# SUMMARY OF SAFETY AND EFFECTIVENESS DATA

## I. GENERAL INFORMATION

Device Generic Name: Automated External Defibrillator

Device Trade Name: X Series®, R Series®, Propaq® MD, AED Pro®, AED 3™ BLS Professional Defibrillators, Pro-Padz Radiotransparent Electrode, SurePower™ Battery Pack, SurePower II™ Battery Pack, AED Pro® Non-Rechargeable Lithium Battery Pack, AED 3™ Battery Pack, SurePower™ Charger, and SurePower™ Single Bay Charger

Device Product Code: MKJ

Applicant's Name and Address: ZOLL Medical Corporation
271 Mill Rd
Chelmsford, MA 01824

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P160022

Date of FDA Notice of Approval: December 27, 2017

The X Series system, which includes an automated external defibrillator (AED), has been commercially available since March 21, 2012, when it was first cleared by FDA under K112432. Propaq MD is an alternate configuration of the X Series that was developed by making insignificant changes to the cleared X Series. The R Series system, which includes an automated external defibrillator (AED), has been commercially available since August 17, 2006, when it was first cleared by FDA under K060559. The AED Pro system has been commercially available since February 4, 2005, when it was first cleared by FDA under K041892. P160022 has been submitted in response to the Final Order issued January 29, 2015, in the Federal Register Volume 80 Number 19, Docket No. FDA-2013-N-0234 and republished February 3, 2015, in the Federal Register Volume 80 Number 22, Docket No. FDA-2013- N-0234. The Final Order required premarket approval of marketed pre-amendment Class III Automated External Defibrillators (AED), product code MKJ. Products affected by this Order are the X Series, R Series and AED Pro systems. The AED 3 BLS system was not commercially available prior to approval of this Premarket Approval Application. A combination of postmarket experience data, relevant literature, clinical data, animal testing, and in-vitro bench testing has been reviewed to demonstrate a reasonable assurance of safety and effectiveness for the X Series, R Series, AED Pro, and AED 3 BLS systems.

## II. INDICATIONS FOR USE

### A. X Series

**Defibrillator Function**

The X Series system is indicated for defibrillation on victims of cardiac arrest where there is apparent lack of circulation as indicated by:

- Unconsciousness.
- Absence of breathing.
- Absence of pulse.

The X Series system in the Manual mode is indicated for synchronized cardioversion of certain atrial or ventricular arrhythmias. A qualified physician must decide when synchronized cardioversion is appropriate.

The X Series system Semiautomatic and Manual mode is indicated for use in early defibrillation programs where the delivery of a defibrillator shock during resuscitation involving CPR, transportation, and definitive care are incorporated into a medically-approved patient care protocol.

The X Series system Semiautomatic and Manual mode is indicated for adult and pediatric patients.

**Electrocardiogram (ECG) Monitoring**

The X Series system is indicated to monitor and/or record 3-, 5-, or 12-lead electrocardiogram (ECG) waveform and heart rate, and to alarm when heart rate is above or below limits set by the operator. ECG monitoring is indicated for patients from newborn (neonate) to adult, with and without heart dysfunction.

**CPR Monitoring**

The X Series system is indicated to provide visual and audio feedback via the CPR Monitoring function, designed to encourage rescuers to perform chest compressions at the AHA/ERC recommended depth and rate of 2 inches (5 cm) and 100 compressions per minute. The CPR Monitoring function is indicated for adult and pediatric patients.

**External Transcutaneous Pacing**

The X Series system is indicated for temporary external cardiac pacing in conscious or unconscious patients as an alternative to endocardial stimulation. External Pacing is indicated for pediatric and adult patients.

**Non-Invasive Blood Pressure Monitoring**

The X Series system is indicated for use to make non-invasive measurements of arterial pressure and heart rate, and to alarm if either parameter is outside of the limits set by the user. The non-invasive blood pressure monitoring feature is indicated for patients from newborn (neonate) to adult.

**Temperature Monitoring**

The X Series system is indicated for use to make continuous temperature measurements of rectal, esophageal, or surface temperatures, and to alarm if the temperature is outside of the limits set by the user. The temperature monitoring feature is indicated for use in patients from newborn (neonate) to adult.

**SpO2 Monitoring**

The X Series system is indicated for use for continuous noninvasive monitoring of functional oxygen saturation of arterial hemoglobin (SpO2), pulse rate, and/or carboxyhemoglobin saturation (SpCO), methemoglobin saturation (SpMet), total hemoglobin (SpHb), oxygen content (SpOC), pleth variability index (PVI), and perfusion index (PI) via the pulse Co-oximeter and accessories. The pulse Co-oximeter and accessories are indicated for use on adult, pediatric, and neonatal patients during both no motion and motion conditions, and for patients who are well or poorly perfused, in hospitals, hospital-type facilities, or in mobile environments.

