	1	0	0
Venous stasis ulcer	0	0	1	1	1	1	0	0
Decubitus ulcer	0	0	0	0	0	0	1	1
Rash	0	0	0	0	0	0	1	2
Skin thinning of	0	0	0	0	0	0	1	1
Benign prostatic hypertrophy	0	0	1	1	1	1	0	0
Reproductive system and breast disorders	0 (0.0%)	0	1 (0.4%)	1	1 (0.2%)	1	3 (0.9%)	3
Enlarged prostate	0	0	0	0	0	0	1	1
Postmenopausal bleeding	0	0	0	0	0	0	1	1
Vaginal bleeding	0	0	0	0	0	0	1	1

Adverse Device Events

Table 14. Unanticipated or Serious Adverse Device Events Over Part 1 and Part 2

	Part 1						Part 2	
	Treatment (270)		Control (280)		All Patients (550)		All Patients (347)	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
Unanticipated Serious Adverse Device Events	0 (0.0%)	0	1 (0.4%)	1	1 (0.2%)	1	0 (0.0%)	0
Serious Adverse Device Events	2 (0.7%)	2	0 (0.0%)	0	2 (0.4%)	2	0 (0.0%)	0

Unanticipated Serious Adverse Device Events

There was one event during Part 1 reported as a USADE by the investigator but determined not to be serious or device system related by the CEC which reviewed the event on 27 Jun 2009. There were no additional USADEs over Part 2 of the clinical trial.

Serious Adverse Device Events

The two SADEs that occurred during Part 1 were hemoptysis during the implant procedure and an in-situ thrombosis during the right heart catheterization procedure. Both patients were treated and recovered without sequela. There were no additional SADEs over Part 2 of the clinical trial.

Cleaning

- Do not submerge the system in water.
- Unplug the electronics unit prior to cleaning.

- To clean the LCD screen, make sure the electronics unit is in the power off mode. Unplug the monitor from the power source before cleaning. Stand away from the LCD monitor and spray cleaning solution onto a clean lint free cloth. Without applying excessive pressure, clean the screen with a slightly dampened cloth.
- To clean the antenna and electronics enclosure, wipe clean with a slightly damp cloth using soap, mild detergent, or water. Make sure parts are dry before turning the electronics unit on.
- Follow the normal biohazard routine per hospital protocol followed for any contaminated parts.

Storage

- Store the system within the environmental limits stated in the Environmental Information section.
- Excessive vibration, impact, or rough handling may damage the system.
- Exposing the screen to rain, water, moisture or sunlight may severely damage the system.
- To avoid potential damage caused by lightning, unplug the electronics unit from any unprotected outlet during electrical storms.

User/Owner Responsibility

The Hospital Electronics System and the authorized replacement parts are designed to work as described in this manual. The user(s) of this equipment should not use parts that have failed, exhibit excessive wear, are contaminated, or otherwise ineffective. Owner's responsibilities:

- Replacement of components as required for safe and reliable operation
- Replacement of ineffective parts with parts supplied by the manufacturer

The system should not be modified. The user of this equipment is responsible for reading, understanding, and following the Warning and Precaution statements presented within this manual.

Electromagnetic Interference and Electromagnetic Compatibility

This section provides a brief overview of Electromagnetic Interference and Electromagnetic Compatibility guidance associated with the use of the CM3000.

Table 15. Electromagnetic Emissions

Guidance and manufacturer's declaration – electromagnetic emissions

The electronics unit is intended for use in the electromagnetic environment specified below.
The customer or the user of the electronics unit should assure that it is used in such an environment.

Emissions test	Compliance	Electromagnetic environment - guidance
RF emissions CISPR 11 CISPR 22	Class A, Group 2 Class B	The electronics unit must emit electromagnetic energy in order to perform its intended function. Nearby electronic equipment may be affected. The electronics unit is suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/ Flicker emissions IEC 61000-3-3	Complies	

Table 16. Electromagnetic Immunity

Guidance and manufacturer's declaration – electromagnetic immunity

The electronics unit is intended for use in the electromagnetic environment specified below. The customer or the user of the electronics unit should assure that it is used in such an environment.

Immunity Test	IEC 60601 Test level	Compliance level	Electromagnetic environment - guidance
Electrostatic discharge (ESD) IEC 61000-4-2	±8 kV contact ±15 kV air	±8 kV contact ±15 kV air	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.
Electrical fast transient/burst IEC 61000-4-4	±2 kV for power supply lines ±1 kV for input/output lines	±2 kV for power supply lines ±1 kV for input/output lines	Mains power quality should be that of a typical commercial or hospital environment
Surge IEC 61000-4-5	±1 kV line(s) to line(s) ±2 kV line(s) to earth	±1 kV line(s) to line(s) Not applicable	Mains power quality should be that of a typical commercial or hospital environment

Table 16. Electromagnetic Immunity

Guidance and manufacturer's declaration – electromagnetic immunity

The electronics unit is intended for use in the electromagnetic environment specified below. The customer or the user of the electronics unit should assure that it is used in such an environment.

