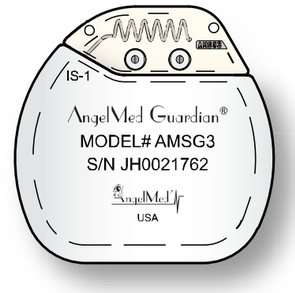
AngelMed Guardian® Implantable Medical Device (IMD) Model AMSG3

User's Guide



Caution: Federal law restricts this device to sale by or on the order of a physician.

Angel Medical Systems®
788 Shrewsbury Ave., Suite 2200
Tinton Falls, NJ 07724 (USA)
+1 561 962-2191
www.angel-med.com

May 2017
P/N 0212-2100-036#P15 Rev C

AngelMed®

Fold Line

Warning

The diagnosis of an acute coronary syndrome (ACS) event should not be based solely on a Guardian Emergency Alarm.

A Guardian Emergency Alarm is an adjunct to symptoms as a prompt for patient presentation for a *potential* ACS event. Interpretation of the Guardian Emergency Alarm may *contribute* to the diagnosis. Any potential ACS event identified by a Guardian Emergency Alarm should be confirmed using the standard of care diagnostic tests and clinical evaluation used to diagnose ACS events (i.e. presence and intensity of symptoms (if present), surface 12 lead ECG, cardiac biomarker, and/or a stress test). This protocol should be followed even when the Guardian Emergency Alarm is not accompanied by symptoms.

A Guardian Emergency Alarm alone should not be the sole basis for performing interventional diagnostic testing or PCI. The decision to perform interventional diagnostic testing and subsequent medical or PCI treatment should be based on the totality of the results of those tests and clinical evaluation.

Contents

1 Introduction

The AngelMed Guardian® Implantable Medical Device (IMD) is an implantable programmable device that monitors the patient's electrogram, vibrates to warn the patient of alarms and alerts, and stores electrogram signals and other data. The IMD is one of the primary components of the AngelMed Guardian system.

How supplied – The IMD is supplied in a sterile tray for introduction into the operating field. The tray contains one IMD and a torque wrench. The outer box contains literature.

About this manual – This document describes the IMD and provides implantation procedures, as well as an outline of the Pre-Implant Check and Post-Implant Setup procedures. For detailed information on these procedures using the Programmer, see the *AngelMed Guardian Programmer Application User's Manual.*

Available Literature

The following documents provide information relevant to the AngelMed Guardian system.

- *AngelMed Guardian® External Device (EXD) Model EXD-001 User's Manual*
- *AngelMed Guardian® Programmer Application User's Manual*
- *Patient Manual for the AngelMed Guardian® System*

2 System Overview

The AngelMed Guardian system monitors and detects changes in patients' electrograms, using baseline electrograms from the previous day for comparison. If a change exceeds a pre-specified threshold, the system warns the patient and stores pertinent data for subsequent review. Two levels of warnings are possible:

- Emergency alarms, for significant events where the patient immediately calls for an ambulance
- See Doctor alerts, for less-significant events where the patient makes an appointment to see the doctor in the next 1 or 2 days

System Components

The AngelMed Guardian system consists of the IMD plus the following components:

Lead – an IS-1, currently-marketed, active fixation, steroid eluding pacing lead that attaches to the apex of the right ventricle.

External Device (EXD) – a hand-held telemetry device that provides alarms and alerts via beeps and a red or yellow flashing indicator light, and is used to silence alarms and alerts. The EXD is also used for communication between the Programmer and the IMD.

Programmer – a customized computer that allows the physician to program IMD parameters and alarm settings for each patient. It also enables the physician to retrieve and review data collected by the IMD.

The IMD is programmed using the AngelMed Guardian Model Prog-003 Programmer running software version 3.6 or higher.

This booklet summarizes some of the tasks that can be performed with the Programmer. For detailed information on Programmer-related tasks, see the *AngelMed Guardian Programmer Application User's Manual*. You may also consult the Programmer online Help.

Indications & Contraindications

Indications:
The AngelMed Guardian System is an implantable cardiac monitor with patient alerting capability and an additional external alarm device. The Guardian System is indicated for use in patients who have had prior acute coronary syndrome (ACS) events and who remain at high risk for recurrent ACS events.

The Guardian System is indicated as an adjunct to patient recognized symptoms. The Guardian System detects potential ongoing ACS events, characterized by sustained ST segment changes, and alerts the patient to seek medical attention for those potential ACS events.

A Guardian System alert is a more accurate predictor of ACS events when compared to patient recognized symptoms alone and demonstrates a reduced rate over time of patient presentations without ACS events (false positives) when compared to patient recognized symptoms alone.

In the absence of symptoms, the Guardian System may identify asymptomatic ACS events and prompt the patient to seek medical attention.

Note:
The ST algorithm has been tested for accuracy of the ST segment data. The significance of the ST segment changes

needs to be determined by a clinician.

Contraindications: Do not implant the IMD in:

- Patients with cognitive impairment that would prevent recognition of alarms
- Patients who cannot feel the vibration from the implanted device (IMD)
- Patients with implanted pacemaker, ICD or CRT devices
- Patients where a pacemaker lead cannot be placed safely

See *Precautions* on page 14 for additional considerations regarding IMD implantation and operation.

3 IMD Device Description

The IMD serves two fundamental functions:

- To detect an ST shift – in other words, a change in the ST deviation of a patient's electrogram[1]
- If an ST shift occurs, to warn the patient to seek immediate medical help, by vibrating in a recognizable pattern

In addition to ST shift, the IMD detects other types of electrogram changes, such as high or irregular heart rates. Each type of electrogram change is called an event. The physician can specify the type of warning – either Emergency alarm or See Doctor alert – that is associated with each event.

See the *AngelMed Guardian Programmer Application User's Manual* for detailed information.

Data Acquisition, Characterization, and Storage

Data Acquisition Modes

The IMD supports the following data acquisition modes:

- Normal data acquisition mode – The usual means by which the IMD collects patient data. The IMD collects a 10-second electrogram segment every 30 or 90 seconds, depending on the characterization of the previous segment.

[1] ST deviation is the voltage difference between the ST and PQ segments. Mathematically: ST deviation = ST segment – PQ segment

- Post-emergency alarm data acquisition mode – Occurs after the IMD has detected an event associated with an emergency alarm. In this mode, the IMD collects a segment every minute for 24 minutes and then every 15 minutes for 6 hours. After 6 hours and 24 minutes, the IMD automatically reverts to normal data acquisition mode. The IMD does not try to detect additional events during this time period.

Data Characterization and Detection of Alarm Conditions

After an electrogram segment has been collected, it is characterized by heart rate and ST shift. The ST shift categorization is made by comparing this electrogram segment to a baseline segment collected nominally over the previous 24 hours. For each patient the physician sets the threshold for designating an ST shift event.

Using the heart rate and ST shift categorizations, the segment is classified, and the classifications of the last several segments are checked to determine if an event has been detected. If, for example, three consecutive segments are classified as "normal heart rate with a positive ST shift," then an event has been detected. Examples of events include positive or negative ST shifts, high heart rate, an ST shift at an elevated heart rate, and low heart rate.

With some exceptions, the events can be mapped to one of the following alarm types:

- Emergency
- See Doctor
- None (i.e., save data in the See Doctor manner but don't alert the patient)
- Ignore (i.e., neither save the data nor alert the patient)

The physician can customize which alarm type is generated for each kind of detected event. For a list of events and their default alarm type assignments, see the *Alarm Configuration Window* on page 52. For a detailed description of alarm type configurations, see the *AngelMed Guardian Programmer Application User's Manual*.

Data Storage

The IMD stores electrogram signals, IMD parameters, and patient data. Electrogram signals are recorded and stored in 10-second segments. In addition to current data, the IMD can save up to two Emergency alarms and up to six See Doctor alerts.

Stored segments may include:

- Current Data – up to 129 electrogram segments that were captured immediately prior to data retrieval
- Pre-Emergency Alarm Data – 24 electrogram segments that occurred prior to the detection of the Emergency alarm event and the hourly baseline segment for the hour in which the event occurred
- Post-Emergency Alarm Data – the 48 electrogram segments that occurred after the detection of an Emergency alarm event
- Pre-See Doctor Alert Data – the three electrogram segments that led up to the detection of a See Doctor alert and the hourly baseline segment for the hour in which the event occurred
- Baseline Segment Memory – 24 electrogram segments, one for each hour of the preceding 24 hours
- Histogram Information – ST deviation histogram information

For a detailed description of data collected by the IMD, see the *AngelMed Guardian Programmer Application User's Manual*.

Vibration Patterns

The IMD vibration pattern is different for emergency alarms than for See Doctor alerts.

Emergency alarms – consist of a repeating sequence of five short vibrations in a 3-2 sequence:

Brrrr–Brrrr–Brrrr ***Brrrr–Brrrr***

See Doctor alerts – consist of a repeating sequence of a half-second vibration, followed by a 7-second pause.

Vibration magnitudes can be set to one of three levels using the Programmer. For more information, see the *AngelMed Guardian Programmer Application User's Manual*.

Wireless Telemetry

The IMD communicates via wireless telemetry to and from the EXD. The IMD is capable of both near- and far-field telemetry.

Near-Field Telemetry

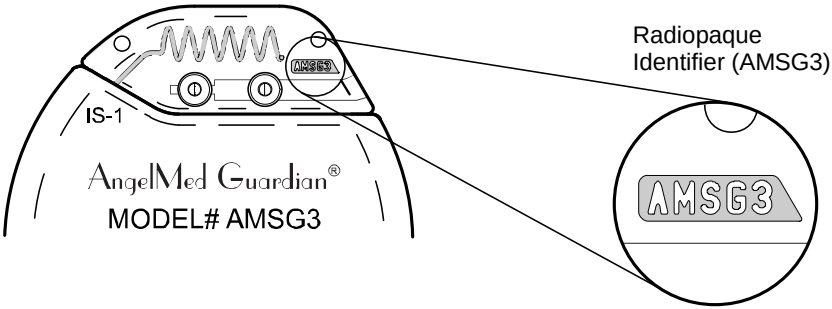
Near-field telemetry is used to silence IMD alarms and establish far-field communication sessions between the IMD and EXD. The EXD initiates all communication sessions. Near-field telemetry is unidirectional (the IMD can only receive) with a communication distance of approximately 2 in (5 cm).

Far-Field Telemetry

Far-field telemetry is bidirectional and is used for sending an alarm or alert from the IMD to the EXD, for retrieving stored IMD data, and for sending configuration parameters from the Programmer to the IMD. The maximum far-field communication distance is approximately 6 ft (1.8 m). The maximum distance for retrieving data and setting IMD parameters may be less depending on the distance and orientation of the EXD. The IMD's far-field communication is enabled by the helical antenna in the IMD header.

Radiopaque Identifier

Each IMD has a tungsten-stamped plate inside the header for non-invasive identification. This radiopaque identifier is the IMD model number, AMSG3.



Certifications

FCC Compliance Statement (Part 15.19)

This device 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.

Warning (Part 15.21): Changes or modifications not expressly approved by the party responsible for compliance could void the user's authority to operate the equipment.

FCC Interference Statement (Part 15.105(b))

This equipment has been tested and found to comply with the limits for a Class B digital device, pursuant to Part 15 of the FCC Rules. These limits are designed to provide reasonable protection against harmful interference in a residential installation. This equipment generates, uses, and can radiate radio frequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to radio communications. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause harmful interference to radio or television reception, the user is encouraged to try to correct the interference by one of the following measures:

- Reorient or relocate the receiving antenna.
- Increase the separation between the equipment and receiver.
- Consult the dealer or an experienced radio/TV technician for help.

(Part 95.1215(a))
This transmitter is authorized by rule under the Medical Device Radiocommunication Service (in part 95 of the FCC Rules) and must not cause harmful interference to stations operating in the 400.150-406.000 MHz band in the Meteorological Aids (i.e., transmitters and receivers used to communicate weather data), the Meteorological Satellite, or the Earth Exploration Satellite Services and must accept interference that may be caused by such stations, including interference that may cause undesired operation. This transmitter shall be used only in accordance with the FCC Rules governing the Medical Device Radiocommunication Service. Analog and digital voice communications are prohibited. Although this transmitter has been approved by the Federal Communications Commission, there is no guarantee that it will not receive interference or that any particular transmission from this transmitter will be free from interference.

(Part 95.1217(a)(1))
This device may not interfere with stations operating in the 400.150-406.000 MHz band in the meteorological aids, meteorological-satellite, and earth exploration-satellite services, and must accept any interference received, including interference that may cause undesired operation.

FCC ID: THL-IMDAMSG3

SAR

This portable transmitter with its antenna has shown compliance with FCC's SAR limits for general population / uncontrolled exposure.

The antenna used for this device must not be co-located or operating in conjunction with any other antenna or transmitter.

4 Storage, Handling, and Resterilization

Device storage

Store the device in a clean area, away from sources of electromagnetic interference. For additional details, see *Environmental Specifications* on page 47.

Drop limits

- **Packaged IMD.** If the packaged IMD is dropped from a height of 3 ft (0.9 m) or more, contact your AngelMed representative for a replacement.
- **Unpackaged IMD.**
  - If the unpackaged IMD is dropped outside the sterile operating field, contact your AngelMed representative for a replacement.
  - If the unpackaged IMD is dropped inside the sterile field, from a height of 12 in (30 cm) or more onto a hard surface, contact your AngelMed representative for a replacement.

Package integrity. Do not use the IMD if the packaging is wet, punctured, opened, or damaged, because the integrity of the sterile packaging may be compromised. Return the device to your AngelMed representative.

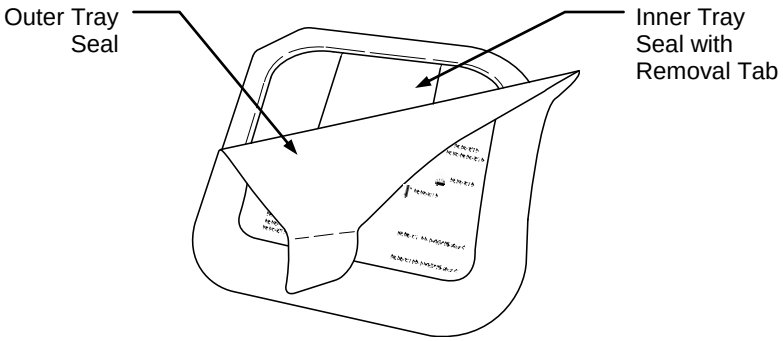
No resterilization. Angel Medical Systems has sterilized the IMD with ethylene oxide prior to shipment. Do not resterilize the device.

Single-use only. Do not re-implant an explanted IMD.

Temperature equilibration. After cold storage, allow the device to reach room temperature before programming or implanting the device. Cold storage temperatures may affect initial device function.

Use By date. Do not implant the device after the "Use By" date because battery longevity may be reduced.

Opening the Package. If the IMD passes its Pre-Implant Check inspection, which is discussed on page 23, you can remove it from its packaging. The package's outer tray can be opened in non-sterile surroundings. When opening the inner tray, you must observe standard sterile practices.



5 Precautions

General

Co-implantation: The AngelMed Guardian system is contraindicated in patients who have previously been implanted with a pacemaker or cardioverter-defibrillator. The AngelMed Guardian system is not designed to monitor electrograms in the presence of pacing signals generated by these devices.

The AngelMed Guardian system has not been evaluated for implantation with other electronic implantable medical devices.

Patient compliance: The AngelMed Guardian system should not be implanted in a patient in whom the physician lacks confidence in the ability or desire of the patient to understand and appropriately respond to the alerts and alarms from the device.

Lead: The IMD is intended for use only with the lead supplied by Angel Medical Systems (i.e., a standard IS-1, currently-marketed, active fixation, steroid eluding pacing lead).

Contraindications: The *Contraindications* section on page 4 lists additional precautions that are associated with the AngelMed Guardian system.

Implantation:

- The IMD is intended for subcutaneous implantation in a left pectoral pocket. Do not implant the IMD in any other location.
- For reliable data transmission, implant the device within 2 in (5 cm) of the surface of the skin.

- Implantation should not be attempted if venous access is inadequate to support placement of the endocardial lead in the apex of the right ventricle.
- The AngelMed Guardian system has not been evaluated for implantation in patients with non-sinus cardiac rhythm, 2nd and 3rd degree atrioventricular blocks, or right or left bundle-branch blocks.

Twiddler's Syndrome: Advise patients against manipulating the IMD since it may result in lead damage or lead displacement.

Adverse Environmental Conditions: Tell patients that they need to be mindful of the effects of adverse environmental conditions such as EMI and extreme temperatures. These topics are discussed in this manual as well as in the patient's manual.

Potential Adverse Effects

- Air embolism
- Bleeding
- Cardiac perforation
- Cardiac dissection
- Damage to the vessel at the catheter insertion site
- Device failure resulting in removal or replacement
- Erosion
- False positive ST shift alarm - device alarms when there is no clinically relevant ST shift
- Allergic reaction
- Body rejection phenomena including local tissue rejection
- Cardiac tamponade
- Chronic nerve damage
- Death
- Endocarditis
- Excessive fibrotic tissue growth
- Extrusion
- False negative ST shift alarm - risk of the device not detecting all ST shift events

- Formation of fibrotic tissue, local tissue reaction
- Fluid accumulation
- Induced ventricular ectopy
- Infection
- Keloid formation
- Lead migration/ dislodgment
- Myocardial irritability
- Nausea and vomiting
- Palpitations
- Pericardial rub
- Procedure related, random component failure
- Stroke (brain attack) from a clot being dislodged by the catheter
- Thrombosis
- Valve damage (particularly in fragile hearts)
- Venous perforation
- Ventricular fibrillation
- Formation of hematomas or cysts
- Ischemia
- Lead abrasion and discontinuity
- Loss of sensing due to dislodgement or mechanical malfunction of the lead
- Myocardial damage
- Pain in shoulder or arm
- Pericardial effusion
- Pneumothorax
- Shunting current or insulating myocardium during defibrillation with internal or external paddles
- Thromboemboli
- Vascular complications, which may require vessel repair
- Venous occlusion
- Vein wall rupture
- Visible bump at implant site, may cause discomfort under clothing (e.g.brassiere straps)

Medical Therapy Precautions

Note:
Therapies where electrical current passes through the body may interfere with IMD operation and cause it to alarm if there is no heart problem, or not alarm if there is a problem. At your discretion, you may advise your patients to visit your office so that you can temporarily disable IMD alarms if they need to undergo such therapy.
Alarms are temporarily disabled from the Programmer's *Edit Alarm Configuration* window. See the *AngelMed Guardian Programmer Application User's Manual* for more information.