**Respiration Monitoring**

The X Series system is indicated for use to continuously monitor respiration rate and to alarm if the rate falls outside of the range set by the operator. Because the measurement method actually measures respiratory effort, apnea episodes with continued respiratory effort (such as obstructive apnea) may not be detected. It is not intended to be used as an apnea monitor. The respiration monitoring feature is indicated for use on patients from newborn (neonate) to adult.

**CO2 Monitoring**

The X Series system is indicated for use in continuous noninvasive measurement and monitoring of carbon dioxide concentration of the expired and inspired breath and breath rate. The CO2 monitoring feature is indicated for use on patients from newborn (neonate) to adult.

**Invasive Pressure Monitoring**

The X Series system is indicated for use to display and make continuous invasive pressure measurements via a compatible pressure transducer. The invasive pressure monitoring feature is indicated for use on patients from newborn (neonate) to adult.

**12-Lead Analysis**

The X series system is indicated for use in acquiring, analyzing and reporting physiological data via 12-lead ECG Analysis, and to provide interpretation of the data for consideration by caregivers. The 12-lead ECG Analysis feature is indicated for use on adults (> 18 years of age).

**Web Console**

The X Series system is indicated for the remote display of physiological data displayed on connected X Series systems via the Web Console feature, including electrocardiogram (ECG), non-invasive blood pressure (NIBP), temperature, and heart rate.

**B. <u>R Series</u>**

**Defibrillator Function**

The R Series system is indicated for defibrillation on victims of cardiac arrest where there is apparent lack of circulation as indicated by:

- Unconsciousness.
- Absence of breathing.
- Absence of pulse.

The R Series system in the Manual mode is indicated for synchronized cardioversion of certain atrial or ventricular arrhythmias. A qualified physician must decide when synchronized cardioversion is appropriate.

The R Series system Semiautomatic and Manual mode is indicated for use in early defibrillation programs where the delivery of a defibrillator shock during resuscitation involving CPR, transportation, and definitive care are incorporated into a medically-approved patient care protocol.

The R Series system Semiautomatic and Manual mode is indicated for adult and pediatric patients.

**ECG Monitoring**

The R Series system is indicated to evaluate the patient's heart rate or ECG morphology via ECG monitoring. In ECG monitoring mode, the feature is indicated for use by personnel who are qualified by training in the use of the R Series defibrillator, basic life and/or advanced life support, or other physician-authorized emergency medical training.

**Real CPR Help**

The R Series system is indicated to provide visual and audio feedback via the CPR Help feature, which is designed to encourage rescuers to perform chest compressions at the AHA/ERC recommended depth and rate of 2 inches (5 cm) and 100 compressions per minute.

**External Pacemaker**

The R Series system is indicated for temporary external cardiac pacing in conscious or unconscious patients as an alternative to endocardial stimulation. External Pacing is indicated for pediatric and adult patients.

**SpO2 Monitoring**

The R Series system is indicated for the continuous, noninvasive monitoring of arterial oxygen saturation (SpO2) and pulse rate during both no motion and patient motion conditions for adult patients, and no motion conditions for pediatric and neonatal patients in a hospital or prehospital environment.

**EtCO2 Monitoring**

The R Series system is indicated for the continuous noninvasive monitoring of end tidal carbon dioxide (EtCO2) and respiration rate in patients requiring ventilator support, in-hospital transport, or anesthesia. EtCO2 Monitoring is indicated for in patients from newborn (neonate) to adult.

**Non-Invasive Blood Pressure Monitoring (NIBP)**

The R Series system is indicated for the non-invasive measurement of arterial blood pressure for resting patients in critical care and in-hospital transport. The NIBP feature is indicated to measure blood pressure for patients from newborn (neonate) to adult.

## C. <u>AED Pro</u>

The AED Pro system is indicated for use on victims of cardiac arrest with apparent lack of circulation as indicated by:

- Unconsciousness
- Absence of breathing, and
- Absence of pulse and other signs of circulation.

The device is also indicated for use when ECG monitoring is indicated to evaluate the patient's heart rate or ECG morphology. The AED Pro system is indicated for adult and pediatric patients.

### D. AED 3 BLS

The ZOLL AED 3 system is indicated for use when a suspected cardiac arrest victim has an apparent lack of circulation as indicated by:

- Unconsciousness
- Absence of breathing, and
- Absence of pulse and other signs of circulation.