Immunity Test	IEC 60601 Test level	Compliance level	Electromagnetic environment - guidance
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	0% U_T[15] (100% dip in U_T) for 0.5 cycle	0% U_T (100% dip in U_T) for 0.5 cycle	Mains power should be that of a typical commercial or hospital environment. If the user of the electronics unit requires continued operation during power mains interruptions, it is recommended that the electronics unit be powered from an uninterruptible power supply or a battery.
	0% U_T (100% dip in U_T) for 1 cycle	0% U_T (100% dip in U_T) for 1 cycle	
	70% U_T (30% dip in U_T) for 25 cycles	70% U_T (30% dip in U_T) for 25 cycles	
	0% U_T (100% dip in U_T) for 5 sec	0% U_T (100% dip in U_T) for 5 sec	
Power frequency (50/60 Hz) Magnetic field IEC 61000-4-8	30 A/m	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
Conducted RF IEC 61000-4-6 Radiated RF IEC 61000-4-3	3 Vrms 150 kHz to 80 MHz ISM Bands 3 V/m 80 MHz to 2.7 GHz	3 Vrms 6 Vrms 3 V/m	Portable and mobile RF communication equipment should be no closer to any part of the electronics unit, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. **Recommended separation distance** **d = 1.2 $\sqrt{P}$** **d = 1.2 $\sqrt{P}$ 80 MHz to 800 MHz** **d = 2.3 $\sqrt{P}$ 800 MHz to 2.7 GHz** where **P** is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and *d* is the recommended separation distance in meters (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey, should be less than the compliance level in each frequency range[16]. Interference may occur in the vicinity of equipment marked with the following symbol:

Electromagnetic site survey- Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the electronics unit is used exceeds the applicable RF compliance level above, the electronics unit should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as reorienting or relocating the electronics unit.

Table 17. Recommended separation distances between portable and mobile RF communications equipment and the electronics unit

The electronics unit is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the electronics unit can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the electronics unit as recommended below, according to the maximum output power of the communications equipment.

[15] UT is the a.c. mains voltage level prior to application of the test level.
[16] Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3V/m.

Rated Maximum output power of transmitter (W)	Separation distance according to frequency of transmitter[17]		
	150 kHz to 80 MHz	80 MHz to 800 MHz[18]	800 MHz to 2,7 GHz
	$d = 1.2 \sqrt{P}$	$d = 1.2 \sqrt{P}$	$d = 2.3 \sqrt{P}$
0.01	0.12 m	0.12 m	0.23 m
0.1	0.38 m	0.38 m	0.73 m
1	1.20 m	1.20 m	2.30 m
10	3.79 m	3.79 m	7.27 m
100	12.00 m	12.00 m	23.00 m

For transmitters rated at a maximum output not listed above, the recommended separation distance (**d**) in meters can be estimated using the equation applicable to the frequency of the transmitter, where **P** is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.

For two electronics units operating simultaneously and in proximity test results indicate that the separation distance should be greater than 4 meters (13 feet and 2 inches).

FCC Statement

This device complies with Part 18 of the FCC rules.

The PA Sensor is approved for wireless transmission under FCC ID number R3PCS-A-000051. The sensor complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions: 1) this device may not cause harmful interference and 2) this device must accept any interference received, including interference that may cause undesired operation.

EU REACH SVHC Disclosure

Current Candidate List (as published July 2014)

REACH - the regulation concerning Registration, Evaluation, Authorization and Restriction of Chemicals - is a law within the European Union. REACH applies to all EU manufacturers, importers and users of chemical substances, as well as EU producers, importers and suppliers of articles such as finished goods, parts and components.

Article 33 of REACH requires us to provide information about certain "substances of very high concern" ("SVHCs") if any SVHCs are present in a concentration of more than 0.1% of the weight of an article that we supply in the EU.

Based on information currently available, no substances from the SVHC candidate list are present in our products as described by Article 33, except as follows:

(DEHP, bis(2-ethyl(hexyl)phthalate), CAS nr.: 117-81-7; EC nr. 204-211-0).

DEHP is found in the following component(s):

Table 18. Component

Component	Part	Amount Present
Rigid Antenna	CS-000132	Less than 0.8% w/w (weight of substance/weight of product)

As a result, there are no restrictions for the user of the rigid antenna in this application.

WEEE Compliance Statement

The 2002/96/EC Directive on Waste Electrical and Electronic Equipment (the WEEE Directive) states that new equipment placed on the market within the European Union must comply with the WEEE directive which aims to ensure that products can be easily broken down or recycled at the end of the life cycle. The manufacturer is committed to complying with the EC WEEE directive. Products put on the market are required to be marked with the crossed through recycling bin symbol and something that identifies that it was put on the market on or after this date.