Diathermy: Avoid diathermy. Diathermy may damage the IMD and injure the tissue near the implanted lead.

Electrosurgical cautery: Electrosurgical cautery may damage or interfere with the IMD. If electrocautery is necessary, keep the current path and ground plate as far away from the IMD and lead system as possible. Confirm IMD operation after treatment.

Electrical therapies: Any treatment that uses therapeutic levels of electricity, like electro-acupuncture or electro-muscle stimulation, may damage or interfere with your IMD. If electrical therapy is performed, medical personnel should keep the current path as far away from the IMD and lead system as possible. Confirm IMD operation after treatment.

External defibrillation: External defibrillation may damage the IMD and myocardium near the lead. Minimize current flowing through the IMD and lead system by observing the following:

- Position defibrillation paddles as far as possible from the IMD and lead system
- Use the lowest clinically appropriate energy output

Confirm IMD operation after treatment.

High radiation sources: Do not direct high radiation sources such as cobalt 60 or gamma radiation at the IMD. If a patient requires radiation therapy in the vicinity of the IMD,place lead shielding over the device to prevent radiation damage. After treatment, you should periodically verify IMD operation since damage from radiation may not be immediately detectable.

Lithotripsy: Lithotripsy may permanently damage the IMD if the focal point of the lithotripsy beam is focused directly on the implant site. Do not focus the focal point of the lithotripsy beam within 6 inches of the implant site.

Magnetic resonance imaging (MRI): Do not use MRI on patients who have an IMD. MRI may damage the device and injure the myocardium near the implanted lead.

Radiofrequency (RF) ablation: The effect of RF ablation on the IMD has not been evaluated. RF ablation may damage the IMD or cause it to malfunction. To minimize RF ablation risks:

- Temporarily turn off all alarms using the Programmer's *Edit Alarm Configuration* window. See the *AngelMed Guardian Programmer Application User's Manual* for instructions.
- Avoid direct contact between the ablation catheter and the IMD and lead.
- Position the ground plate so that the current pathway does not pass through or near the IMD and lead.
- After completing the procedure, turn the alarms back on.

Confirm IMD operation after treatment.

Transcutaneous Electrical Nerve Stimulation (TENS): TENS may interfere with device function. To reduce interference, place the TENS electrodes close to one another and as far as possible from the IMD and lead system. Confirm IMD operation after treatment.

Ultrasound therapy: Avoid exposing the IMD to therapeutic ultrasound because it can damage the device and harm the patient. If the patient needs ultrasound therapy, medical personnel should not direct the therapy at the IMD.

Electromagnetic Interference Precautions

The AngelMed Guardian system is protected against most sources of electromagnetic interference (EMI). However, sources of strong EMI can damage the IMD and EXD, and interfere with the wireless communication between them.

Sources of Strong EMI

Home appliances that are not in good working order.

High-voltage power lines.

Automobile ignition systems. Patients should not work under the hood of a car when the engine is running. Patients can, however, drive or be a passenger in a car.

Ignition systems of other internal combustion engines, like gasoline-powered lawn mowers and leaf blowers. It's generally safe to work around running internal combustion engines, but patients should limit their exposure to ignition-system parts.

Industrial equipment such as arc welders, large electro-magnets, induction furnaces, and very large or defective electric motors.

Small motor-driven appliances like hair dryers, electric shavers, power tools, radio transmitters, and transmitters for radio-controlled equipment or toys. Patients should not hold small motor-driven appliances closer than 6 inches from their IMD and/or EXD when the appliances are active.

Some medical equipment such as MRIs. See *Medical Therapy Precautions* on page 17 for further details.

Warning:
Patients should stay away from high-powered energy sources like MRIs and large industrial motors and generators. These energy sources can damage the IMD and injure the myocardium near the implanted lead. Do not enter any room with an active MRI machine. Stay at least 10 feet from other high powered energy sources such as large industrial motors and generators.

Warning:
Advise patients to be aware of any signage that warns those with pacemakers and other implanted devices to stay away. Such environments often have high-powered energy fields, which can interfere with the operation of the IMD.

Cell Phone Precautions

Cell phones emit EMI, but can safely be used with the AngelMed Guardian system provided that patients do the following:

- Hold the phone at least 6 in (15 cm) away from the IMD and EXD. If the cell phone transmits above 3 watts, patients should hold the phone at least 12 in (30 cm) away from the IMD and EXD.

  If the patient does not know the transmit power of the cell phone, the patient should assume that the cell phone transmits at the higher power and should hold the phone at least 12 in (30 cm) away from the IMD and EXD.

- Store the phone at least 6 in (15 cm) away from the IMD and EXD. This is important because some phones send signals when in the Listen or Standby mode.

- Patients should never carry the phone in a shirt or breast pocket, which would place the device over the IMD.

Anti-theft Systems

Anti-theft systems that are used in stores, libraries, and other places can interfere with the IMD and EXD if the patient stays within 2 feet of them. Patients should observe the following precautions.

- Pedestal systems are usually placed at store exits. Patients should walk past the pedestals at a normal pace and not linger.
- Tag deactivator systems are often used at stores and library checkout counters. Patients should stay at least 2 feet away from them while conducting business.
- Patients should not operate the checkout counter at a store or library where such systems are used.

Security Systems

Security systems such as those used in airports will probably not interfere with the IMD and EXD. Patients should walk through them at a normal pace, and not linger near them.

The IMD and EXD have metal parts that may set off an airport security system alarm. If this happens, the patient should show the Identification Card to the security officers. If they use a handheld wand to perform a search, the patient should ask them to work quickly and avoid holding the wand over the IMD.

Physical Activity Precautions

Patients should be advised to not engage in contact sports like football since the EXD, IMD, or lead may get damaged. Also, they should be encouraged to consult with you before doing strenuous or repetitive upper-body exercise like weight lifting or softball.

6 Implant and Setup Procedures

Proper surgical procedures and sterile techniques are the responsibility of the physician. The following procedures are provided for information only. Each physician must apply the information in these procedures according to professional medical training and experience.

Refer to the *AngelMed Guardian Programmer Application User's Manual* for detailed information about all of the implant and setup procedures performed using the Programmer. This *IMD User's Manual* provides only an outline of these procedures.

IMD implant and setup procedures include the following steps:

1. Conduct the Pre-Implant Check procedure.
2. Implant the lead.
3. Connect the lead to the IMD.
4. Implant the IMD.
5. Conduct the Implant Verification procedure.
6. Secure the IMD and close the incision.
7. Verify transdermal communication.
8. Conduct the Post-Implant Setup procedure.
9. Set an Appointment for Initial Programming.

1. Conduct the Pre-Implant Check Procedure

Note:
This procedure should be performed with the IMD in its sealed sterile tray.

Refer to the *Pre-Implant Check* chapter of the *AngelMed Guardian Programmer Application User's Manual* for detailed information about these procedures.

1. Create a new patient record in the Programmer and enter the relevant details in the *New Patient Record* window.

2. Select the new patient on the Main Programmer window.

3. With the IMD in its sealed sterile tray, establish a session between the Programmer and the IMD. The session may be established with the sterile tray still in the IMD's outer box.

   Warning:
   If you cannot establish a session between the Programmer and the IMD, do not implant the IMD. Obtain another IMD for implantation. Return the IMD to your AngelMed representative.

4. Select *Implant* → *Pre-Implant Check*.
   - The Programmer automatically populates the IMD serial number into the patient record (if it was not manually entered in Step 1).
   - Ensure the *Diagnostics* area of the *Pre-Implant Check* window indicates that the *IMD Diagnostics* have passed.

– Verify that the IMD *Battery Status* indicator is green (i.e., Good).

Warning:
If the Programmer's IMD *Battery Status* indicator is yellow (i.e., Low) or red (i.e., Replace), do not implant the IMD. Obtain another IMD for implantation. Return the IMD with the low battery to your AngelMed representative.

2. Implant the Lead

Warning:
To ensure the proper operation of the IMD, you should review the *Precautions* section on page 14 for information on the implant site.

Warning:
Ensure that an external defibrillator is immediately available.

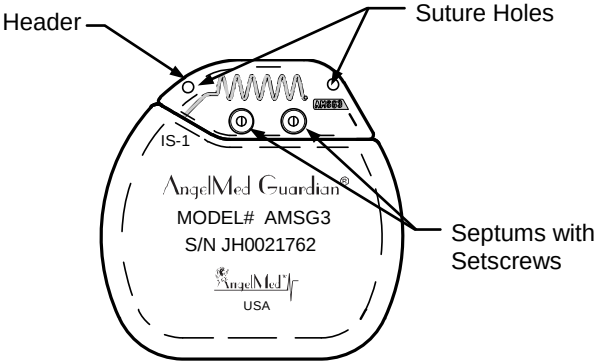
1. Implant the endocardial lead using standard lead implantation techniques, ensuring that the lead tip is actively fixated into the apex of the right ventricle. This location is necessary for proper functioning of the IMD.

2. Conduct both unipolar and bipolar lead testing to confirm proper placement and fixation. For detailed instructions, see the documentation that accompanies the endocardial lead.

Warning:
Improper lead placement may affect the AngelMed Guardian System's ability to function as intended.

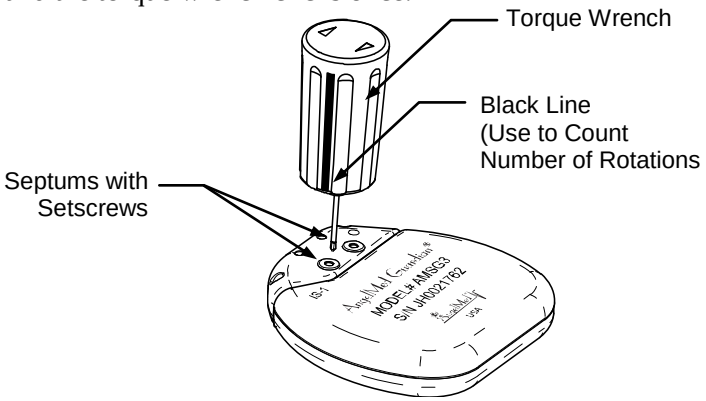
3. Connect the Lead to the IMD

In this procedure, use the supplied torque wrench to connect the lead to the IMD.



Caution:
Only use the torque wrench supplied with the IMD. This wrench is designed to prevent damage to the device from over-tightening a setscrew.

1. Insert the torque wrench through either of the IMD header septums and turn the corresponding setscrew clockwise until it stops and the torque wrench clicks once.



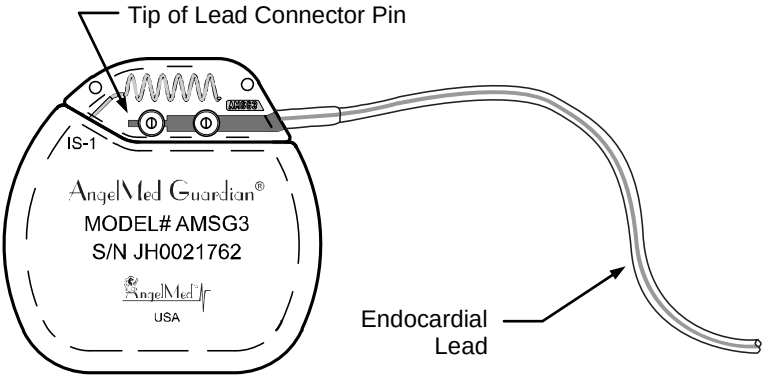
2. Observing the black line on the torque wrench handle, turn the same setscrew counterclockwise six full rotations to provide clearance for the lead connector pin.

3. Repeat Steps 1 and 2 for the other setscrew.

4. Wipe off any body fluids on the connector pin of the lead.

> **Note:**
> To facilitate insertion, sterile water may be used to lubricate the lead connector pin.

5. Insert the lead connector pin into the IMD header receptacle until the connector pin tip is fully seated inside the header. You can see the end of the connector pin through the header. Ensure that the end of the connector pin extends beyond the innermost setscrew and all the way to the end of the header cavity.



6. Insert the torque wrench through either IMD header septum and into a setscrew. Turn the setscrew clockwise until the torque wrench clicks once.

7. Repeat Step 6 for the other setscrew.

8. Test the connection by gently pulling on the header while holding the lead. If there is movement, loosen the setscrews and reinsert the lead as described in Steps 1 through 6.

4. Implant the IMD

1. Prepare a pocket subcutaneously or submuscularly in the left pectoral region. Ensure that the pocket will position the device header within 2 in (5 cm) of the surface of the skin.

2. Coil any excess lead length behind the IMD while inserting the IMD into the pocket. The IMD can be positioned with the etched label facing either toward or away from the skin surface; however, the IMD header should be proximal to the clavicle.

5. Conduct the Implant Verification Procedure

Note:
Detailed information for these procedures is provided in the *Implant Verification* chapter of the *AngelMed Guardian Programmer Application User's Manual*.

Prior to closing the incision, you need to ensure the IMD can sense the cardiac signal and can communicate with the Programmer through the skin. To do this, perform the following steps.

1. Open the patient's record in the Programmer.

2. Establish a communication session with the IMD. Since the IMD will be in the sterile field, hold the EXD inside a sterile bag (e.g., video camera drape) while establishing the session.

3. Select the *Retrieve Data* button on the Main Programmer window to retrieve data.

4. From the *Dataset Retrieval Amount* window, select *Minimum* for the quickest data retrieval.

5. After the data retrieval completes, select *Close* on the *Retrieve Implant Data* window.

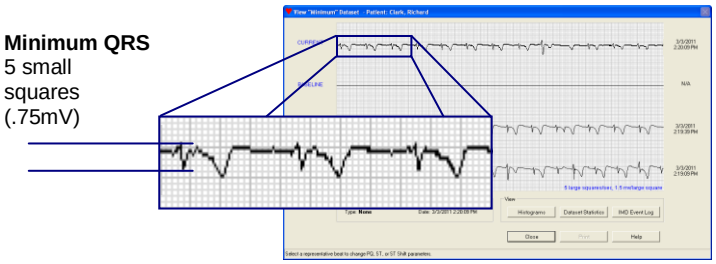
   Note:
   If the Programmer reports any dataset anomalies in the *Retrieve Implant Data* window, you should ignore them at this time.

6. From the Main Programming window, open the dataset that you just retrieved.

7. Look at the most recent segment, which appears along the top of the window, and check for the following:

a. The segment shows a continuous cardiac signal that has no gaps.

b. The signal's QRS complex is at least five small squares (0.75mV) in height. An example is shown in the following figure.

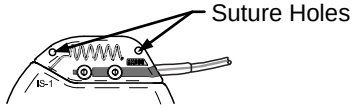


8. Do one of the following:

- If the Programmer shows a continuous cardiac signal with the proper minimum amplitude, proceed to the next step to close the incision.
- If the Programmer shows either no cardiac signal (i.e., flat line) or a cardiac signal that is not continuous:
  - Recheck the lead and IMD header connections. To obtain an adequate amplitude, you may need to reposition the lead tip.
  - Verify the IMD is making good contact with the surrounding tissue in the pocket.
  - Wait at least 30 seconds. Then retrieve and review the segments again. If you are still unable to obtain a continuous cardiac signal, exchange the IMD for another one and again verify the IMD senses the cardiac signal.

6. Secure the IMD and Close the Incision

1. To prevent migration, suture the IMD securely within the pocket, using the IMD suture holes.
2. Suture the pocket incision closed.



7. Verify Transdermal Communication

Establish a final communication session between the IMD and Programmer to ensure that you can communicate with the IMD through the skin.

1. Ensure the patient's record in the Programmer is open.
2. Establish a communication session with the IMD.
3. Select the *Retrieve Data* button on the Main Programmer window to retrieve data.
4. From the *Dataset Retrieval Amount* window, select *Minimum*.
5. After the data retrieval completes, select *Close* on the *Retrieve Implant Data* window.

> **Caution:**
> Under some circumstances, it is possible for the *Retrieve Implant Data* window to display some messages about anomalies being detected in the retrieved data. These messages are in red type. If they appear during this phase of Implant Verification, you can ignore them by selecting the *Defer Issues* button.

The data retrieval process verifies that you can communicate with the IMD through the skin. If you cannot retrieve the IMD data, contact your AngelMed representative.

8. Conduct the Post-Implant Setup Procedure

Post-Implant Setup typically occurs on the day following implantation because you need to provide sufficient time for the patient's heart signal to stabilize. Post-Implant Setup comprises two main tasks:

- Setting the IMD's signal gain
- Setting the heart rate bins

Setting the Signal Gain

1. Open the patient record in the Programmer.
2. Establish a communication session with the IMD.
3. Select the *Retrieve Data* button on the Main Programmer window to retrieve data.
4. From the *Dataset Retrieval Amount* window, select *Some* to retrieve all the hourly baselines plus the eight most recent electrograms.
5. After the data retrieval completes, check the status messages in the *Diagnostics* pane of the *Retrieve Implant Data* window. Expect to see:
   - *Number of baselines stored* – Check that the number of stored baselines roughly equals the number of hours since the implant.
   - *Patient's current heart rate* – Verify that the indicated heart rate matches the patient's actual heart rate
   - *Default Baseline R-Wave Height/ST Deviation* – Indicates the values used for the default baseline. No action on your part is required.
   - *Current Gain Setting* – Indicates the current IMD gain setting.