The AED 3 system is indicated for adult and pediatric patients.

## III. CONTRAINDICATIONS

**X Series and R Series**

**Semiautomatic Operation Contraindications for Use**

The rhythm analysis function may not reliably identify ventricular fibrillation in the presence of an implanted pacemaker. Inspection of the electrocardiogram and clinical evidence of cardiopulmonary arrest should be the basis for any treatment of patients with implanted pacemakers. Do not use the rhythm analysis function during patient movement on a stretcher. A patient must be motionless during ECG analysis. Do not touch the patient during analysis. Cease all movement of the stretcher prior to analyzing the ECG.

**AED Pro and AED 3 BLS**

**Defibrillation**

Never use the unit for defibrillation when the patient

- Is conscious;
- Is breathing; or
- Has a detectable pulse or other sign of circulation.

**CPR Monitoring**

The CPR monitoring function is not intended for use on patients under 8 years of age.

## IV. WARNINGS AND PRECAUTIONS

Warnings and Precautions for AED Plus and Fully Automatic AED Plus can be found in the device's Operator's and Administrator's Guides.

## V. DEVICE DESCRIPTION

### A. X Series

The currently marketed ZOLL® X Series™ unit is a portable defibrillator that combines defibrillation and external pacing with the following monitoring capabilities: ECG, CO-Oximeter, Noninvasive Blood Pressure, IBP, CO2, Temperature, and Respiration. Functions are offered as options and functions can be configured to meet the needs of a particular application. The product is designed for use in both the hospital and EMS environment.

The X Series is powered by auxiliary power as well as a rechargeable battery pack that quickly recharges when the X Series is connected to auxiliary power. In addition, user can use a ZOLL SurePower Battery Charger or SurePower Single Bay Charger to recharge and test the X Series battery.