System Specifications

Electrical Characteristics

Power

- Power Supply: Input: Class II 100-240V, 50-60 Hz, Output: 12 VDC, 6A
- Manufacturer part number: CS-001301
- Only use power cord (CM3020) supplied by the manufacturer

Radiofrequency (RF) Characteristics

- Transmitted Electrical Power: < 1 mW e.r.p.
- Operating Frequency: 30-37.5 MHz. Under normal operating conditions the measurement bandwidth is approximately 1 MHz within the operating frequency range.

---

[17] These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects, and people.
[18] At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.

Mechanical Characteristics

Main Unit

- Weight: approximately 8 pounds
- Dimensions: Height:11.5 inches Width: 10.5 inches Length: 5.5 inches
- Product Life: 5 years
- I/O: 2 USB, RS-232
- Printer: FP-900064
- Optional WIFI adapter: CM3040

Display

- Touchscreen: Resistive
- Brightness: approximately 250 cd/m2
- Resolution: 800 x 480, color

Antenna

- Weight: approximately 4 pounds
- Diameter: 9 inches
- Cable: Reference manufacturer's part number CS-000135

Environmental Information

- Operation: 5º to 40ºC (41º to 104ºF), 15% to 93% humidity (non-condensing), 700-1060 hPa (Electronics), 800-1150 hPa (implanted sensor)
- Transportation: -25º to 70ºC (-13º to 158ºF), 15% to 93% humidity (non-condensing)
- Storage: -25º to 70ºC (-13º to 158ºF), 15% to 93% humidity (non-condensing)

Classification

- Class II equipment
- Type BF insulation
- Ordinary Equipment IP 21
- Continuous Use

Testing

System Testing

- System Accuracy (under typical environmental conditions): +/- 2 mmHg at baseline and +/-3% of difference between measured pressure and baseline
- System Accuracy: +/-4 mmHg over the range of environmental conditions
- The CM3000 was issued an ETL/cETL Listing Mark

Safety Testing

- IEC 60601-1
- ANSI ES 60601-1
- CENELEC EN 60601-1
- CAN/CSA-C22.2 No. 60601-1

EMI/EMC Testing

- CENELEC EN 60601-1-2
- ETSI EN 301 489-1

Wireless Testing

- FCC part 18 (Electronics System)
- FCC part 15 (Sensor)
- ETSI EN 301 489-3
- ETSI EN 302 510
- CISPR 11
- CISPR 22

Software

This device contains open source software. Source code is available upon request.

Technical Support

In North America:

For Merlin.net™ PCN patients, telephone Technical Support is available Monday through Friday (8AM to 8PM Eastern Standard Time). For clinicians, telephone Technical Support is available 24-hours a day.

For Merlin.net Patient Care Network support:

- 1 877 696 3754 (1 877 MY MERLIN) (toll-free within North America)

In Europe:

Telephone Technical Support is available Monday through Friday (8:00 to 17:00 Central European Time).

- +46 8 474 4756 (Sweden) (Support in English and Swedish)

St. Jude Medical maintains 24-hour phone lines for technical questions and support:

- 1 818 362 6822
- 1 800 722 3774 (toll-free within North America)
- + 46 8 474 4147 (Sweden)

For additional assistance, call your local St. Jude Medical representative.

Symbols

The following symbols are used on the system labels.

Symbol	Description
REF	Reorder number
	Consult instructions for use
	Keep dry
	Date of Manufacture
	Manufacturer
	Temperature limitations
	Humidity limitation
SN	Serial number
Made in USA.	Made in USA
	Momentary pushbutton
	Quantity, package contents
	Do not use if package is damaged
	The device contains a battery and the label is affixed to this device in accordance with European Council Directives 2002/96/EC and 2006/66/EC. These directives call for separate collection and disposal of electrical and electronic equipment and batteries. Sorting such waste and removing it from other forms of waste lessens the contribution of potentially toxic substances into municipal disposal systems and into the larger ecosystem. Return the device to St. Jude Medical at the end of its operating life.
	Direct current
	Federal Communication Commission Number (FCC ID: #)
	Non-ionizing radiation
	Type BF Patient Applied Part
IP21	IEC 60529 Ingress Protection Level
	Class II equipment

Symbol	Description
	Manufacturing Facility
	Australian Communications and Media Authority (ACMA) and New Zealand Radio Spectrum Management (RSM) Regulatory Compliance Mark (RCM)
R͓x ONLY	For prescription use only
ETL CLASSIFIED C US Intertek 4002966	Conforms to AAMI Std ES60601-1 IEC Std 60601-1-11 Certified to CAN/CSA std C22.2 No. 60601-1

2017-07
ARTEN600007895 A

600007895

ST. JUDE MEDICAL™