6. Do one of the following:

- If the gain setting is good (*Current Gain setting is OK*.), select either *Defer Issues* or *Close* (whichever is available) and then proceed to *Setting the Heart Rate Bins* on page 33.
- If the gain setting requires adjusting (*Current Gain setting is too High/Low and should be adjusted*.), select *Address Issues* and continue to the next step.

7. From the *Gain Check* window, select the *Adjust Gain* button.

8. Observe the progress bar in the *Evaluating Gain Change* window.

9. When the progress bar completes, re-establish a communication session with the IMD and select *OK*.

10. Again, check the gain status in the *Gain Check* window and perform Step 6 in this procedure.

> **Note:**
> Depending on the magnitude of the heart signal, the Programmer may need more than one opportunity to adjust the gain setting.

> **Note:**
> It is possible for the gain setting to be at its limit and still report that the gain is either too high or low. If this condition occurs, the Programmer will display an explanatory message and you should contact your AngelMed representative for assistance.

11. Continue with the next task, *Setting the Heart Rate Bins*.

Setting the Heart Rate Bins

1. Retrieve data by selecting the *Retrieve Data* button on the Main Programmer window.
2. From the *Dataset Retrieval Amount* window, select *Minimum* for the fastest retrieval.
3. After the data retrieval completes, close the window by selecting the *Close*, *Defer Issues*, or *Address Issues* button. The retrieved data are automatically saved to the Programmer.
4. From the Main Programmer window, open the *None* dataset that you just retrieved.
5. From the *View Minimum Dataset* window, select any beat from the first, third, or fourth segments.
6. From the *Edit Implant Parameters* window, review the Low, Normal, and High heart rate bin current settings and change them if appropriate.
7. Save the new settings by selecting the *Save* button. (If you have elected to keep the original settings, select *Cancel* and then go to Step 12.)
8. The Programmer may display the *Select Data to Clear* window. If it does, leave all items checked and select *OK*.

> **Note:**
> Leave all items checked on the *Select Data to Clear* window unless instructed otherwise by an AngelMed representative.

9. The Programmer saves the heart rate parameter settings to the patient's IMD.
10. Re-establish a communication session with the patient's IMD.

11. Retrieve IMD data again by selecting Retrie*ve Data* from the Main Programmer window, using the *Minimum* retrieval option.

> **Note:**
> You should always perform a data retrieval when you change any IMD parameter. Doing so ensures that the Programmer has a dataset that contains the most recent parameter values.

12. The Post-Implant Setup process has concluded. Be sure to complete the *AngelMed Guardian IMD Patient Information Card* and review its contents with the patient. Tell him or her to keep it close by at all times in a convenient place, such as a wallet.

9. Set an Appointment for Initial Programming

Establish a time for the patient to return for Initial IMD Programming. Initial Programming sets most of the IMD's operating parameters and is conducted about 7 to 14 days after Post-Implant Setup. (For further details, see the *AngelMed Guardian Programmer Application User's Manual*.)

7 Patient Follow-up

Follow-up Frequency

Patients should be seen for follow-up at 1, 3, 6, and 12 months after the implant, and every 6 months thereafter.

Follow-up Tasks

During follow-up visits, physicians should:

- Check IMD battery status.
- Retrieve and review stored electrograms.
- Confirm that IMD parameters are set appropriately and modify them if necessary.
- Replace the patient's EXD battery every 6 months if the patient has not already done so.
- Confirm the IMD vibration settings are still appropriate
- Review key instructions with the patient. For example:
  - Responding to Emergency alarms and See Doctor alerts
  - Checking EXD battery power
  - Ensuring the patient has their ID card and knows where their Patient Manual is.

For details on these procedures, see the *AngelMed Guardian Programmer Application User's Manual*.

8 Explant Procedure

After about 3.2 years (typical use), the IMD sets the elective replacement indicator (ERI) flag, indicating a low battery. When the ERI flag is set, the IMD issues a See Doctor alert to the patient. At this time, the patient must be scheduled to have his or her IMD replaced within a month's time. (For additional details on the ERI flag, see page 48.) You can also determine IMD battery status any time you retrieve IMD data. The battery status is reported by the *Retrieve Implant Data* window on the Programmer.

The IMD should also be explanted after the death of a patient.

Warning:
In the event of patient death, the IMD must be explanted for either or both of the following reasons.

- Some jurisdictions require that battery-operated devices be explanted due to environmental concerns.
- IMDs contain sealed chemical power cells and capacitors that may explode if incinerated.

Before you Begin

Ensure that you have the required tools and replacement devices before starting the procedure.

If replacing an IMD, verify that you have a:

- Replacement IMD (sterile torque wrench supplied in package)
- Programmer to retrieve data from the old IMD and program the replacement IMD

If explanting an IMD without replacing it, verify that you have a:

- Sterile torque or hex wrench to loosen the connector screw that secures the lead to the IMD
- Lead cap to cover the proximal end of the lead (if the lead is to be abandoned)
- Programmer to retrieve data from the old IMD

Explanting the IMD

This section describes how to:

- Replace a Model AMSG3 IMD with another Model AMSG3 IMD
- Replace a Model AG101 IMD with a Model AMSG3 IMD
- Explant and not replace a Model AMSG3 IMD

For additional information on the Model AG101 IMD, see the *AngelMed Guardian® Implantable Medical Device (IMD) Model AG101 User's Guide*.

To replace an IMD, perform the following procedure in its entirety.

To explant an IMD without replacing it, you need only complete Steps 4 through 9.

Always return any explanted device(s) as discussed in *After Explanting the IMD* on page 44.

1. Prior to the date of explantation, contact Angel Medical Systems and identify the serial number of the IMD that you intend to replace. Angel Medical Systems uses this information to determine if any internal parameters have been set for the patient. If they have, an AngelMed representative will arrange to set these parameters in the replacement IMD.

2. On the date of explantation, create another patient record and conduct a Pre-Implant Check on the replacement IMD to prepare it for use.

> **Note:**
> When creating another patient record, the Programmer does not allow you to use the same first name-middle initial-surname combination. You will need to add one or more characters to make the name combination unique. For example, add -2 to the surname (e.g., Meyer-2). You will also need to specify a different patient ID.

Instructions for this step are provided in *Conduct the Pre-Implant Check Procedure* on page 23.

3. Leave the properly working replacement IMD in its sterile packaging and set it aside for now.

4. Retrieve data from the IMD using the following instructions:

a. From the Programmer, open the patient's original patient record and establish a communication session with the implanted IMD.

b. From the Main Programmer window, select the *Retrieve Data* button.

c. Select *All* on the *Dataset Retrieval Amount* dialog box.

d. When the data have been retrieved, select either *Close* or *Defer Issues* on the *Retrieve Implant Data* window.

5. Record the IMD parameter settings using the following instructions:

a. Open a communication session with the IMD and record the following parameter values from the associated windows (in parentheses). These values need to be returned with the explanted device. They are also needed for programming the replacement IMD as described in Step 12. Use the provided tables to record the values.

- IMD Vibration settings (*Alarm Tests*)

Event	Low	Med	High
Emergency Alarm			
See Doctor Alert			

- Alarm mappings (*Edit Alarm Configuration*)

Event	Emer-gency	See Dr	None	Ignore
Positive ST Shift & Non-Elevated HR				
Negative ST Shift & Non-Elevated HR				
ST Shift & Elevated HR				
ST Shift & Elevated HR Persists				
High Heart Rate				
Low Heart Rate				
Irregular Heart Rate				
Flat Line				
Not Enough Beats				
Cannot Get Baseline				
ST Deviation Trending				

b. Open the dataset that you retrieved and record the following parameter values from the associated windows.

- Heart rate bin settings (*Edit Implant Parameters*)
  Low _____bpm
  Normal _____bpm
  High _____bpm
- PQ/ST Start and Duration values for Normal heart rate bin only (*Edit Implant Parameters*)

Heart Rate Bin	Start (ms)	Duration (ms)
Normal bin, PQ segment		
Normal bin, ST segment		

6. Turn off alarms on the IMD to be explanted or replaced using the following instructions:

a. From the Main Programmer window, select *Implant* → *Alarm Configuration*.

b. From the *Edit Alarm Configuration* window, set all *Events* to *Ignore* and then select *Save* to save your changes. Doing so ensures the IMD will not signal an alarm or alert when it detects an event. (Because the IMD will not be connected to the endocardial lead once it is explanted, events such as Flat Line will occur.)

7. Verify that a sterile torque or hex wrench is available, so that you can loosen the required setscrews.

Note:
A sterile torque wrench is provided in the replacement IMD packaging, but is also available separately from AngelMed.

8. Dissect the IMD and coiled lead from the surgical pocket, taking care not to damage the lead insulation.

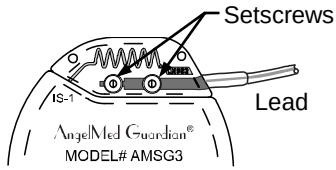
9. Do one of the following:

– **If you are replacing a Model AMSG3 IMD with another Model AMSG3 IMD:**

> **Warning:**
> Do not twist the lead when disconnecting it from the IMD header. Doing so may rotate the lead's connector pin and helix.

a. Loosen the two setscrews in the IMD header.

b. Withdraw the lead from the header.



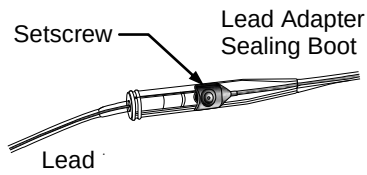
c. Set the IMD aside for now so that it can be later returned to Angel Medical Systems. Then proceed to Step 10.

– **If you are replacing a Model AG101 IMD with a Model AMSG3 IMD:**

> **Warning:**
> Do not twist the lead or lead adapter when disconnecting them. Doing so may rotate the lead's connector pin and helix.

a. Loosen the setscrew in the lead adapter sealing boot.

b. Withdraw the lead from the lead adapter sealing boot.



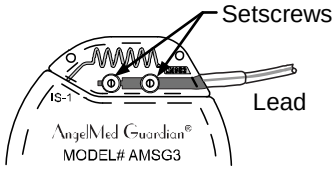
c. Set the IMD and lead adapter aside for now so that they can be later returned to Angel Medical Systems. (The AMSG3 IMD does not use a lead adapter.) Then proceed to Step 10.

– **If you are explanting and not replacing a Model AMSG3 IMD:**

> **Warning:**
> Do not twist the lead when disconnecting it. Doing so may rotate the lead's connector pin and helix.

a. Loosen the two setscrews in the IMD header.

b. Withdraw the lead from the header.



c. Set the IMD aside for now so that it can be later returned to Angel Medical Systems.

d. Cap the lead and secure with sutures.

> **Warning:**
> To prevent patient injury, cap any abandoned lead and secure the lead caps with sutures to prevent unwanted transmission of electrical signals from the electrode to the heart. Seal the remaining open end of any severed lead with medical adhesive and a lead cap. Suture the remnant to adjacent tissue using heavy, non-absorbable suture to prevent migration of the lead fragment.

e. Suture the pocket incision closed.

f. Skip the remaining steps and proceed to *After Explanting the IMD* on page 44.

10. Inspect the connector pin on the lead and verify that it is free from corrosion or other physical damage.

> **Caution:**
> To ensure a proper connection between the lead and replacement IMD, clear the connector pin of any bodily fluids or tissue.

11. Finish the implantation by completing the following steps. These steps are the same as those for initial implantation and appear on pages 25 through 31.

- **a.** Attach the lead to the header of the replacement IMD. (See *Connect the Lead to the IMD*, page 25.)
- **b.** Place the new IMD and lead into the surgical pocket. (See *Implant the IMD*, page 27.)
- **c.** Using the Programmer, conduct the Implant Verification procedure for the replacement IMD. (See *Conduct the Implant Verification Procedure*, page 28.)
- **d.** Suture the IMD securely within the pocket and close the incision. (See *Secure the IMD and Close the Incision*, page 30.)
- **e.** Verify that you can still communicate with the IMD through the skin. (See *Verify Transdermal Communication*, page 30.)
- **f.** Conduct a Post-Implant Setup. (See *Conduct the Post-Implant Setup Procedure*, page 31.) Note that because you are leaving the original lead in place, you can perform this procedure anytime after re-implantation. You do not have to wait until the following day, although you may if you wish.

12. Enter the IMD parameter values of the original IMD into the replacement IMD. Refer to the values that you recorded in Step 5 starting on page 39. For assistance on entering the parameter values into the IMD, see the *Initial Programming* chapter of the *AngelMed Guardian Programmer Application User's Manual*.

13. Perform Initial Programming on the replacement IMD for long-term operation. (If necessary, see the *AngelMed Guardian Programmer Application User's Manual* for details on Initial Programming procedures.)

After Explanting the IMD

- Clean all explanted devices with disinfectant solution, but do not submerge the IMD. Fluid in the IMD header receptacle can impede analysis of the device.
- Return the explanted device(s) using the Product Return Kit. (Your AngelMed representative can provide the Product Return Kit if you do not have one.)
- When returning an IMD, please include a record of the IMD's Programmer settings that you recorded in Step 5.

9 Service and Support

Service

If the IMD does not operate correctly, contact your AngelMed representative.

Technical Support

For technical support, contact your AngelMed representative or Angel Medical Systems.

Angel Medical Systems, Inc.
788 Shrewsbury Ave., Suite 2200
Tinton Falls,, NJ 07724 USA
Phone: +1 800 508-5206 (USA toll-free)
+1 561 962-2191

10 IMD Specifications

Physical & Mechanical Specifications

Item	Specification
Dimensions Height (Vertical) Width (Horizontal) Depth	 2.10 in (53 mm) 2.13 in (54 mm) 0.40 in (10 mm)
Weight	1.1 oz (32 grams)
Volume	23.4 cm3
Drop Limit Packaged IMD Unpackaged IMD	 3 ft (0.9 m) 30 cm (12 in)
Lead Compatibility	Angel Medical Systems-supplied endocardial pacing lead
Materials in contact with human tissue Can Header Septum	 Titanium Tecothane® polyurethane resin* Silicone

* Tecothane is a registered trademark of Lubrizol Corporation.

Environmental Specifications

Item	Specification
Operating Conditions Temperature Humidity Atmospheric pressure	 77°F to 113°F (25°C to 45°C) N/A 10.20 psi to 15.58 psi (703 hPa to 1074 hPa)
Storage Conditions Temperature Humidity Atmospheric pressure	 14°F to 131°F (-10°C to +55°C) N/A 7.35 psi to 15.58 psi (507 hPa to 1074 hPa)

Battery Type and Longevity Specifications

Item	Specification
Battery Type	3.6V lithium thionyl chloride
Manufacturer	EaglePicher
Model	LTC-15MC-S7
Voltage$_{\text{(Beginning of Life(BOL))}}$	3.6V
Voltage $_{\text{(ERI)}}$	3.4V
Voltage $_{\text{(EOS)}}$	3.0V
Capacity (BOL to EOS)	1463mAh
Battery Longevity	3.2 years, assuming nominal program parameters and typical use

Device Longevity

There are three activities that affect the expected longevity of the IMD:

- Normal data collection and analysis
- Generating vibrations when alarms and alerts are detected
- Communicating with the Programmer

Battery capacity is constantly used to perform normal data collection and analysis. The rate of consumption is low, but somewhat variable, depending primarily on how often a patient's electrocardiogram is normal.

By contrast, battery capacity is used at a relatively high rate when the device is vibrating, but the device is expected to vibrate for a small percentage of time. Similarly, when communicating with the Programmer, the IMD uses battery capacity at a relatively high rate on an infrequent basis.

The IMD monitors its battery voltage and also maintains an estimate of cumulative battery capacity usage. Depending on these parameters, the IMD sets the following service flags:

- Elective replacement indicator (ERI) flag
- End of service (EOS) flag

ERI Flag

When the elective replacement indicator (ERI) flag is set, the IMD issues a See Doctor alert. The ERI flag is activated if the battery voltage falls below 3.4V, in which case the estimated time remaining before EOS is usually 30 days, but can range from 14 to 70 days.

EOS Flag

The end of service (EOS) flag is set if either the battery voltage falls below 3.0V or the estimated battery capacity has been used. The IMD does not operate when battery voltage is less than 3.0V.

11 Programmable Parameters: Defaults and Ranges

Programmable IMD parameters are set from the Programmer. The following tables show the possible ranges for these parameters and their default values where applicable.

Edit Implant Parameters Window

HR-Max (BPM)

Heart Rate Bin	Min	Max	Default
Elevated (A4)	110	220	160
Elevated (A3)	90	190	140
Elevated (A2)	70	160	125
Elevated (A1)	55	130	110
Normal (A0)	40	115	100
Low (LO)	25	95	50

Start of PQ (ms)

Heart Rate Bin	Min	Max	Default
Elevated (A4)	70	200	75
Elevated (A3)	70	200	85
Elevated (A2)	70	200	95
Elevated (A1)	70	200	105
Normal (A0)	70	200	150

Note: Start of PQ ≥ (Duration of PQ + 30)

Duration of PQ (ms)

Heart Rate Bin	Min	Max	Default
Elevated (A4)	40	90	40
Elevated (A3)	40	90	45
Elevated (A2)	40	90	50
Elevated (A1)	40	90	55
Normal (A0)	40	90	80

Note: Duration of PQ ≤ (Start of PQ – 30)

Start of ST (ms)

Heart Rate Bin	Min	Max	Default
Elevated (A4)	40	160	40
Elevated (A3)	40	160	45
Elevated (A2)	40	160	50
Elevated (A1)	40	160	55
Normal (A0)	40	160	80

Note: Start of ST ≤ (200 – Duration of ST)

Duration of ST (ms)

Heart Rate Bin	Min	Max	Default
Elevated (A4)	40	90	55
Elevated (A3)	40	90	60
Elevated (A2)	40	90	65
Elevated (A1)	40	90	70
Normal (A0)	40	90	80

Note: Duration of ST ≤ (200 – Start of ST)

ST-Pct Positive/Negative (ST Shift Thresholds) (%)

Heart Rate Bin	Min	Max	Default
Elevated (A4)	0	127	100
Elevated (A3)	0	127	100
Elevated (A2)	0	127	100
Elevated (A1)	0	127	100
Normal (A0)	0	127	100

Lo HR Decrement (BPM)

Min	Max	Default
0	7	5

ST Trends Histogram Window

Parameter	Min	Max	Default
Moving Average Size (Days)	1	14	7
Check Hour*****	0	23	9
Ignore Data Older Than (Days Ago)	1	192	192
Detection Threshold	10	50	20

*****Hour of the day.

Alarm Tests Window (Vibration Settings)

Parameter	Min	Max	Default
Emergency Alarm Test	Low	High	Low
See Doctor Alert Test	Low	High	Low

Alarm Configuration Window

Time Interval Parameters

Parameter	Min	Max	Default
ST Shift and Elevated HR becomes persistent after (minutes)	3	20	10
Alarms and alerts will be enabled in (days) *	Now	7	Never**

* Now means immediately or upon re-entering normal data acquisition mode

** The Programmer automatically changes this parameter to Now at Initial Programming. The value Never disables alarming and can only be set by an AngelMed representative.