**Figure1: Front Panel**

**A.** **B.**

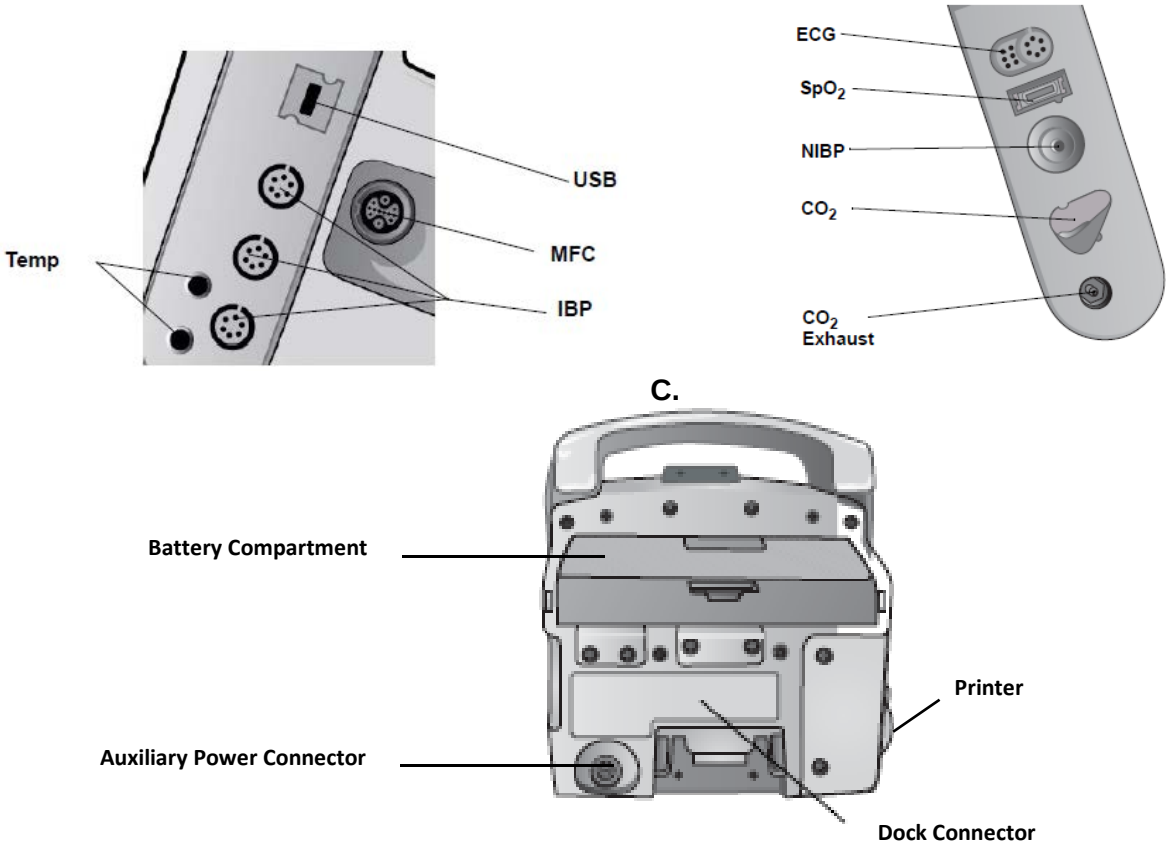



**Figure 2:** (A) Right Side Patient Connector; (B) Left Side patient connector; (C) Back view of device.

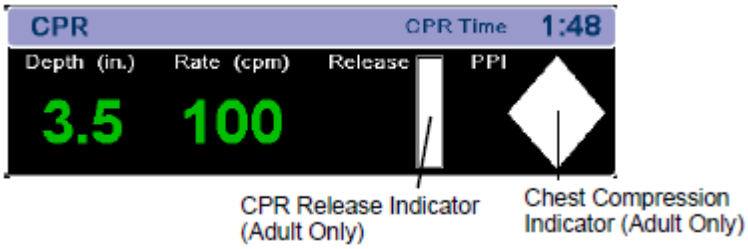
The X Series device is an automated external defibrillator with manual capabilities and may be configured to operate in Manual, Advisory or Semiautomatic modes. In Advisory and AED modes, some features of the device are automated and an ECG detection algorithm is used to analyze a patient's presenting rhythm and determine the appropriateness of defibrillation shock. Units may be configured to automatically charge, analyze, recharge, and prompt the operator to "PRESS SHOCK," depending on local protocols. The unit is switched from AED mode to Manual mode for ACLS use by pressing the appropriate key on the front panel.

When operating in manual configuration, the device operates as a conventional defibrillator where the device's charging and discharging is fully controlled by the operator. In manual mode operation, the device may be also used to perform synchronized cardioversion using the patient's R-wave as a timing reference.

The X Series units utilize a biphasic defibrillation waveform with a shape that varies slightly depending upon selected energy and patient impedance.

The X Series defibrillators contain an external pacemaker for the emergency treatment of hemodynamically compromising bradycardia, bradycardia with escape rhythms that are unresponsive to pharmacological therapy, refractory tachycardia (supraventricular or ventricular) and bradyasystolic cardiac arrest. The X Series has two pacer mode settings: Demand and Fixed.

When used with ZOLL electrodes with built-in CPR Sensor, the CPR monitoring function of the device assists caregivers during cardiopulmonary resuscitation (CPR) by evaluating the rate and depth of chest compression and providing audio and visual feedback to encourage rescuers to perform chest compressions at the American Heart Association (AHA) and European Resuscitation Council (ERC) recommended rate and depth. For Pediatric patients, the functionality is limited to CPR timer and the numeric display of the actual rate and depth of chest compression. The CPR features that the X Series unit provides differ depending whether adult or pediatric CPR electrodes are attached to the unit. The X Series unit automatically senses which type of CPR electrode is attached, and provides the CPR features as follows:

| **CPR Feature** | **Adult CPR Features (Available when Adult CPR Electrodes are attached)** | **Pediatric CPR Features (Available when Pediatric CPR Electrodes are attached.)** |
|---|---|---|
| **CPR Voice Prompts**<br>Issues voice prompts related to the depth of chest compressions as feedback to rescuers performing CPR. Two voice prompts are available for this purpose:<br>• Push Harder<br>• Good Compressions | + | |
| **CPR Metronome**<br>Used to encourage rescuers to perform chest compressions at a rate consistent with AHA/ERC recommended guidelines | + | + |
| ***FULLY RELEASE* Prompt**<br>Display the text prompt FULLY RELEASE, which instructs rescuers to lift (fully release) their hands from the patient's chest after compressions to allow full recoil. | + | |
| ***CPR Dashboard***<br>  | | |
| • CPR Rate and Depth Measurements<br>Displays the CPR rate and depth measurements. With pediatric CPR electrodes, the values always display in green. For adult, default display of values is in green. However, if the unit detects CPR Performance (compression rate and/or rate) is below the AHA/ERC recommended value, the corresponding value(s) displays in yellow (needs improvement). | + | + |
| • CPR Release Indicator<br>The CPR Release Indicator is intended to provide feedback on the rescuer's ability to fully lift his hands off the sternum during the upstroke of the compression. The release indicator is filled when | + | |