Alarm Type Association (Recommended Settings)

Event	Emergency	See Dr	None	Ignore
Positive ST Shift & Non-Elevated HR	**X**		*	
Negative ST Shift & Non-Elevated HR **	**X**		*	
ST Shift & Elevated HR	N/A	**X**	*	
ST Shift & Elevated HR Persists	**X**		*	
High Heart Rate	**X**		*	
Low Heart Rate		**X**	*	
Irregular Heart Rate		**X**	*	
Flat Line	**X**			*
Not Enough Beats	N/A	**X**		*
Cannot Get Baseline	N/A	**X**	*	
ST Deviation Trending	N/A	**X**	*	

* Denotes the factory setting of each event. (X is the recommended setting.)

**If detected while the patient's heart rate is decreasing, the IMD automatically reclassifies the event as a Recovery event, which is internally mapped as a See Doctor alert.

A. Clinical Investigations

There have been six human clinical studies related to the AngelMed Guardian system was developed to provide patient alerting for ischemia and heart rate related cardiac events. These are:

- A Proof of Concept Study [1]
- A First-in-Man Study in Brazil (CARDIOSAVER) [3-6]
- A US IDE Safety Study (DETECT) [3-4]
- A Prospective Randomized Pivotal IDE Study (ALERTS)
- An **A**LERTS **Q**uality **o**f **L**ife (AQOL) sub-study

Proof of Concept Study (2001) [1]

The first study in humans used a temporary pacemaker lead to measure RV apical voltage (referenced to left pectoral region) during a two-minute occlusion obtained during scheduled balloon angioplasty of 17 lesions in 14 subjects (who were receiving the angioplasty for clinical reasons).

CARDIOSAVER [3-6]

In 2005, based on successful GLP animal results, AngelMed initiated the CARDIOSAVER study in collaboration with the Dante Pazzanese Hospital of Cardiology in Sao Paulo, Brazil. The CARDIOSAVER study was designed to better understand the proper functioning of the AngelMed Guardian system as it responds to an occlusion of a human coronary artery. The study included 20 subjects at high risk for heart attack, with the added indications that each had:

1. demonstrated ischemia on an exercise stress test and
2. an angiogram showing a stenosed coronary artery and

3. a clinical indication for angioplasty and/or stenting.

The Guardian was implanted in these subjects with initial device programming performed shortly thereafter. Some of the subjects then underwent a repeat stress test with both intracardiac and surface ECG recordings used to assess ST segment changes with elevated heart rate. Next, each subject underwent PCI. The PCI procedures included balloon occlusion of the target artery. These occlusions lasted up to three minutes in order to provide intracardiac recording of ST segment changes associated with the resultant ischemia evoked by the balloon occlusion of the coronary artery. In addition to this proof of concept, a number of significant improvements in the device and algorithm were made following the lessons learned in CARDIOSAVER.

DETECT [3-4]

In late 2006, AngelMed submitted an IDE (G060259) to the FDA requesting approval to begin a US based 20 subject safety study (the DETECT Clinical Study) with two primary objectives:

- Show that the AngelMed Guardian maintains a high safety profile when implanted in US patients
- Demonstrate that the Autopick function in the Physician Programmer would provide a reliable means for objectively selecting ST shift ischemia detection thresholds based upon statistical measures of each subject's normal daily range of ST segment variability

The DETECT study met its objective, demonstrating that the Autopick function provided greater specificity regarding ST shift detections.

The inclusion and exclusion criteria for the US DETECT study were different from those used in Brazilian CARDIOSAVER study. The DETECT subjects were survivors of a prior ACS event or bypass with additional risk factors that increased their probability of having a heart attack. DETECT was successful in showing that the IMDs could be implanted successfully and safely. Results from the DETECT and CARDIOSAVER studies provided the basis for the design of the ALERTS randomized prospective pivotal study with enrollment of 1020 subjects, conducted between 2008 and 2013. Multiple articles have been published describing the results from the CARDIOSAVER and DETECT studies in terms of the Guardian's ability to detect ST changes from coronary blockages including thrombotic occlusions from ruptured plaques.

ALERTS

ALERTS Clinical Study Design

Angel Medical Systems conducted the ALERTS clinical study to establish a reasonable assurance of safety and effectiveness of the AngelMed Guardian System to monitor a patient's intracardiac electrogram for ST segment shifts indicating coronary ischemia in the US (under IDE # G060259). The following two major analyses of data collected from ALERTS study patients were presented to FDA and are summarized below.

I. A pre-specified, randomized analysis; and
II. A post-hoc analysis of study subject ED visits (termed "additional analysis of ALERTS ED visits")

A. ALERTS Study Design

Randomized Analysis

The ALERTS Clinical Study was a Bayesian adaptive, randomized controlled trial. Patients in the ALARMS ON group had the device's alerts enabled while patients in the ALARMS OFF group had those alerts disabled initially.

A total of 1020 subjects were enrolled in the ALERTS Clinical Study with 910 subjects actually implanted and 907 subjects both implanted and randomized (1:1) into ALARMS ON (Treatment) and ALARMS OFF (Control) groups. Patients in both groups were implanted with a Guardian System device and those in the ALARMS ON group had the Guardian alarms activated at the time of randomization (7-14 days post implantation) while those in the ALARMS OFF group had their alarms deactivated and devices placed in a monitoring mode for the first six months for randomized comparison between the two groups. After the six-month randomized period the alarms in all trial devices were activated and patients were followed per IDE protocol.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the ALERTS study was limited to patients who met the following inclusion criteria:

a. Advanced multi-vessel Cardiac Disease
b. An index ACS event (e.g., Myocardial Infarction (MI), Unstable Angina or Coronary Artery Bypass Graft (CABG) within six months of enrollment)
c. Additional risk factors/co-morbidities (diabetes, TIMI risk score≥3, or renal insufficiency).
d. Lives in a geographic area in close proximity (within 60 minutes by EMS) to any hospital that can treat AMI.
e. Greater than 21 years of age.

f. Women of childbearing age must have a negative pregnancy test or confirmation of one of the following:
    i. Post-menopausal or amenorrheic during the past year
    ii. Surgical sterilization
    iii. Use of effective contraceptive method

Patients were not permitted to enroll in the ALERTS study if they met any of the following exclusion criteria:

a. In the investigator's opinion, subject lacks ability to respond appropriately to alarms, e.g., illiteracy, poor memory or cognitive function, dementia or other condition affecting memory function, etc.
b. There is known compromised tissue at the site of lead implantation in the apex of the right ventricle, e.g., prior infarct affecting the RV apex location.
c. A permanent pacemaker or ICD is already in place or the patient is indicated for ICD or pacemaker implantation based on the guidelines published by the American College of Cardiology as Class I and IIa recommendations. Class IIb recommendations are at the investigator's discretion.
d. Subject cannot feel the IMD vibration when placed on top of the skin on the left pectoral side of the chest.
e. Subject has recurrent or persistent atrial fibrillation.
f. Subject has recurrent or persistent non-sinus cardiac rhythm, second or third degree atrioventricular blocks, QRS duration greater than 120 msec, Benign Early Repolarization (BER), or Brugada Syndrome.
g. Subject has left ventricular hypertrophy evidenced by ECG criteria.
h. Subject has any condition preventing the subcutaneous implantation of the Guardian System in a left pectoral pouch, such as: superior vena cava thrombosis, subcutaneous tissue deemed inappropriate for the procedure or prior central venous access via portacath, Hickman, Groshong, or similar placed in a left pectoral location or left side PICC line.

i. Subject has extremely heavy alcohol consumption (participates in binge drinking that leads to alcohol intoxication) or has history of alcohol or illicit drug abuse within past 5 years.
j. There is evidence of unresolved infection (fever > 38^{o} C and/or leukocytosis > 15,000).
k. Subject has history of bleeding disorders or severe coagulopathy (platelets < 100,000 plts/ml; APTT or PT > 1.3 x reference range).
l. Subject has had a hemorrhagic stroke or transient ischemic attack (TIA) in the past 6 months.
m. Subject has other severe diseases, such as cancer or refractory congestive heart failure, associated with limitation of life expectancy (less than 1 year), which may lead to inadequate compliance to the protocol or confusing data interpretation.
n. Subject has clinical conditions such as heart diseases, difficult-to-control blood pressure, difficult-to-control insulin-dependent diabetes or serious prior infections attributed to the diabetes, or others that, at the investigator's discretion, could seriously affect the subject's current clinical condition during study procedures.
o. Subject has previous participation in the DETECT Study, current participation or previous participation in another drug or device study in the past 30 days that conflicts with this study as determined by the study sponsor.
p. Subject has experienced gastro-intestinal hemorrhage in the past 6 months.
q. Subject has any situation in which the use of aspirin is contraindicated for at least 6 months.
r. Subject has epilepsy.
s. Subject has known severe allergies, e.g., peanut, bee sting, etc.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 7-14 days and 1, 3 and 6 months and every 6 months after that postoperatively. It should be noted that the effectiveness evaluation for the additional analysis of ALERTS ED visits does not rely on data from scheduled visits but only on adjudication of emergent visits in the ED.

Preoperatively, all patients were seen in clinic and a baseline 12-lead ECG was taken. Postoperatively, the objective parameters measured during the study included any ACS standard of care testing that was performed during an emergent ED visit. Adverse events and complications were recorded at all pre-specified follow-up examinations noted above.

3. Clinical Endpoints

The following were the primary endpoints for the ALERTS Clinical Study:

3.1 Primary Safety Endpoint

- Proportion of subjects free from system-related complications is greater than 90%.

3.2 Composite Primary Effectiveness Endpoint (ALARM ON < ALARM OFF)

- Cardiac/Unexplained Death
- New Q-Wave MI (QWMI)
- Late Arrival – Time-to-door (time between device alarm and medical presentation) > 2 Hours for an ACS Event (confirmed by ECG, Stress test, Angiogram, or Enzymes)

Additional Analysis of ALERTS ED Visits

After presentation to the Advisory Panel, FDA engaged AngelMed to create an additional analysis of ALERTS ED visits that would include events in ALERTS patients from both the randomized and non-randomized period of the trial. This additional clinical analysis of ALERTS ED visits as a retrospective analysis of all ED visits for study patients that met specific criteria from the entirety of the follow up period from the ALERTS study; therefore, the additional analysis of ALERTS ED visits included data that were collected

outside the pre-specified original randomization period and thus were not reviewed by, or presented to, the Advisory Committee. The additional clinical analysis of Alerts ED visits compares device functionality related to Emergency Department (ED) visits for patients whose device alarm initiated (with or without symptoms) the visit (ALARMS ON), shown in the green below, and patients whose device alarms were inactive and whom presented due to symptoms alone (ALARMS OFF), shown in blue below. For a study subject's ED visit to be included in the analysis at least one standard of care test for ACS had to have been performed on the study subject. It was not necessary for an ED visit in the ALARMS OFF group to have been initiated by symptoms typically associated with cardiac events to be included in the analysis.

Figure 1: ALERTS Trial (Original and New Clinical Analysis) Diagram

The figure shows how the assignment of the Control and Treatment groups during the 6-month randomization period relates to the ALARMS OFF and ALARMS ON groups used by the additional analysis of ALERTS ED visits protocol. In the post-randomization period the Control group patients were re-categorized into the ALARMS ON group.

The ALARMS ON patients represent the treatment group for this new clinical analysis and were compared using frequentist statistics to the ALARMS OFF patients which represent the control group for both Positive Predictive Value (PPV) and False Positive Rate (FPR).

Each ED visit was evaluated by an independent Clinical Events Committee (CEC) based on pre-specified criteria and adjudicated as either an ACS event or a false positive presentation to the ED.

The database for the additional analysis of ALERTS ED visits to support the PMA data was collected through May 2016 and included the 907 implanted and randomized patients.

1. Clinical Inclusion and Exclusion Criteria

The Inclusion and Exclusion Criteria did not change from the randomized analysis. See above.

2. Follow-up Schedule

All patients that were included in the additional analysis of ALERTS ED visits followed the follow-up schedule noted for the pre-specified ALERTS study noted above. This new clinical analysis focused on data collected during emergent visits to the ED rather than on data collected during regularly scheduled follow-up visits that occurred every 6 months.

3. Clinical Endpoints

With regards to safety, complication rates (system-related, replacement-related, and explant-related complication rates) and mortality (all cause and cardiac death) were collected for the entire ALERTS study follow up period independent of randomized group. No formal statistical tests were performed on the collected safety data.

With regards to effectiveness, the co-primary endpoints were Positive Predictive Value (PPV) and False Positive Rate (FPR) analyzed as follows:

a. PPV – Superiority

H_O: $PPV_{Alarm\ ON} \leq PPV_{Alarm\ OFF}$

H_A: $PPV_{Alarm\ ON} > PPV_{Alarm\ OFF}$

b. FPR – Non-Inferiority

H_O: $\beta \geq 1.50$

H_A: $\beta < 1.50$

Where β is a regression coefficient used to approximate

$$\frac{FPR(Alarm\ ON)}{FPR(Alarm\ OFF)}$$

B. <u>Accountability of PMA Cohort</u>

At the time of database lock, of 1020 patients enrolled in the PMA study, 88.9% (907) patients were available for analysis. Figure 2 and 3 below depicts the accountability of patients throughout the follow up of the ALERTS study.

Figure 2: Patient Accountability during Randomized Period of the ALERTS Study/Original Follow-up

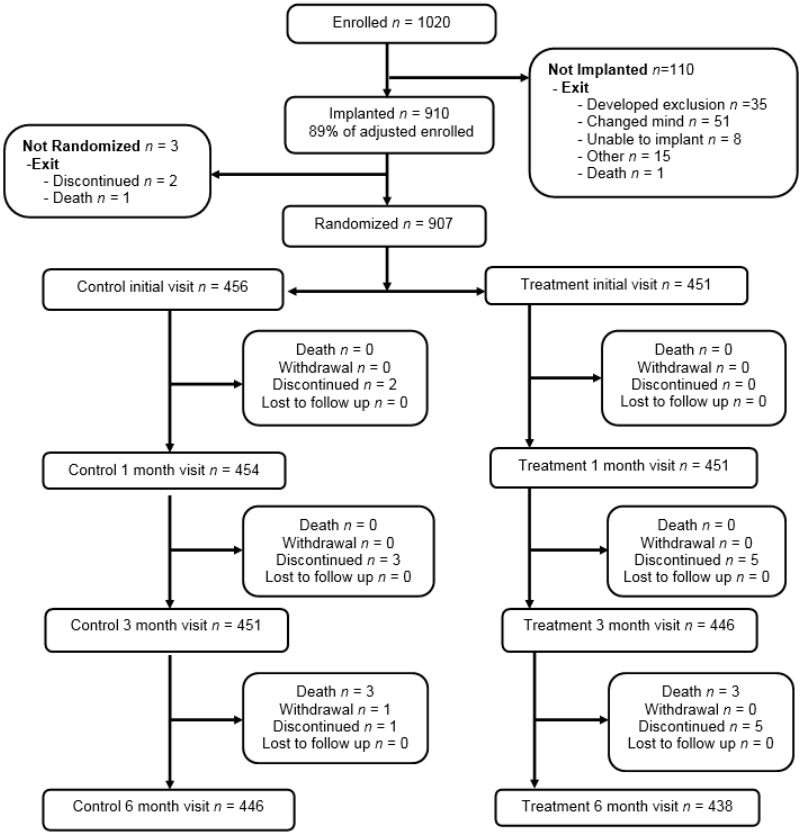
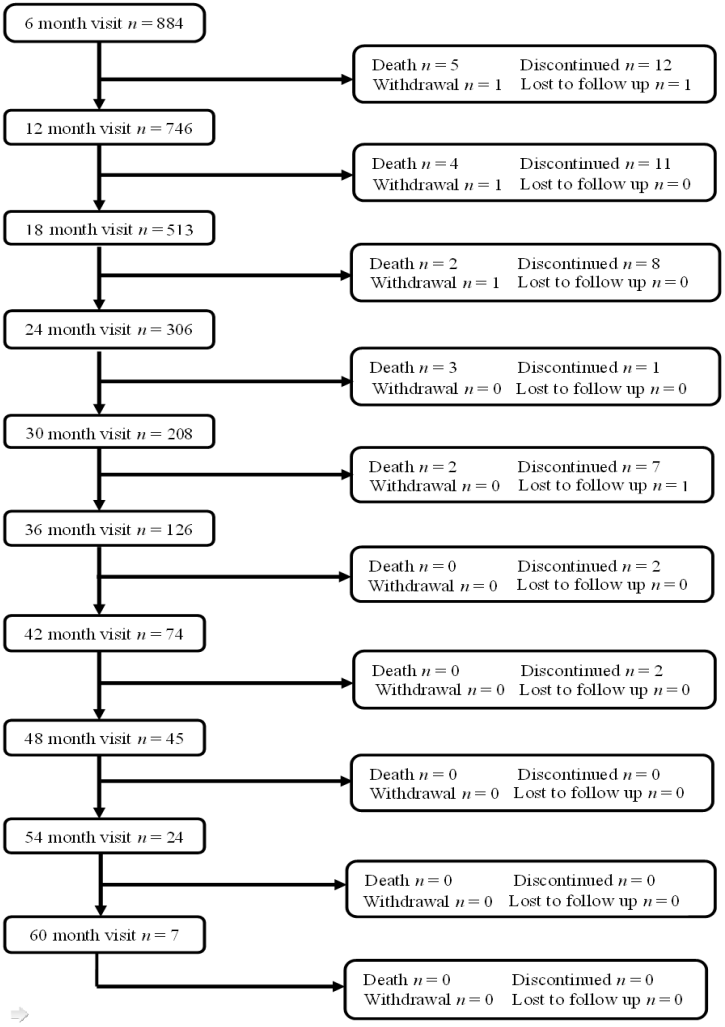


Figure 3: Patient Accountability after the Randomized Period of the ALERTS Study/Extended Follow-up



Note: This patient accountability represents the number of patients who had reached each time point at the time of database lock. All patients were followed through the IDE until study exit.