| CPR Feature | Adult CPR Features (Available when Adult CPR Electrodes are attached) | Pediatric CPR Features (Available when Pediatric CPR Electrodes are attached.) |
|---|---|---|
| rescuers release compressions more quickly, whereas the indicator will only fill partially if chest compression release is slow. | | |
| • Chest Compression Indicator<br>This diamond-shaped figure provides a quick, overall indicator of how well the rescuer's combined rate and depth of chest compressions match the AHA/ERC recommendations for adult CPR. | + | |
| • CPR Countdown Timer<br>Indicate the time (in minutes and seconds) left in the current CPR interval. | + | + |
| **CPR Depth Idle Time Display**<br>This display indicates the elapsed time in minutes and seconds since the last detected chest compression. | + | + |
| **CPR Compression Bar Graph**<br>display a CPR compression bar graph next to the dashboard that is computed from the CPR sensor signals | + | |

**Table 1: Listing of CPR features with Adult CPR Electrode vs. Pediatric CPR Electrode when used with X Series device**

When used with ZOLL electrodes with built-in CPR Sensor, See-Thru CPR functionality allows the rescuer to see a close approximation of the patient's underlying ECG rhythm while performing CPR by removing not all, but much of the CPR artifact from the ECG signal.

X Series units can perform ECG monitoring through ECG electrodes connected to the 3-, 5-, or 12-lead ECG patient cables or through Multi-Function electrodes, or standard defibrillation paddles.

The X Series device incorporates features such as 12-Lead ECG Interpretive Analysis, $SpO_2$ Monitoring, CO2 Monitoring, and Non-Invasive Blood Pressure (NIBP) Monitoring which are cleared OEM technology. When CO2 monitoring is not available, the X Series derives the respiration rate through impedance pneumography. A brief description of X Series features, mentioned above, is provided below:

- The device supports up to 3 Invasive Blood Pressure (IBP) measurement channels. These channels can be used to measure arterial, venous, or intracranial pressures using invasive traducers with 5uV/V/mmHg sensitivity (AAMI BP-22). The functionality is intended for Newborn (neonate) to adults.

- X Series supports two simultaneous temperature measurements. YSI400/YSI700 series probes (reviewed and cleared by FDA under K883793) are used to make temperature measurements.

- X Series also provides a Web Console functionality allows remote personnel to view the content of one or multiple (up to forty) X Series device screens. Users of the new Web Console features can only view the data on monitors remotely, and cannot operate the X

Series device, silence device alarms, or initiate any patient treatment remotely – this can only be done directly on the device, at the patient's bedside.

- The X Series provides TBI Dashboard functionality which creates an embedded web page that consolidates concurrently displayed data on the X Series for SBP (systolic blood pressure), $SpO_2$, EtCO2 data, and timer into graphical trend formats and a countdown timer for ventilations. The web page can be requested, through a Bluetooth connection, using a standard web browser on a viewing device for display.

- The device is equipped to communicate through a Wi-Fi access point, Bluetooth-equipped device, Ethernet cable, or USB cellular modem. User can send data through a wireless connection to a remote recipient via a ZOLL server configured for their unit or user can transfer data to a PC through a wireless connection or via an Ethernet cable. The data available to transmit to a remote location includes 12-lead report snapshots (including trend data) as well as the Disclosure logs for up to 15 cases at one time.

- A wide-format 80 mm printer option is available in the X Series. The printing option allows user to print the following patient information:
    - Waveforms;
    - Reports; and
    - Trends.

Propaq MD is an alternate configuration of the X Series that was developed by making insignificant changes to the cleared X Series. The differences between the X Series and the proposed Propaq MD device are as follows:

- The Propaq MD keypad has a Sync button in the same place as the Analyze button of the X-Series. There is a soft key on the Propaq MD for Analyze and a soft key on the X Series for Sync.
- The silicone keypad in the Propaq MD is a dark blue instead of the X-Series lighter blue color. The keypad goes over the exact same set of electronic keys as the X Series.
- The housing parts are molded from the same molds but come in a slightly different shade of gray.

Apart from the changes described above, both the devices are identical from a hardware standpoint and use the same software (See Figure 3).

**Front View X Series**

**Front View Propaq MD**

**Figure 3: Front view of X Series and Propaq MD**

### B. R Series

The ZOLL R Series® External Defibrillator is intended for defibrillation, Noninvasive Transcutaneous Pacing, multi-parameter monitoring of patient vital signs, including ECG Monitoring, Pulse Oximetry, Non-Invasive Blood Pressure measurement, End Tidal CO2, CPR performance and data printing and recording for resting patients in critical care and transport. The ZOLL R Series is intended for use by qualified medical personnel who are trained and authorized to respond to medical emergencies, to facilitate the ability to monitor and assess the physiological characteristics of the indicated patients in a critical care environment. The design facilitates table top use while still providing a light weight and easy to carry device for transport.