C. Study Population Demographics and Baseline Parameters

Table 1 provides a summary of demographic characteristics according to group within the randomized period (0-6 months). All ALARMS OFF patients crossed over to the ALARMS ON group at their 6-month visit.

Table 1: ALERTS Study Subject Demographics

Characteristic	ALARMS OFF (Control) Group (N=456)		ALARMS ON (Treatment) Group (N=451)		Difference (ON – OFF)
	N	Mean ± S.D. or N (%)	N	Mean ± S.D. or N (%)	95% BCI
Age at Randomization	456	59.5 ± 10.2	451	59.4 ± 10.5	(-1.4, 1.3)
Sex (Female)	456	154 (33.8%)	451	137 (30.4%)	(-9.4%, 2.7%)
Race/Ethnicity	456		451		
- American Indian		1 (0.2%)		0 (0.0%)	(-1.0%, 0.5%)
- Asian/Pacific Islander		2 (0.4%)		5 (1.1%)	(-0.6%, 2.0%)
- Black – Not of Hispanic Origin		32 (7.0%)		30 (6.7%)	(-3.7%, 2.9%)
- Caucasian – Not of Hispanic Origin		391 (85.7%)		391 (86.7%)	(-3.7%, 5.5%)

Characteristic	ALARMS OFF (Control) Group (N=456)		ALARMS ON (Treatment) Group (N=451)		Difference (ON – OFF)
	N	Mean ± S.D. or N (%)	N	Mean ± S.D. or N (%)	95% BCI
- Hispanic – any race		30 (6.6%)		22 (4.9%)	(-4.7%, 1.3%)
- Other		0 (0.0%)		3 (0.7%)	(-0.2%, 1.7%)
Presentation of ACS (Qualifying Event)	456		451		
- STEMI		113 (24.8%)		109 (24.2%)	(-6.2%, 5.0%)
- NSTEMI		127 (27.9%)		126 (27.9%)	(-5.7%, 5.9%)
- Unstable Angina		199 (43.6%)		199 (44.1%)	(-6.0%, 6.9%)
- Other		15 (3.3%)		15 (3.3%)	(-2.4%, 2.4%)
- Unknown		2 (0.4%)		2 (0.4%)	(-1.1%, 1.1%)
History of Silent MI	455	28 (6.2%)	451	25 (5.5%)	(-3.7%, 2.5%)
Diabetes	456	224 (49.1%)	451	206 (45.7%)	(-9.9%, 3.0%)
Dyslipidemia Requiring Medication	456	421 (92.3%)	451	416 (92.2%)	(-3.6%, 3.4%)

Characteristic	ALARMS OFF (Control) Group (N=456)		ALARMS ON (Treatment) Group (N=451)		Difference (ON – OFF)
	N	Mean ± S.D. or N (%)	N	Mean ± S.D. or N (%)	95% BCI
Hypertension Requiring Medication	456	426 (93.4%)	451	414 (91.8%)	(-5.1%, 1.8%)
History of Smoking	456	315 (69.1%)	451	322 (71.4%)	(-3.6%, 8.2%)
Currently Smoking	456	121 (26.5%)	451	117 (25.9%)	(-6.3%, 5.1%)
History of Heart Failure	452	60 (13.3%)	451	79 (17.5%)	(-0.5%, 8.9%)
NYHA	452		451		
- I		18 (4.0%)		34 (7.5%)	(0.5%, 6.6%)
- II		32 (7.1%)		36 (8.0%)	(-2.6%, 4.4%)
- III		10 (2.2%)		9 (2.0%)	(-2.2%, 1.8%)
- None		392 (86.7%)		372 (82.5%)	(-9.0%, 0.5%)
Killip Class	448		446		
- I		425 (94.9%)		410 (91.9%)	(-6.3%, 0.4%)
- II		20 (4.5%)		34 (7.6%)	(0.0%, 6.3%)
- III		3 (0.7%)		2 (0.4%)	(-1.4%, 0.9%)

Characteristic	ALARMS OFF (Control) Group (N=456)		ALARMS ON (Treatment) Group (N=451)		Difference (ON – OFF)
	N	Mean ± S.D. or N (%)	N	Mean ± S.D. or N (%)	95% BCI
Ejection Fraction (LVEF, %)	418	53.9 ± 8.8	411	54.1 ± 9.4	(-1.1, 1.4)
History of Renal Insufficiency	456	75 (16.4%)	451	83 (18.4%)	(-3.0%, 6.9%)
History of Reperfusion/ Revascularization	456	444 (97.4%)	451	442 (98.0%)	(-1.4%, 2.7%)
Angina in previous six months	456	400 (87.7%)	451	395 (87.6%)	(-4.4%, 4.1%)
Average Frequency of Angina	399		394		
- > 10 times/month		63 (15.8%)		58 (14.7%)	(-6.0%, 3.9%)
- 6-10 times/month		44 (11.0%)		37 (9.4%)	(-5.9%, 2.6%)
- 3-6 times/month		87 (21.8%)		101 (25.6%)	(-2.1%, 9.7%)
- < 3 times/month		205 (51.4%)		198 (50.3%)	(-8.0%, 5.8%)
Angina Status	398		389		

Characteristic	ALARMS OFF (Control) Group (N=456)		ALARMS ON (Treatment) Group (N=451)		Difference (ON – OFF)
	N	Mean ± S.D. or N (%)	N	Mean ± S.D. or N (%)	95% BCI
(most recent episode as of pre-procedure exam)					
- Stable		233 (58.5%)		228 (58.6%)	(-6.8%, 6.9%)
- Unstable		165 (41.5%)		161 (41.4%)	(-6.9%, 6.8%)
History of Silent Ischemic Changes	456		451		
- Yes		34 (7.5%)		28 (6.2%)	(-4.6%, 2.1%)
- No		309 (67.8%)		338 (74.9%)	(1.3%, 13.0%)
- Unknown		133 (24.8%)		85 (18.8%)	(-11.2%,-0.5%)
TIMI Risk Score (mean)	454	3.623 ± 0.968	449	3.706 ± 1.023	(-0.048, 0.213)
History of Atrial Arrhythmia	456	25 (5.5%)	450	18 (4.0%)	(-4.3%, 1.3%)
History of Ventricular Arrhythmia	456	26 (5.7%)	450	25 (5.6%)	(-3.2%, 2.9%)
History of Ectopic	456	6 (1.3%)	450	5 (1.1%)	(-1.8%, 1.4%)

Characteristic	ALARMS OFF (Control) Group (N=456)		ALARMS ON (Treatment) Group (N=451)		Difference (ON – OFF)
	N	Mean ± S.D. or N (%)	N	Mean ± S.D. or N (%)	95% BCI
Arrhythmia					

The new clinical analysis also included six secondary clinical efficacy endpoints:

1. The false positive rate (FPR) for Guardian alerting (with or without symptoms) would be superior to the FPR of symptoms in patients without the Guardian.

2. The Guardian would provide the ability to detect asymptomatic (silent) ACS events and cause the patient to seek urgent medical care in less than 12 hours.

3. The adjunctive detection and patient prompting of the Guardian would cause patients with or without symptoms to arrive at a medical facility in a timely manner for treatment of a CEC identified STEMI.

4. The adjunctive detection and patient prompting of the Guardian would cause patients with or without symptoms to arrive at a medical facility in a timely manner for treatment of a CEC identified NSTEMI.

5. The adjunctive detection and patient prompting of the Guardian would cause patients with or without alarms to arrive at a medical facility for treatment of a CEC identified ACS event in a timely manner.

6. The Guardian would have the ability to prompt presentation for other clinically meaningful medical conditions.

The following sections present the Safety results (associated with the original PMA design and the additional analysis of ALERTS ED visits) and the co-primary and secondary efficacy endpoint data associated with the additional analysis of ALERTS ED visits.

Safety Results

Six Month Randomized Period

The 31 system-related complication events in 30 subjects (3.3%) observed during the randomized period of the study are presented in Table 2 below. as defined for the primary safety endpoint. The primary safety endpoint for the randomized period of the trial was met with a posterior probability of >0.9999.

Table 2: System-Related Complications – Original Follow-Up

Complication	**# of Events (%)**
Cardiac Perforation	2 (0.22%)
Erosion	3 (0.33%)
Infection	11 (1.21%)
Lead migration/dislodgement	4 (0.44%)
Device Malfunction	2 (0.22%)
Lead Malfunction	1 (0.11%)
Loss of sensing due to dislodgement or malfunction of the lead	2 (0.22%)
Pain at or near the pocket site	5 (0.55%)
Visible bump where implanted in the chest	1 (0.11%)
Total – % (# of Subjects)	3.30% (30/910)

Additional Safety Analysis of ALERTS ED Visits/Extended Follow-up

The following analysis of long-term device safety was based on events from the implanted cohort of 910 patients that occurred after the randomization period and thus were not included in the safety results from the Original Follow-Up summarized above. This long term device safety and adverse event data are presented in Tables 3 to 6.

The 34 system-complications observed in 33 patients that occurred during the post-randomization period of the study are

presented in Table 3 below. 12 of the device malfunctions listed below were due to IMD replacement due to battery depletion.

Table 3: System-Related Complication Rate – Extended Follow-Up

Complication	# of Events (%)
Infection	4 (0.44%)
Erosion	1 (0.11%)
Device Malfunctions	16 (1.76%)
Hematoma (requiring drainage)	3 (0.33%)
Lead Malfunction	2 (0.22%)
Pain	4 (0.44%)
Signal Capture Problem	4 (0.44%)
Total (# of Subjects)	3.63% (33/910)

A total of 463 IMD replacement procedures were performed for patients in the ALERTS clinical trial. 12 adverse events in 12 patients were observed during those procedures and are summarized in Table 4.

Table 4: Replacement Implant System-Related Complication Rate

Complication	# of Events (%)

Infection	1 (0.22%)
Erosion	1 (0.22%)
Device Malfunctions	6 (1.30%)
Pain	2 (0.43%)
Signal Capture Problem	2 (0.43%)
Total	2.59% (12/463)

A total of 703 explant procedures were performed for patients in the ALERTS study. Four adverse events were observed during those procedures and are summarized in Table 5 below.

Table 5: Explant Procedure System-Related Complication Rate

Complication	**# of Events (%)**
Hematoma (requiring drainage)	3 (0.43%)
Lead Malfunction	1 (0.14%)
Total	0.57% (4/703)

The 65 system-related complications in 63 patients that were observed for the entire follow-up period of the ALERTS study are summarized in Table 6 below. Overall the acute procedural and long-term implantation risks of the device are comparable to a single chamber pacemaker.

Table 6: System-Related Complication Rate – All Follow-Up

Complication	**# of Events (%)**
Cardiac perforation	2 (0.22%)

Device Malfunction	18 (1.98%)
Erosion	4 (0.44%)
Hematoma (requiring drainage)	3 (0.33%)
Infection	15 (1.65%)
Lead malfunction	3 (0.33%)
Lead migration/dislodgment	4 (0.44%)
Loss of sensing due to dislodgement or malfunction of lead	2 (0.22%)
Pain at or near the pocket site	9 (0.99%)
Signal capture problem	4 (0.44%)
Visible bump where implanted in the chest	1 (0.11%)
Total (# of Subjects)	6.92% (63/910)

There were no serious complications of a cardiac catheterization following a patient ER visit prompted by an alarm during the nearly 3 years of average patient follow-up in approximately 900 patients.

Effectiveness Results – Six Month Randomized Period

Primary Efficacy Endpoint

Table 7 below presents the results from the primary effectiveness endpoint for the randomized analysis of the ALERTS clinical study.

Table 7: ALERTS Randomized Effectiveness Results

	ALARMS OFF	ALARMS ON	Posterior

		(N=456)		(N=451)		Probability*
		N	Pts (%)	N	Pts (%)	
Component – Cardiac or Unexplained Death						
		447	1 (0.2%)	441	3 (0.7%)	
Component – New QWMI (dual baseline analysis)						
		427	13 (3.0%)	420	7 (1.7%)	
Component – Time-to-door > 2 hours						
Look-back Window	**7-Day**	446	8 (1.8%)	439	4 (0.9%)	
	90-Day	446	17 (3.8%)	439	4 (0.9%)	
Composite Primary Endpoint Events (with dual baseline analysis)**						
Look-back Window	**7-Day**	428	20 (4.7%)	423	13 (3.1%)	0.8833
	90-Day	428	28 (6.5%)	423	13 (3.1%)	0.9908

* The significance threshold for the posterior probabilities of event reduction is 0.983 for the primary effectiveness endpoint.

** The dual baseline analysis incorporated both pre-implant and randomization ECGs as baseline to more accurately identify new, persistent Q-waves observed during the study

Effectiveness Results - Additional Analysis of ALERTS ED Visits/Extended Follow-up

Co-Primary Endpoints

The analysis of effectiveness was based on ED visits from the 907 patients from the entire randomized and non-randomized follow up period for the ALERTS Trial.

Table 8 below shows the results from both components of the co-primary effectiveness endpoint of the additional analysis of ALERTS ED visits. The device failed to reject the null hypothesis for PPV and did reject the null hypothesis for FPR. As a secondary endpoint the FPR for the ALARMS ON group showed superiority with respect to ALARMS OFF group (p<0.001).

Table 8: Primary Effectiveness Endpoint Results

	ALARMS OFF – Symptoms Only	**ALARMS ON – Alarm w/ or w/o Symptoms**	**P-Value**
ED Visits	181	345	
True Positive	33	89	
False Positive	148	256	
PPV	18.23%	25.80%	0.0313*
FPR (FP/pt. year)	0.678 FP/pt. year	0.164 FP/pt. year	<0.001**

*One-sided Fisher's exact test for **superiority** (Significance level = 0.025)

**Generalized linear model based on a Poisson distribution and the canonical log link function.

These data can further be broken down into whether a patient with an alarm also experienced symptoms as shown in Table 9 below.

Table 9: Additional PPV Results

	ALARMS OFF – Symptoms Only	ALARMS ON – Alarm and Symptoms	ALARMS ON – Alarm Only	ALARMS ON – Symptoms Only
ED Visits	181	135	210	625
True Positive	33	47	42	104
False Positive	148	88	168	521
PPV	18.23%	34.81%	20.00%	16.64%

Further analysis of the false positive (FP) alarms revealed that a relatively small group of patients drove the FPR as shown in Table 10. Based on the data collected it was not possible to determine an adequate predictor for patients likely to experience multiple FP alarms.

Table 10: False Positive Frequency

# of FP Alarms/Patient	# of Patients

0	744
1	106
2	37
3	9
4	8
5	2
6	0
7	1

Table 11 presents the False Negatives (FNs) or missed ACS events that were recorded during the study period for the ALARMS ON group. A FN for either symptoms only or a Guardian System alarm could only be observed if the patient presented to the ED. If an ACS event occurred and neither symptoms nor the guardian device prompted the patient to seek medical care it would not be captured in the following data.

Table 11: False Negatives in Additional Analysis of ALERTS Study ED Visits

	Alarm	**Symptoms**
FN - All ACS Events	104	42
FN - MIs	59 (3 STEMIs)	13 (1 STEMI)

The diagnostic performance of the device should be considered in clinical context and in comparison to the available alternatives.

For all ALERTS study patients, the presence of the device with ALARM ON increased the diagnostic accuracy (the PPV) compared to symptomatic patients without monitoring (ALARM OFF), (25.80% vs. 18.23%). Further, symptomatic patients with a positive alarm had a PPV that was higher than symptomatic patients with a negative alarm (34.81% vs. 16.64%). Among patients without symptoms, those who presented to the ED had a 20.00% PPV. Without an alarm, these patients very likely would have gone undiagnosed.

The FPR (FP/patient year) was lower in the ALARMS ON group than in the ALARMS OFF group (0.164 vs. 0.678 FP/pt. year, $P<0.001$ for non-inferiority).

There were 625 ER visits due to symptoms alone (ALARMS ON) compared to 345 ER visits for alarms (with or without symptoms) as shown in Tables 8 and 9. Also 521 False Positive ER visits were due to symptoms only (ALARMS ON). Across 1558 patient monitoring years this corresponds to an FPR of 0.334. The total FPR for all ALARMS ON presentations (regardless of reason for ER visit) is 0.499 (0.164 + 0.334). This is less than the FPR of 0.678 (shown in Table 8 for the ALARMS OFF cohort) and is statistically superior ($p<0.0001$).