The R Series is powered by auxiliary power as well as an easily replaceable battery pack that quickly recharges when the R Series is connected to auxiliary power. In addition, user can use a ZOLL SurePower Battery Charger or SurePower Single Bay Charger to recharge and test the R Series battery.

R Series has 3 different models: R Series ALS, R Series BLS and R Series Plus. All 3 models are essentially identical from a hardware standpoint, except for the difference in the front panel assembly (discussed below), and use the same software.

- **R Series ALS** is a manual/advisory external defibrillator which also supports Transcutaneous Pacing, multi-parameter monitoring of patient vital signs, including ECG Monitoring, Pulse oximetry, Non-Invasive Blood Pressure measurement, End Tidal CO2, CPR performance and data printing and recording for resting patients in critical care and transport. Refer to Table 3 for complete list of features offered by R Series ALS. Front panel contains silicone buttons and all the controls and indicators are fully viewable for the ALS user (See Figure 4).

**Figure 4: R Series ALS and its Front Panel**

- **R Series BLS and R Series Plus** are designed to provide personnel trained and familiar with the equipment a simplified operator interface. The devices are dual mode defibrillator that combines an AED operating mode with manual override capability. The ZOLL R Series BLS/Plus Defibrillator have a front panel which contains lighted buttons that are illuminated when Manual Mode is selected and the Confirm Manual Mode softkey is selected by the operator. Both devices power up in AED Mode as shown in Figure 5 and Figure 7. Once the operator switches to Manual Mode a set of control buttons are illuminated and activated on the front panel of the unit (refer to Figure 6 and Figure 8). Additionally, the pacer controls, which were recessed and covered with the pacer door (identified in Figure 8) in AED mode, are available once the user switches to manual mode. While changing from AED Mode to Manual mode, the previously selected energy level is maintained. R Series Plus differs from BLS in the features offered with the model. Refer to Table 3 for more details.

The difference between R Series ALS and BLS/Plus Front Panel is discussed in Table 2.