Secondary Endpoint Results

Secondary Endpoint #1, found that the FPR of 0.164 for alarms (with or without symptoms) was significantly lower than (i.e. superior to) the FPR for symptoms only in ALARMS OFF patients ($p<0.001$).

Secondary Endpoint #2 found that there were 42 ACS events detected for patients who were prompted to present by an alarm alone. The median alarm-to-door time for these 42 ACS events was 1.38 hours (82.5 minutes).

Secondary endpoints #3, #4 and #5 included a summary of symptom-to-door and alarm-to-door times for all ACS events and also MI only events, presented as distributions, median and mean.

Figure 4 (all ACS) and Figure 5 (MI only) present four distribution data sets from ALERTS:

1. the symptom-to-door distributions for patients with both symptoms and alarms in the ALARMS ON group
2. the symptom-to-door distribution for symptoms only presentations in the ALARMS OFF group
3. the symptom-to-door distribution for symptoms only presentation in the ALARMS ON group. and
4. the alarm-to-door distribution for alarm (with or without symptoms) presentations in the ALARMS ON group.

Figure 5 also includes the arrival distribution of published data for MI symptom-to-door (adopted from Table 3 of DeVon et al. (2010) [7]) to contextualize the symptom-to-door times for ALARMS OFF reported here. Some studies report median symptom-to-door time of 2 hours, but this is optimistic and artificially short due to analysis characteristics such as rejecting all pre-hospital delays longer than 12 or 24 hours.

Figure 4: Arrival Distribution for All ACS Events

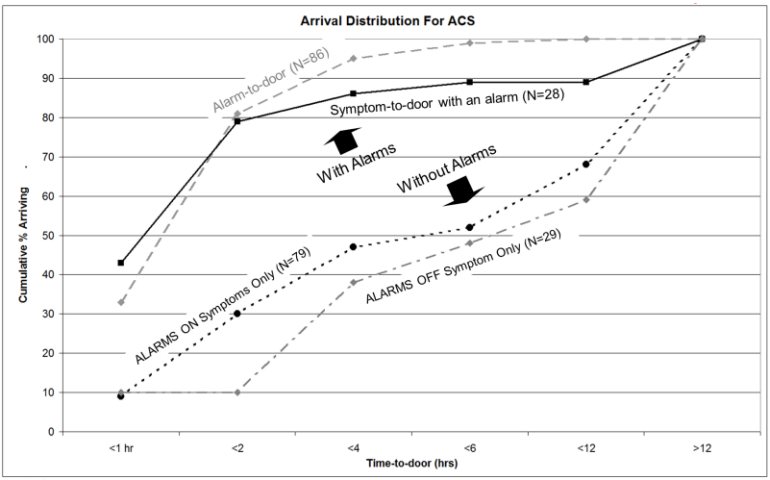
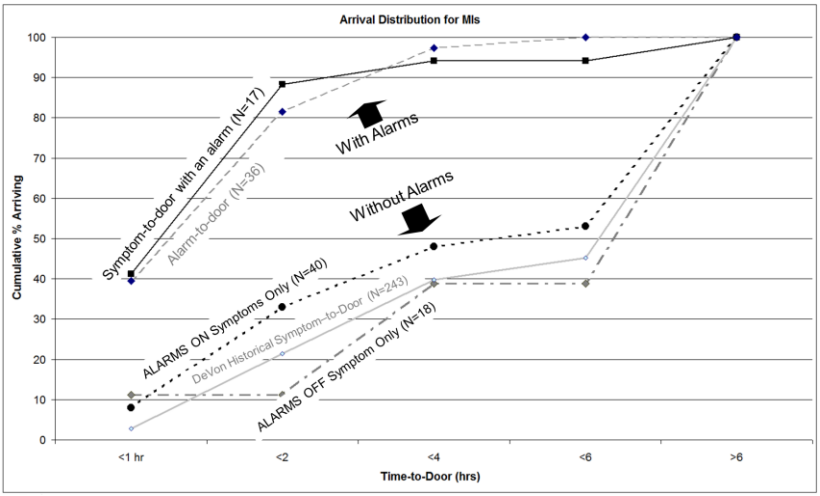


Figure 5: Arrival Distribution for MI Only Events



The median symptom-to-door times for CEC adjudicated ACS, MI and STEMI are presented in Table 12.

Table 12: Median Symptom-to-Door (with alarms) Times (ALARMS ON)

TYPE OF EVENT	Symptom-to-Door with an alarm (Median hours)
STEMI (n=7)	**0.75**
All MI (n=17)	**1.00**
ACS (n=28)	**1.04**

As seen in Table 13, Guardian alerts prompted 108 events in 79/910 (8.68%) of ALERTS patients to seek medical attention resulting in

the identification of a number of non-ACS events. Guardian alerts also resulted in the identification of the need for therapeutic devices such as pacemakers and ICDs in ~5% of ALERTS patients.

Table 13: Other Medical Conditions Diagnosed Following Guardian Alerts

Medical Condition Detected	Number of Events*	Number of Patients
Anemia	12	1.21% (11 / 910)
Atrial Fibrillation	33	2.86% (26 / 910)
Bradycardia	18	1.87% (17 / 910)
Bundle Branch Block	9	0.88% (8 / 910)
Hypokalemia	9	0.88% (8 / 910)
Tachycardia	25	2.09% (19 / 910)
Transient Heart Block	2	0.22% (2 / 910)
Total*	108	8.68% (79 / 910)

*Patients can experience multiple events so the event total and total number of patients will not be equal.

AQOL: Quality of Life Sub-Study

The ALERTS Quality Of Life (AQOL) sub-study was designed and run as an independent study using ALERTS study subjects during the final two years of the ALERTS study. The AQOL study included the MacNew [8-10] QOL instrument that has been used and validated to evaluate heart-related therapies. A custom QOL survey (the AngelMed Quality of Life - Frequency of Emergency Department Usage (AMQOL-FEDU)) was also designed to measure QOL changes related specifically to AngelMed Guardian heart-monitoring and alerting. Surveys were given to a subset of ALERTS subjects to prospectively examine changes in QOL at both six

months ("Post-1") and 12 months ("Post-2") after their alerting features were activated, compared to each subject's QOL during the year prior to implantation. Likert scales were used and responses were scored relative to baseline as improving ("Pos"), staying the same ("Neutral"), or worsening ("Neg").

The survey materials were given to both Treatment and Control subjects prior to implant. Treatment subjects were assessed again at six months (i.e., Post-1 time-point) and at 12 months (i.e., Post-2 time-point). Control subjects were tested 12 and 18 months later since Control subjects did not have alerts enabled for the first six months. Repeated measures analysis of variance (ANOVA) was carried out, with significant main effects followed-up using post-hoc t-tests.

The study enrolled 157 subjects at 21 ALERTS study sites with 133 having Post-1 completion and 108 having Post-2 completion.

AQOL Results

The MacNew showed a global improvement of 0.6 at 6 months and 0.5 at 12 months compared to pre-implant baseline ($p<0.0001$). The minimum clinically important difference is 0.5 points. Both 6- and 12-month MacNew results indicate a statistically and clinically significant benefit in QOL. The results from the customized AMQOL-FEDU are summarized in Table 14.

Table 14: AMQOL-FEDU Survey Results

	6 Months			1 Year		
	Pos	**Neutral**	**Neg**	**Pos**	**Neutral**	**Neg**
More Control Since Alarms on	90%	5%	5%	89%	8%	3%
Safer Since Alarms on	90%	6%	3%	90%	6%	5%
QOL Improved	69%	23%	6%	71%	20%	8%
More Productive	48%	38%	14%	55%	28%	18%
Less Depressed	47%	27%	11%	44%	29%	11%
Slept Better	50%	29%	12%	50%	22%	15%
Less Anxiety	73%	16%	8%	69%	12%	11%
Less Anxiety (symptoms)	62%	13%	7%	49%	14%	14%
Worried Less About Overdoing It	62%	20%	13%	66%	16%	12%
Exercise	56%	21%	8%	61%	20%	10%
Sexual Activity	34%	17%	14%	34%	15%	10%
Average	62%	20%	9%	62%	17%	11%

Study Conclusions

A. Effectiveness Conclusions

The diagnostic performance of the device should be considered in clinical context and in comparison to the available alternatives. While the Advisory Panel voted that there was not a reasonable assurance of effectiveness, this re-analysis includes data that were collected outside the pre-specified randomization period and thus were not reviewed or presented to the Advisory Committee.

For all ALERTS study patients, the presence of the device with ALARM ON increased the diagnostic accuracy (the PPV) compared to symptomatic patients without monitoring (ALARM OFF), (25.80% vs. 18.23%). Further, symptomatic patients with a positive alarm had a PPV that was higher than symptomatic patients with a negative alarm (34.81% vs. 16.64%).

Among patients without symptoms, those who presented to the ED had a 20.00% PPV. Without an alarm, these patients very likely would have gone undiagnosed.

The FPR (FP/patient year) was lower in the ALARMS ON group than in the ALARMS OFF group (0.164 vs. 0.678 FP/pt. year, $p<0.001$ for non-inferiority and $p<0.001$ for superiority as well).

Including symptoms only ALARMS ON presentations, the overall FP/patient year for all ALARMS ON presentations was is lower than that of the ALARMS OFF group (0.499 vs 0.678 FP/patient year.

The device improved the diagnostic accuracy (PPV) for patients both with and without symptoms, and the device did not increase the false positive rate (FPR) and may reduce it.

B. Safety Conclusions

The risks of the device are based on pre-clinical laboratory and animal studies as well as data collected in a clinical study conducted to support PMA approval as described above.

In the randomized portion of the study, there were 31 system-related complication events in 30 subjects (3.30%) as defined for the primary safety endpoint. The primary safety endpoint of the trial was met with a posterior probability of >0.9999 which was above the significance threshold of 0.954. The primary safety endpoint was met.

In the extended follow-up portion of the study, there were an additional 34 system-related complications in 33 subjects (3.63%). These safety data represent data collected from 3450 implant years from the original and extended follow-up.

The risks of the device have been well characterized and relate both to the procedural and device-related aspects as described above. Risks may also result from false positive or false negative results from the device.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in the ALERTS clinical study conducted to support PMA approval as described above.

The ALERTS data submitted in support of the PMA for the Angel Medical Guardian System demonstrate the following notable benefits:

a. Improved positive predictive value for ACS events in subjects presenting with symptoms

b. Improved positive predictive value for ACS events in subjects without symptoms
c. No increase, and a possible reduction, in the false positive ED visit rate in subjects with device alarms ON compared to subjects with device alarms OFF.

While there is some uncertainty in assessing and quantifying these benefits, including the lack of statistical significance of some measures, the overall uncertainty regarding the benefits is acceptable.

Similarly, the risks of the device have been well characterized and relate both to the procedural and device-related aspects as described above. The risks also relate to the false positive and false negative device results. Overall, the uncertainty pertaining to the magnitude of these risks is low.

When considering the overall benefits and risks of the device, the FDA concluded that the benefits outweigh the risks for the intended population.

An important consideration is that the device fills an unmet medical need by providing more effective diagnosis of a life-threatening condition compared to relying on patient symptoms alone.

References

1. Fischell TA, Fischell DR, Fischell RE et al. Potential of an intracardiac electrogram for the rapid detection of coronary artery occlusion. *Cardiovasc Revascul Med.* 2005; 6:14-20.

3. Fischell TA, Fischell DR, Avezum A, John MS, Holmes D, Foster M 3rd, Kovach R, Medeiros P, Piegas L, Guimaraes H, Gibson CM.Initial clinical results using intracardiac electrogram monitoring to detect and alert patients during coronary plaque rupture and ischemia. J Am Coll Cardiol. 2010 Sep 28;56(14):1089-98.

4. Hopenfeld B, John MS, Fischell DR, Medeiros P, Guimarães HP, Piegas LS. The Guardian: an implantable system for chronic ambulatory monitoring of acute myocardial infarction. J Electrocardiol. 2009;42(6):481-6. Chronic Intracardiac Ischemia Detection 26

5. Gibson M, Guimarães VS, John MS, Keenan D, Feitosa AM, Medeiros P, Piegas LS, Krucoff MW, Holmes D. Magnitude and Duration of Ischemic Events Detected Using Permanent Intracardiac ST-Segment Monitoring: First In Human Experience. American College of Cardiology (ACC), 2012, Chicago.

6. Guimarães VS, Feitosa A, Portela NM, Sobrinho D, Ramires J. Monitor intracardíaco implantável (AngelMed Guardian) para detectação de isquemia miocárdica, Revista Brasileira de Medicina, RBM Volume 71, Number 4, April 2014, pp109-116.

7. DeVon HA, Hogan N, Ochs AL, Shapiro M. Time to Treatment for Acute Coronary Syndromes: The Cost of Indecision. The Journal of cardiovascular nursing. 2010;25(2):106-114.

8. Dixon T, Lim LL, Oldridge NB. The MacNew heart disease health-related quality of life instrument: reference data for users. Qual Life Res. 2002 Mar;11(2):173-83.

9. Höfer S, Lim L, Guyatt G, Oldridge N. The MacNew Heart Disease health-related quality of life instrument: a summary. Health Qual Life Outcomes. 2004 Jan 8;2:3.

10. Oldridge N, Guyatt G, Jones N, Crowe J, Singer J, Feeny D, McKelvie R, Runions J, Streiner D, Torrance G. Effects on quality of life with comprehensive rehabilitation after acute myocardial infarction. Am J Cardiol. 1991 May 15; 67(13):1084-9.

Index

Reminders

- ☑ Emergency Alarms: The IMD vibrates and EXD beeps 5 times, and then repeats. Call for an ambulance immediately.
- ☑ See Doctor Alerts: The IMD vibrates and EXD beeps one time, pauses for 7 seconds, and then repeats. See your doctor in the next 1 or 2 days.
- ☑ EXD Low Battery Warning: The EXD makes a very short beep every 30 seconds. Replace the EXD battery.
- ☑ Heart Attack Symptoms: If you have heart attack symptoms, call for an ambulance immediately – even if your AngelMed Guardian system is not alarming.
- ☑ If you can't tell what the alarm is, call for an ambulance immediately.
- ☑ Keep your EXD within 6 feet (1.8m) of your IMD at all times.
- ☑ Check your EXD's battery power once a week.
- ☑ Carry your AngelMed Guardian System Patient Identification Card with you at all times.

Angel Medical Systems®
788 Shrewsbury Ave. Suite
Tinton Falls, NJ 07724 (USA)
+1 561 962-2191

May 2017
0201-2100-001#P15 Rev. C

Patient Manual for the AngelMed Guardian® System

Caution: Federal law restricts this device to sale by or on the order of a physician.

AngelMed®

Fold Li

Warning

NEVER ignore any symptoms of a heart attack.

Call for an ambulance immediately and seek emergency care whenever heart attack symptoms occur (whether accompanied by a Guardian Emergency Alarm or not).

Symptoms include[1]:

- Chest discomfort. Most heart attacks involve discomfort in the center of the chest that lasts more than a few minutes, or that goes away and comes back. It can feel like uncomfortable pressure, squeezing, fullness or pain.
- Discomfort in other areas of the upper body. Symptoms can include pain or discomfort in one or both arms, the back, neck, jaw or stomach.
- Shortness of breath. May occur with or without chest discomfort.
- Other signs. These may include breaking out in a cold sweat, nausea or lightheadedness.

NEVER ignore a Guardian Emergency Alarm.

Call an ambulance immediately and seek emergency care:

- if you have symptoms (with or without an Emergency Alarm),
- if there is an Emergency Alarm (whether or not you have heart attack symptoms), or
- you have both symptoms and there is an Alarm.

1 From the American Heart Association (2007). *Know the Facts, Get the Stats*

Contents

1 Responding to Alarms and Heart Attack Symptoms

The next two pages provide a quick reference for

- How you know if you're getting an Emergency alarm and See Doctor alert – and what to do when each occurs
- What to do if you can't tell whether it's an Emergency alarm or See Doctor alert
- What to do if you experience heart attack symptoms

Heart attack symptoms are described on the inside front cover.

Important reminders on how to use your AngelMed Guardian system are summarized on the back cover.

Responding To Alarms and Alerts

If You Experience	Do This
♦ A repeating pattern of – 5 vibrations on IMD **Brrr Brrr Brrr Brrr Brrr** – 5 beeps on EXD **Beep Beep Beep Beep Beep** ♦ A flashing red EXD light	**Call for an ambulance immediately.** This is an **Emergency** alarm. See page 25 for more information.
♦ A repeating pattern of – 1 vibration and a 7-second pause on IMD **Brrr** (7 seconds) **Brrr** – 1 beep and a 7-second pause on EXD **Beep** (7 seconds) **Beep** ♦ A flashing yellow EXD light	**See your doctor in the next one or two days.** This is a **See Doctor** alert. See page 28 for more information.
♦ A very short beep every 30 seconds (EXD) – and the IMD does not vibrate **Short Beep** (**30** seconds) **Short Beep**	**Replace your EXD battery** or have your doctor replace it for you in the next 1 to 2 days. This is a **Low EXD Battery** warning. See pages 33 and 34 for more information.

If you	Do this
Don't know which alarm it is (For example, you may be stressed and confused.)	**Call for an ambulance immediately.** Treat the alarm as an Emergency alarm.

Responding To Heart Attack Symptoms

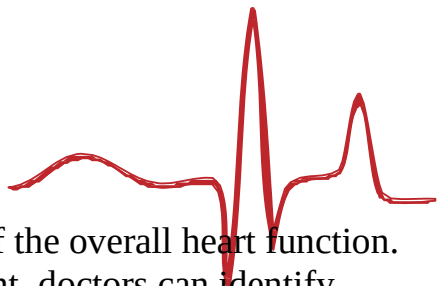
If you	Do this
Have any heart attack symptoms like: ♦ Chest discomfort ♦ Discomfort in the upper body ♦ Shortness of breath	**Call for an ambulance immediately.** You may be having a heart attack – even if your AngelMed Guardian system isn't alarming. See the inside front cover for more information.