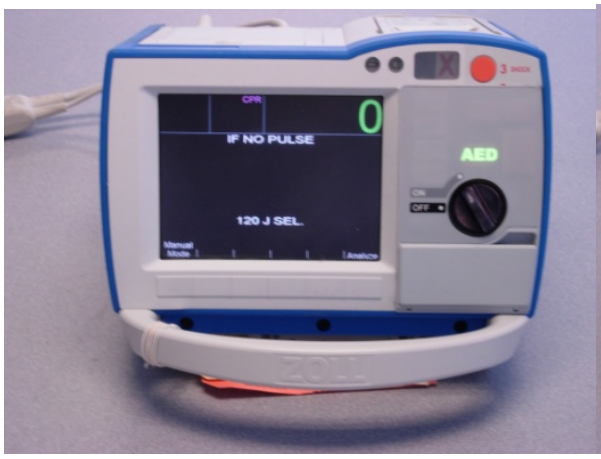



***Figure 5: BLS/Plus in AED mode***

***Figure 6: BLS/Plus in Manual Mode***

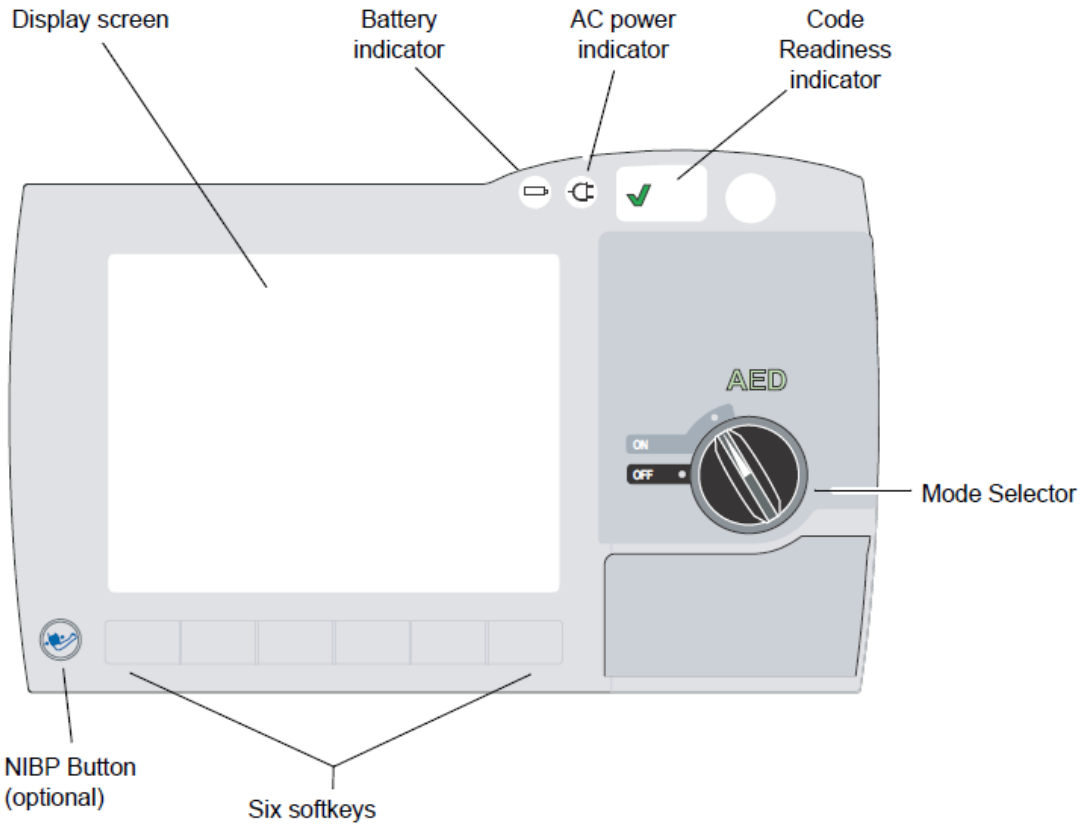



**Figure 7: R Series BLS/Plus Front Panel (AED Mode)**

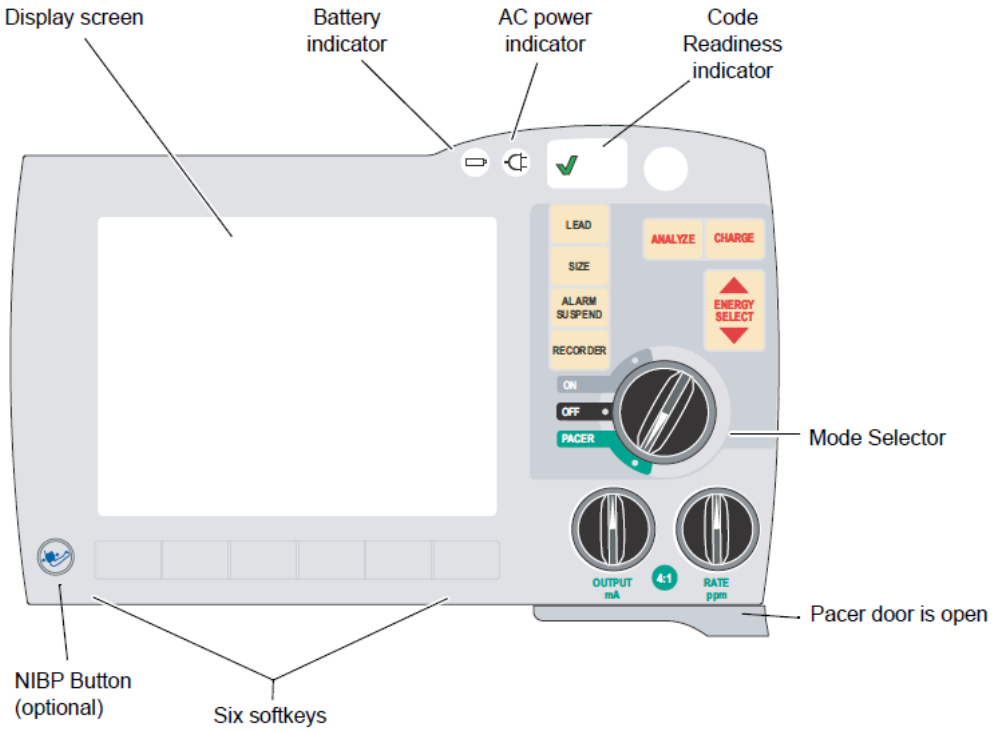


**Figure 8: R Series BLS/Plus Front Panel (Manual Mode)**

Front Display panel of ZOLL R Series ALS differs from BLS/Plus in following manner.