2 About the AngelMed Guardian System

Your doctor has prescribed the AngelMed Guardian® system to monitor and record your heart's electrical signals, 24 hours a day. The device is indicated for use in patients who have had prior acute coronary syndrome (ACS) events and who remain at high risk for recurrent ACS events. This manual describes the system and provides instructions on how to use it.

Your heart is a muscular organ which pumps blood throughout your body. The pumping is controlled by electrical signals from within the heart. While these signals vary from person to person, they all share similar characteristics. It is these characteristics that the AngelMed Guardian system monitors.

A typical heart signal, shown here, can provide vital information on the heart's overall health. Each area of the signal indicates a different part of the overall heart function. Using diagnostic equipment, doctors can identify many heart problems.



In a similar way, the AngelMed Guardian system continuously monitors your heart. It warns you of changes that may indicate that your heart is not

getting enough oxygen – a condition called myocardial ischemia. Myocardial ischemia can lead to a heart attack. It often occurs when a blockage develops in one of the heart arteries. Clinical studies suggest that this condition often changes the shape of the signal. If the signal shape changes too much, the AngelMed Guardian system warns you to seek medical help.

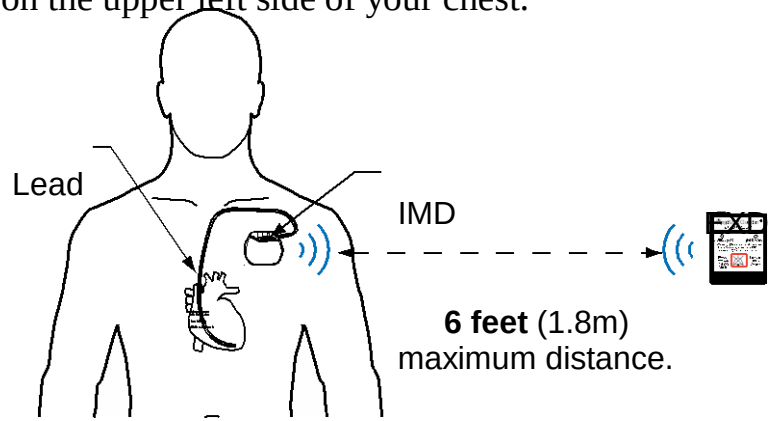
The AngelMed Guardian system also records your heart signals. These recordings can be reviewed by your doctor during office visits.

How the System Works

Your AngelMed Guardian system has two main parts:

- Implantable Medical Device (IMD Model AMSG3)
- External Device (EXD, Model EXD-001)

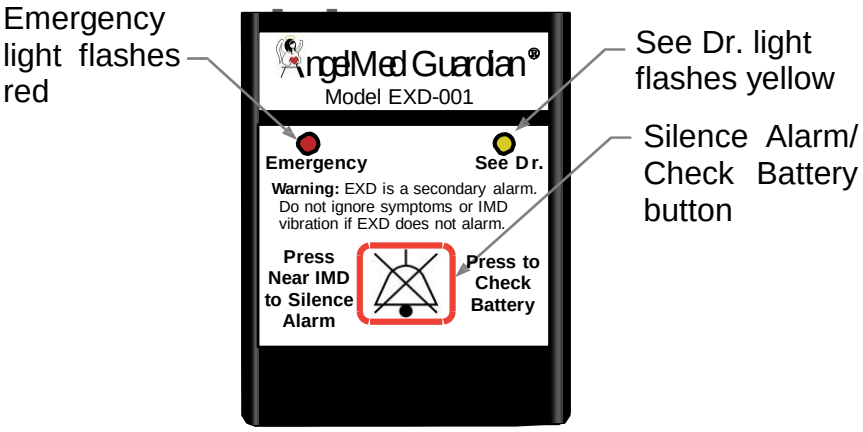
The IMD is surgically implanted just under the skin on the upper left side of your chest.



A lead is also implanted. One end of the lead is attached to the inside of your heart, and the other end connects to the IMD. The lead allows the IMD to monitor the electrical signals directly from your heart, 24 hours a day. The IMD gently vibrates if it detects specific changes in your heart signal.

When this occurs, the IMD communicates with the EXD, and the EXD beeps when the IMD vibrates. However, the EXD can only beep if it is within 6 feet (1.8 meters) of the IMD. That is why you must carry the EXD with you at all times. Note that your IMD will still beep even if your EXD is out of range.

As shown in the figure below, the EXD has Emergency and See Doctor lights, plus a *Silence Alarm/Check Battery* button. These features are described in detail later in this manual.



How Long Will Your IMD Last?

Your IMD is powered by an internal battery, which is expected to last about 3.2 years under normal conditions. However, excessive alarming and data retrievals (conducted by your doctor) may reduce IMD battery longevity. When the battery gets low, the IMD needs to be replaced. An incision is made where your current IMD is located, and your current IMD is replaced with a new one. The lead inside your heart remains in place.

Your IMD continuously monitors its own battery. When the IMD battery gets low, the IMD issues a See Doctor alert. Your doctor will then schedule a time to replace the IMD. The IMD is designed to last about 1 month after warning of low battery power. (The EXD has its own battery, which is discussed in *EXD Battery* on page 31.)

How the System Warns You of a Problem

Your AngelMed Guardian system provides three kinds of warnings.

- Emergency alarm
- See Doctor alert
- Low EXD Battery warning

An overview of each of these three alarms is provided in Section 1 – *Responding to Alarms and Heart Attack Symptoms* on page 1.

The AngelMed Guardian system signals an Emergency alarm or See Doctor alert when a change occurs in your heart's electrical signal. When these warnings occur, the IMD gently vibrates under your skin. In addition, the EXD warns you with beeps and a red or yellow flashing light.

Emergency alarms are used for life-threatening heart conditions, so you should call for an ambulance immediately. See Section 6 – *Emergency Alarms* on page 25 for more information.

See Doctor alerts are not as serious, but you should make an appointment to see your doctor in the next 1 or 2 days. See Section 7 – *See Doctor Alerts* on page 28 for more information.

Low EXD Battery warnings mean that the EXD battery power is low. The EXD beeps, but the IMD does not vibrate. You should either replace the EXD battery with the custom battery supplied by your doctor or call your doctor to replace the battery for you. The Low EXD Battery warning is described in Section 8 – *EXD Battery* on page 31. Battery replacement instructions are provided in Section 8 – *How to Replace the EXD Battery* on page 34.

3 When Not to Use this Product

The AngelMed Guardian system may not be implanted in the following circumstances:

- In patients with cognitive impairment that would prevent recognition of alarms
- In patients who cannot feel the vibration from the implanted device (IMD) when it is placed on top of the skin and just under the left collarbone
- In patients who have previously been implanted with a device that regulates heart rhythm such as a pacemaker or cardioverter-defibrillator (ICD). The AngelMed Guardian system is not designed to monitor your heart if these devices are also implanted.
- In patients where a pacemaker lead cannot be placed safely

4 Risks and Benefits

What are the Benefits?

The major benefit of the AngelMed Guardian system is that it constantly monitors the heart and warns you to seek medical help when it detects specific changes in your heart signal. Early treatment can save your life.

The AngelMed Guardian system also records your heart signal. This feature should help your doctor to manage your heart condition going forward.

What are the Risks?

Your doctor can best explain the risks involved with the AngelMed Guardian system. Some possible risks are as follows:

- Implanting the AngelMed Guardian IMD presents the same risks as any surgery. A small percentage of patients will develop a complication because of the implant surgery. These may include infection, reaction to a drug used during surgery, blood loss, or damage to a blood vessel, heart wall, or other organ.

- After surgery, you will feel some discomfort. This should lessen as you recover. Some patients however, continue to feel discomfort where the IMD is implanted.
- You should follow certain precautions with your AngelMed Guardian system. Your doctor will discuss them with you and many are discussed in this booklet. Please read this booklet completely. Pay close attention to sections that are labeled Warning or Caution because they contain important safety information.

Note that some coronary artery blockages may not cause your AngelMed Guardian system to warn you to get help. This is why you should **always get immediate medical attention if you experience heart attack symptoms,** even if your AngelMed Guardian system hasn't warned you.

5 General Warnings and Precautions

Your AngelMed Guardian system contains small electrical components. Under some circumstances, these parts can be affected and even damaged by external factors such as equipment that is used in medical settings, industry, and around the house.

This section explains the practices and environments that can adversely affect your AngelMed Guardian system. It covers:

- Medical therapy precautions
- Physical exercise precautions
- Interference from electrical devices and engines

Where possible, this section also explains steps that you or others can take to minimize any damaging effects.

Medical Therapy Precautions

Your AngelMed Guardian system will not be harmed by diagnostic x-rays (including fluoroscopy, dental and chest x-rays), computed tomography (CT) scans, mammographies, or ultrasonic dental cleaners.

However, some medical procedures can affect your IMD and the heart tissue near your lead. These procedures are listed in this section. Always tell the medical staff that you have an IMD and show them this booklet.

Diathermy is a medical procedure that uses microwaves or sound waves to heat body tissue. Do not have diathermy treatments. Diathermy may damage your IMD and injure the tissue near your implanted lead.

Electrosurgical cautery is a medical procedure that uses electrical currents to burn body tissue. Electrosurgical cautery may damage or interfere with your IMD. If electrosurgical cautery is necessary, medical personnel should keep the current path and ground plate as far away from the IMD and lead system as possible.

Because this treatment can cause your IMD to alarm, ask your doctor if alarms should be disabled prior to treatment. After treatment, see your doctor to confirm the IMD is operating properly.

Electrical therapies – Any treatment that uses therapeutic levels of electricity, like electro-acupuncture or electro-muscle stimulation, may damage or interfere with your IMD. If you undergo an electrical therapy, medical personnel should keep the current path as far away from the IMD and lead system as possible.

Because these treatments can cause your IMD to alarm, ask your doctor if alarms should be disabled prior to treatment. After treatment, see your doctor to confirm the IMD is operating properly.

External defibrillation uses external equipment to deliver an electrical shock to stop rapid heartbeats. External defibrillation may damage the IMD and heart tissue near the lead. Medical personnel should minimize current flowing through the IMD and lead system by:

- Positioning defibrillation paddles as far as possible from the IMD and lead system.
- Using the lowest clinically appropriate energy output.

After treatment, see your doctor to confirm the IMD is operating properly.

High radiation sources – High radiation sources such as cobalt 60 or gamma radiation should not be directed at the IMD. If you require radiation therapy near your IMD, medical personnel should put lead shielding over the device to prevent radiation damage. After radiation therapy, your doctor should periodically verify that your IMD is working properly since damage from radiation may not be immediately detectable.

Lithotripsy is a medical procedure that uses shock waves to break up hardened bodily secretions such as kidney stones. Lithotripsy may permanently damage the IMD. Avoid it unless the therapy site is not near your IMD or lead.

MRI (magnetic resonance imaging) is a diagnostic technique that uses radio waves to produce images of the body. Do not have an MRI. An MRI creates a very powerful magnetic field that can damage your IMD and injure the tissue near your implanted lead.

Radiofrequency (RF) ablation is a medical procedure that uses heat energy to destroy a small area of body tissue. RF ablation may damage your IMD or cause it to malfunction. To minimize RF ablation risks, medical personnel should avoid direct contact between the ablation catheter and your IMD and lead system. In addition, they should position the ground plate so that the current pathway does not pass through or near your IMD and lead system.

Because this treatment can cause your IMD to alarm, ask your doctor if alarms should be disabled prior to treatment. After treatment, see your doctor to confirm the IMD is operating properly.

Transcutaneous Electrical Nerve Stimulation (TENS) is the electrical stimulation of the skin to relieve pain. TENS may damage your IMD. If you need TENS, medical personnel should place the TENS electrodes close to one another and as far as possible from your IMD and lead system.

Because this treatment can cause your IMD to alarm, ask your doctor if alarms should be disabled prior to treatment. After treatment, see your doctor to confirm the IMD is operating properly.

Ultrasound therapy is a diagnostic technique that uses sound waves to produce images of the body. Ultrasound therapy, if directed at the IMD, may damage the device and cause you harm. If you need ultrasound therapy, the therapy should not be directed at the IMD. After treatment, see your doctor to confirm the IMD is operating properly.

Physical Activity Precautions

After surgery, the surgical site is likely to be sore. You need time to heal and you should keep this in mind whenever you exercise or stretch your upper body. Speak with your doctor about the kinds of physical activities you should avoid until you heal.

After you heal, you should be able to resume most of your usual activities. However, because you have an implanted device, avoid playing contact sports like football since the EXD, IMD or lead may get damaged. Also, consult your doctor before doing strenuous or repetitive upper-body exercise like weight lifting or softball.

Warning

Avoid contact sports after you get your IMD. Also, get your doctor's approval before starting an exercise program, especially if it involves upper-body activity. Strenuous activity may damage the implanted components, which may prevent the AngelMed Guardian system from warning you when it should.

Interference from Electrical Devices and Engines

All electrical devices generate some amount of electromagnetic interference (EMI). The AngelMed Guardian system protects against most sources of EMI. However, you should follow certain precautions as discussed in this section. Also, speak with your doctor if you want to learn more about these precautions.

What is Electromagnetic Interference?

Electromagnetic interference (EMI) is waves of energy from electrical equipment that interfere with the proper operation of nearby equipment. No doubt, you have already experienced EMI. For example, you may have heard static on the radio when you used an electrical appliance in the kitchen. This is an example of EMI.

Electrical equipment in good working order does not usually produce enough EMI to interfere with your IMD and EXD. This includes small and large kitchen appliances, stereo equipment, washers, dryers, computers, and similar items.

Sources of Strong EMI

Some types of equipment produce strong EMI. The following equipment can damage or interfere with your IMD and EXD:

Home appliances that are not in good working order.

High-voltage power lines.

Automobile ignition systems. Do not work under the hood of the car when the engine is running. However, it is okay to drive or be a passenger in a car.

Ignition systems of other internal combustion engines, like gasoline-powered lawn mowers and leaf blowers. It's generally safe to work around running internal combustion engines, but limit your exposure to ignition-system parts.

Industrial equipment such as arc welders, large electro-magnets, induction furnaces, and very large or defective electric motors.

Radio transmitters and transmitters for radio-controlled equipment or toys.

Small motor-driven appliances like hair dryers, electric shavers, power tools. Do not hold small motor-driven appliances close to your IMD and EXD.

Some medical equipment such as MRIs. See *Medical Therapy Precautions* on page 12 for details.

Warning

Stay away from high-powered energy sources like MRIs and large industrial motors and generators. Getting too close can damage the IMD and injure the tissue near your implanted lead.

Warning

Be aware of any signs that warn those with pacemakers and other implanted devices to stay away. Such environments often have high-powered energy fields, which can interfere with the operation of the IMD. Speak with your doctor before entering such areas.

Cell Phones

Cell phones can safely be used with your AngelMed Guardian system, provided that you do the following:

- Hold the phone at least 6 inches (15 centimeters) away from your implanted IMD. Typically, that can be done by holding the phone on the right side of your body – opposite the IMD. If your cell phone transmits above 3 watts, hold the phone at least 12 inches (30 centimeters) away from your IMD.
- If you do not know the transmit power of your cell phone, check the cell phone manual. If you still do not know the transmit power, assume the cell phone transmits at the higher power and hold the phone at least 12 inches (30 centimeters) away from the IMD and EXD.
- Store the phone at least 6 inches (15 centimeters) away from the IMD. For example, store the phone on the right side of your body – opposite the IMD. This is important because some phones send signals when in the Listen or Standby mode.
- Never carry your phone in a shirt or breast pocket, which would place the device over the IMD.

Security Systems

Anti-Theft Systems (in Stores and Libraries)

Anti-theft systems that are used in stores, libraries and other places can interfere with your IMD and EXD if you stay within 2 feet of them. Please observe the following precautions.

- Pedestal systems are usually placed at store exits. Walk past the pedestals at a normal pace and do not linger.
- Tag deactivator systems are often used at stores and library checkout counters. Stay at least 2 feet away from them while conducting business.
- Do not work at the checkout counter of a store or library where such systems are used.
- Avoid self-checkout counters where such systems are used. Store management should be able to tell you if the self-checkout counters are equipped with an electronic security system.

Security Systems (in Airports and Other Public Buildings)

Security systems such as those used in airports and some public buildings will probably not interfere with your IMD and EXD. Walk through them at a normal pace, and do not linger near them.

The IMD and EXD have metal parts that may set off a security system alarm. If this happens, show your Identification Card to the security officers. If they use a handheld wand to perform a search, ask them to work quickly and avoid holding the wand over your IMD.

What Happens if IMD or EXD Operation is Impaired?

If you experience any of the conditions warned against in the previous sections, your IMD or EXD may be affected. When affected by these outside factors, the IMD or EXD may do the following:

- Issue a warning even if no medical problem exists
- Not issue a warning if a medical problem does exist

If the impairment is caused by electrical devices like cell phones, security systems, or sources of strong EMI (see page 19), the IMD or EXD generally returns to normal operation when the condition no longer exists. For example, when you step away from a store's security system or move away from the ignition system of a running automobile, the IMD and EXD will operate normally.

If you had one of the medical therapies discussed previously (see page 12) or if you sustained a physical shock or injury over the implant site, see your doctor to ensure the IMD is operating properly.

Warning

If you think your IMD or EXD may be damaged, call your doctor so that he or she can examine them. A damaged IMD or EXD may not warn you if a heart problem occurs.

6 Emergency Alarms

If you have an Emergency alarm, call for an ambulance immediately.

Alarm Pattern

During an Emergency alarm, the IMD vibrates in a repeating pattern of five short vibrations. The five vibrations are in a 3-2 pattern like this:

Brrrr- Brrrr- Brrrr Brrrr- Brrrr

If your EXD is within 6 feet (1.8 meters) of the IMD, the EXD will beep like this:

Beep-Beep-Beep Beep-Beep

Also, the **red light**, labeled "Emergency", on the EXD will flash.

These alarms will continue for up to 5 minutes, unless you turn them off with the EXD.

How to Respond

If you have an Emergency alarm, do the following:

1. Call for an ambulance immediately.

2. Look at the back of your EXD and follow any instructions written on the label.

3. Turn off the alarm by holding the EXD within 2 inches (5 centimeters) of your IMD. Then press the *Silence Alarm/Check Battery* button.

4. Take your EXD with you to the hospital.

5. At the Emergency room, tell the medical staff that you have an implanted device that vibrates when you have a heart problem. Also, show them your Patient ID card and this booklet, if available.

Turning Off an Emergency Alarm

You can turn off an Emergency alarm after it has been on for at least 30 seconds.

To turn off an Emergency alarm, hold the EXD within 2 inches (5 centimeters) of your IMD and push the *Silence Alarm/Check Battery* button on your EXD.

Turning Off an Emergency Alarm

If the EXD beeps twice, you have successfully turned off the alarm. If it beeps only once, move the EXD a little and try again. After the alarm has been turned off, your IMD will stop vibrating and the EXD will stop beeping.

Reminder Alarms

After 15 minutes, the IMD will vibrate again and the EXD will beep again with the pattern of five short vibrations. This is called a reminder alarm. It reminds you to call for an ambulance immediately, if you haven't done so already.

As before, you can turn off the reminder alarm after it has been on for at least 30 seconds. If you don't turn it off, the alarm will continue for about two minutes and then stop automatically.

For your safety, reminder alarms will recur every 15 minutes for up to 2 hours. They will stop after you have turned off two separate alarms.

Flashing Red Light Remains On

The EXD's red Emergency light will flash for 25 hours, unless your doctor turns it off. Your doctor is the only person who can turn off the EXD's flashing light.

7 See Doctor Alerts

If you have a See Doctor alert, make an appointment to see your doctor in the next one or two days.

Alert Pattern

The See Doctor alert is very different from the Emergency alarm. The IMD vibrates one time, pauses for about 7 seconds, vibrates again, and so on, like this:

Brrrr 7 sec **Brrrr**

If your EXD is within 6 feet (1.8 meters) of the IMD, the EXD will beep like this:

Beep 7 sec **Beep**

Also, the **yellow light**, labeled "See Dr.", on the EXD will flash.

These alerts will continue for up to 5 minutes, unless you turn them off with the EXD.

How to Respond

If you have a See Doctor alert, do the following:

1. Make an appointment to see your doctor in the next 1 or 2 days.
2. Look at the back of your EXD and follow any instructions written on the label.
3. Turn off the alert by holding the EXD within 2 inches (5 centimeters) of your IMD. Then press the *Silence Alarm/Check Battery* button.
4. Bring your EXD to your appointment.

Turning Off a See Doctor Alert

You turn off a See Doctor alert the same way you turn off an Emergency alarm.

You can turn off a See Doctor alert after it has been on for at least 30 seconds.

To turn off the alert, hold the EXD within 2 inches (5 centimeters) of your IMD and push the *Silence Alarm/Check Battery* button.

Turning Off a See Doctor Alert

If the EXD beeps twice, you have successfully turned off the alert. If the EXD beeps only once, move the EXD a little and try again. After the alert has been turned off, your IMD will stop vibrating and the EXD will stop beeping.

No Reminder Alarm

There are no reminder alarms for the See Doctor alert. The vibrations and beeps will not restart after you turn them off.

Flashing Yellow Light Remains On

The EXD's yellow See Dr. light will flash for 25 hours, unless your doctor turns it off. Your doctor is the only person who can turn off the EXD's flashing See Dr. light.

8 EXD Battery

The EXD uses a custom battery that lasts about six months. This battery is available only from your doctor. Your doctor will provide you with a spare battery so that you can replace the battery between appointments should the need arise. If you don't feel comfortable changing the battery yourself, ask your doctor to replace it for you.

You should however check your EXD battery power once a week. If this check shows that the battery is dead (see page 32) or if you hear a low EXD battery warning (see page 33), either replace the battery yourself (see page 34) or have your doctor do it for you.

Warning

Use only the battery supplied by your doctor in your EXD. The EXD will not work with a different battery. Using a different battery can also damage your EXD. An EXD that isn't working properly cannot warn you when it should.

Checking EXD Battery Power

Check your EXD's battery power once a week.

To check battery power, press the *Silence Alarm/Check Battery* button on your EXD. You do not need to hold the EXD near your IMD when you press the button.

- If the battery is working, the EXD will make **one** very short beep ("chirp") at the same time you press the button.
- If the battery is not working, the EXD will not beep when you press the button. Call your doctor to replace the battery.

Warning

Check the EXD's battery power once a week to avoid losing power to your EXD. An EXD with a depleted battery cannot warn you when it should.

Low EXD Battery Warning

If you get a Low EXD Battery warning, see your doctor in the next day or two for a replacement battery.

If your EXD battery has low power, the EXD will make a very short beep ("chirp") every 30 seconds, until it runs out of power or until you turn the warning off.

Short Beep ← 30 sec → **Short Beep**

The IMD does not vibrate during a Low EXD Battery warning.

You can turn off a Low EXD Battery warning at any time. When you turn it off, the Low EXD Battery warning remains off for 12 hours and then starts beeping again.

To turn off the Low EXD Battery warning for 12 hours, press the *Silence Alarm/Check Battery* button on the front of your EXD. You do not need to hold the EXD near the IMD to turn off the Low EXD Battery warning.

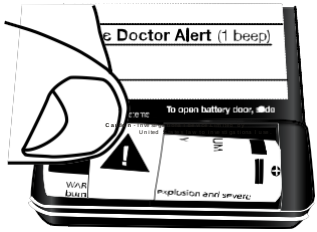
Turning Off a Low Battery Warning

How to Replace the EXD Battery

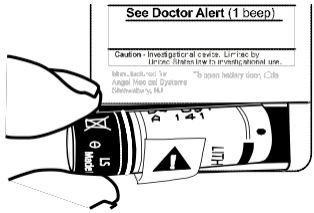
To replace the EXD battery:

1. Open the EXD's battery compartment by pushing down on the right-side of the battery cover and sliding it to the left.

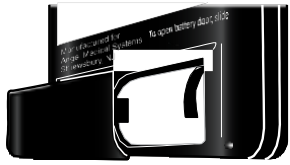
2. Gently pull the tab to lift the negative (–) end of the old battery. **Note:** If the pull-tab is under the battery or missing, use a small screewdriver to gently lift the battery.



3. Insert the positive (+) end of the new battery into the battery compartment, then push down on the battery's negative (–) end.
Caution: Your EXD will only operate when you use the battery supplied by your doctor. Do not use a common household battery.



4. Close the battery compartment by sliding the battery cover completely to the right.



5. To confirm that the battery was correctly inserted and is working, push the *Silence Alarm/Check Battery* button. The EXD will beep one time if the battery is working.
   Note: You may need to press the button up to 20 times before the EXD beeps. This is a characteristic of a new battery when it is being used for the first time.

6. Discard the depleted battery according to local environmental regulations.

Warning

If you replaced the EXD battery and the EXD no longer beeps when pressing the *Silence Alarm/Check Battery* button, perform the steps in the *Troubleshooting* section on page 44. If the EXD still does not beep, your EXD is not functioning properly and you should contact your doctor for assistance. Note however, that your IMD can still vibrate if it detects a heart problem even if your EXD is not working properly.

9 Keeping the EXD Close By

Keep the EXD within 6 feet (1.8 m)

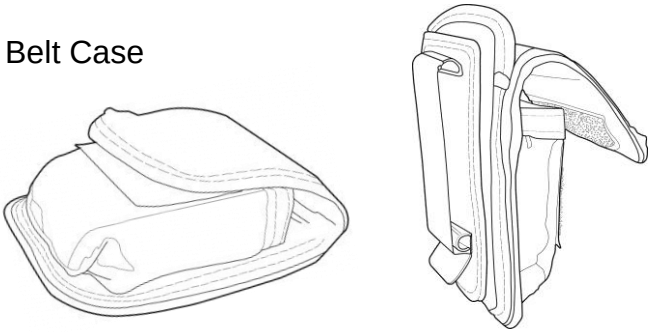
It is important for you to keep the EXD within 6 feet (1.8 meters) of your IMD at all times. You should carry it with you during the day, and keep it by your bed at night. Doing so allows the EXD to beep and flash if your IMD signals an Emergency alarm or See Doctor alert. Keeping the EXD close by also allows you to stop the EXD and IMD warnings if they occur.

Do not expose the EXD to extreme temperatures or water as these may interfere with its operation. For information on ways to care for your EXD, see *Care and Maintenance* on page 40.

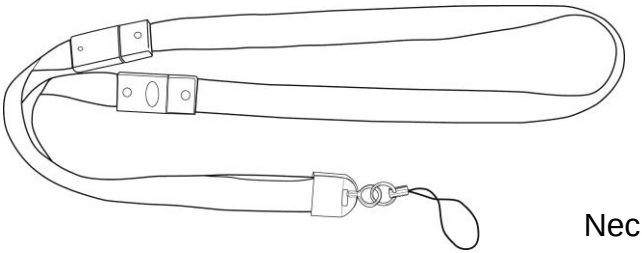
Belt Case and Neck Cord

Your AngelMed Guardian system includes a neck cord and a belt case for carrying the EXD. These accessories help you to keep the EXD close by at all times. The belt case has a built-in belt clip.

Belt Case



The neck cord has a break-away safety feature. If you pull hard on the neck cord, it automatically opens and falls from your neck. This feature protects you if the neck cord or EXD gets caught on something.



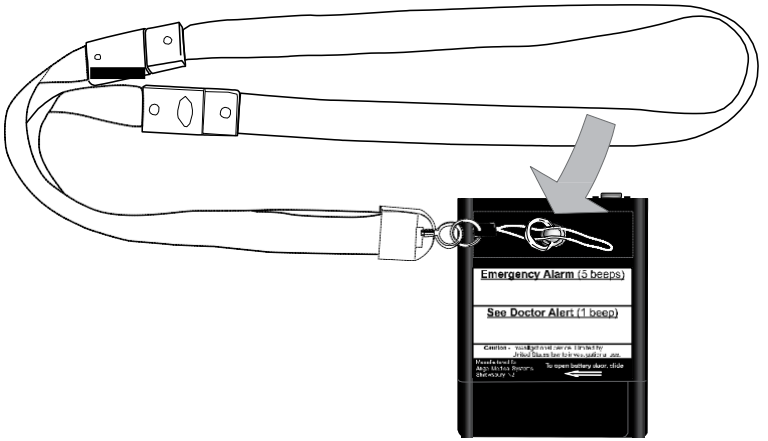
Neck Cord

Warning

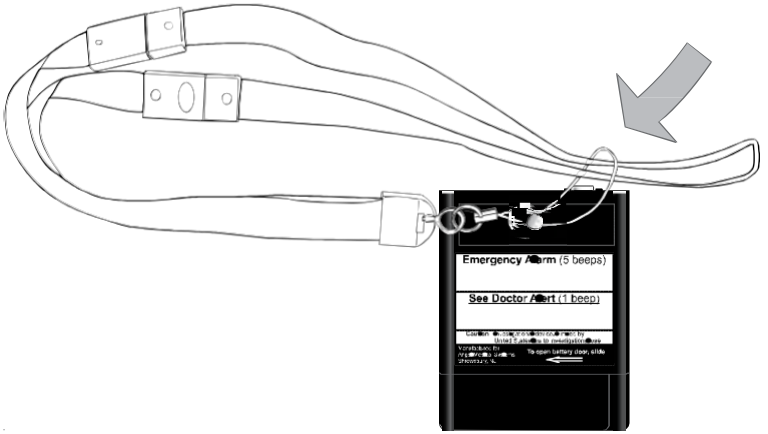
Do not use any neck cord except the one supplied by Angel Medical Systems. Many neck cords do not have a breakaway safety feature, which protects you from injury if your EXD or neck cord gets caught on something.

How to Attach the Neck Cord to the EXD

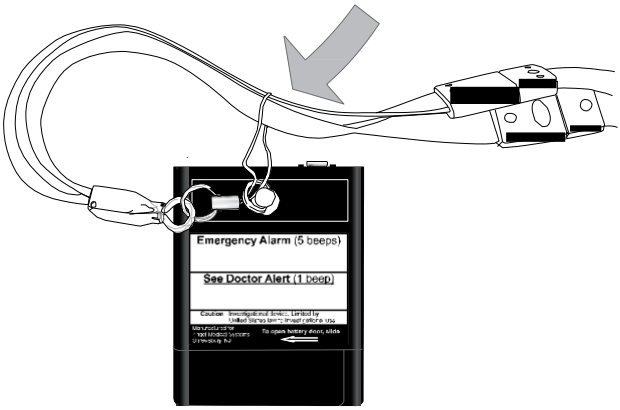
7. Insert the string loop at the end of the neck cord through the EXD's metal attachment ring.



8. Insert the neck cord through the string loop.



9. Slide the string loop down the neck cord.



10 Care and Maintenance

Warning

Contact your doctor if any of these statements are true:

- You sense any problems with your IMD.
- Your EXD is damaged.
- If after replacing the battery, you don't hear the short beep ("chirp") when you press the EXD's *Silence Alarm/Check Battery* button.
- Your EXD battery power is low and you need help replacing the EXD battery.

These conditions indicate your AngelMed Guardian system is not functioning properly and may fail to warn you when it should.

Take care of your AngelMed Guardian system as follows:

Check the EXD's battery power once a week See Section 8, *EXD Battery* on page 31 for details.

Keep the EXD dry. The EXD is not waterproof, so getting it wet may damage its electronics. If you accidentally drop the EXD into a sink, tub, or similar place, call your doctor.

Never use strong cleaners or solvents to clean the EXD. If the surface of the EXD gets dirty, you can clean it with a cloth lightly dampened in clean water.

Don't expose your EXD to extreme temperatures. It may stop operating.

- In cold climates (below 32°F (0°C)), keep your EXD underneath your outer clothing so that it does not come into contact with the frigid air.
- In hot climates (above 122°F (50°C)), keep your EXD out of direct sunlight.

If the EXD is dropped from a height of greater than 3 feet (0.9 meters) or if it strikes another object sharply, see your doctor for a replacement EXD. If the EXD is dropped from a lesser height, push the *Silence Alarm/Check Battery* button. If the device beeps one time, it is okay; if it does not beep, see your doctor for a replacement.

Don't expose your IMD and EXD to atmospheric pressures below 10.2 psi (703 hPa) or above 15.58 psi (1074 hPa). Operation of these devices outside this range is not recommended.

11 Travel Information

Your AngelMed Guardian system is designed to go anywhere you go. With only a few of points to keep in mind, you can travel freely.

Travel Restrictions: Follow any travel restrictions that are recommended by your doctor.

EXD Temperature Ranges: Observe the EXD temperature ranges described on page 41 when visiting hot or cold climates.

Change the EXD Battery? Your EXD battery can work for about 6 months. Depending on when it was last replaced, the battery could run out of power while you are away. If you intend to travel for an extended time period, we recommend that you change the battery before you leave. It's also a good idea to take a spare battery along with you whenever you travel. For instructions on changing the battery, see *How to Replace the EXD Battery* on page 34. If you need help changing the battery, contact your doctor for assistance.

Security Systems: Your IMD may trigger security systems like those found at airports. Always carry your ID card, which you can show the security officer, if necessary. For more details on this topic, see *Security Systems* on page 22.

Patient Manual: Take this manual with you when you travel. It contains information that may be helpful to you as you come across places, environments, or circumstances that you don't normally encounter.

Different Time Zone: If you travel to another time zone, ask your doctor if your AngelMed Guardian system's trending check should be set for another time.

This check occurs every day at the same time and warns you if it finds a problem. Ideally, this check should occur when you are awake. If you travel to another time zone, this check may no longer occur when you are awake.

12 EXT Battery Troubleshooting

Problem	Possible Causes	What to Do
EXD does not beep when the *Silence Alarm/Check Battery* button is pushed.	Battery power is depleted.	Replace the battery.
	Battery has been inserted backwards.	Reinsert the battery.
	Wrong battery has been installed.	Replace the battery with the AngelMed custom EXD battery.
EXD beeps once every 30 seconds.	Battery power is low.	Replace the battery.

13 Glossary

Diathermy

A medical procedure that uses microwaves or sound waves to heat body tissue for therapeutic purposes.

Electromagnetic interference (EMI)

Waves of energy from electrical equipment that interfere with the proper operation of nearby equipment.

Electrosurgical cautery

A medical procedure that uses electrical currents to burn body tissue for surgical purposes.

External Device (EXD)

The pager-sized device that uses sound (i.e., beeps) and a flashing light to warn you to seek medical attention.

External defibrillation

The use of external equipment designed to stop rapid heartbeats.

Implanted cardioverter-defibrillator (ICD)

An implanted device used to stop rapid heartbeats.

Implantable Medical Device (IMD)

The device that is implanted under the skin to monitor your heart. It vibrates to warn you to seek medical attention.

Lithotripsy

A medical procedure that uses shock waves to break up hardened bodily secretions.

Magnetic resonance imaging (MRI)

A diagnostic technique that uses radio waves to produce images of internal body tissues.

Myocardial ischemia

A condition where a portion of the heart has insufficient blood flow. This can lead to a heart attack.

Pacemaker

An implanted device used to speed up a slow heartbeat.

Radiofrequency (RF) ablation

A medical procedure that uses heat energy to destroy a small area of body tissue.

Transcutaneous Electrical Nerve Stimulation (TENS)

The electrical stimulation of the skin to relieve pain.

Ultrasound therapy

A diagnostic technique that uses sound waves to produce images of internal body tissues.

Index

Notes

Notes

Notes

Notes
Patient Instructions

Physician:
Copy and write the EXD back label instructions here.