| ZOLL R Series ALS | ZOLL R Series BLS and Plus |
|---|---|
| Silicone buttons and all the controls and indicators are fully viewable for the ALS user. | Polyester key covering with backlit control keys for BLS & ALS users, recessed and covered pacer controls until manual mode is switched on. |

**Table 2: Difference between R Series ALS and BLS/Plus Front Panel**

| Feature | ALS Model | BLS Model | Plus Model |
|---|---|---|---|
| Defibrillator | | | + |
| • Manual Defibrillator | + | + | + |
| • Advisory Defibrillator | + | + | + |
| • AED | | + | + |
| Real CPR Help | + | + | + |
| See-Thru CPR | + | | + |
| Perfusion Performance Indicator™ | + | | + |
| OneStep system | + | + | + |
| Code Readiness testing system | + | + | + |
| Integrated hands free electrode mounting | + | + | + |
| Universal operating system | + | + | + |
| Defib activity log | + | + | + |
| CPR voice prompts | + | | + |
| 5.8 Ah rechargeable lithium-ion battery | + | + | + |
| 90mm strip chart writer | + | + | + |
| Integrated AC power | + | + | + |
| Built-in test port | + | + | + |
| Compact Flash card slot | + | + | + |
| USB device port | + | | + |
| Wi-Fi communication | + | | + |
| EtCO2 | + | | + |
| NIBP | + | | + |

| Feature | ALS Model | BLS Model | Plus Model |
|---|---|---|---|
| Pacing | + | + | + |
| SpO2 | + | + | + |

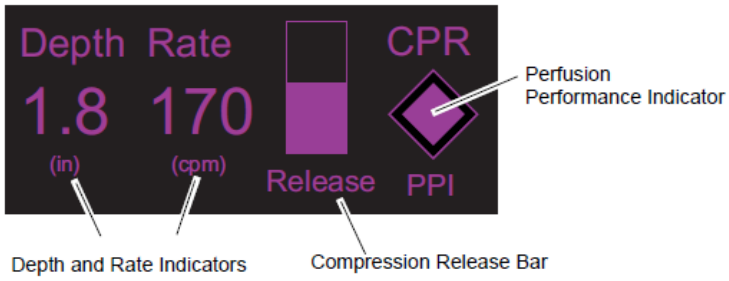
**Table 3: List of features offered with each R Series Model**

The R Series ALS device is an external defibrillator that may be configured to operate in manual or advisory mode while the R Series BLS and Plus are external defibrillators that may be configured to operate in AED, Manual or Advisory modes. In Advisory and AED modes, some features of the device are automated and an ECG detection algorithm is used to determine the appropriateness of defibrillation shock. Depending on local protocols, the unit may be configured to automatically analyze the ECG, charge the defibrillator (if appropriate), and prompt the operator to PRESS SHOCK between periods of CPR.

When operating in manual configuration, the device operates as a conventional defibrillator where the device's charging and discharging is fully controlled by the operator. In manual mode, the device may be also used in synchronized mode to perform synchronized cardioversion using the patient's R-wave as a timing reference.

The currently marketed R Series device utilizes a biphasic defibrillation waveform with a shape that varies slightly depending upon selected energy and patient impedance. R Series defibrillators contain an external pacemaker for the emergency treatment of hemodynamically compromising bradycardia, bradycardia with escape rhythms that are unresponsive to pharmacological therapy, refractory tachycardia (supraventricular or ventricular) and bradyasystolic cardiac arrest. The R Series has two pacer mode settings: Demand and Fixed.

When used with ZOLL electrodes with built-in CPR Sensor, the CPR monitoring function of the R Series device assists caregivers during cardiopulmonary resuscitation (CPR) by evaluating the rate and depth of chest compressions and providing audio and visual feedback to encourage rescuers to perform chest compressions at the AHA/ERC recommended rate and depth. For Pediatric patients, the functionality is limited to CPR timer and the numeric display of the actual rate and depth of chest compressions. The CPR features that the R Series unit provides differ depending whether adult or pediatric CPR electrodes are attached to the unit. The R Series unit automatically senses which type of CPR electrode is attached, and provides the CPR features as follows:

| CPR Feature | Adult CPR Features (Available when Adult CPR Electrodes are attached) | Pediatric CPR Features (Available when Pediatric CPR Electrodes are attached.) |
|---|---|---|
| **CPR Voice Prompts**<br><br>Issues voice prompts related to the depth of chest compressions as feedback to rescuers performing CPR. Two voice prompts are available for this purpose:<br><br>• Push Harder<br>• Good Compressions | + | |
| **CPR Metronome**<br><br>Used to encourage rescuers to perform chest compressions at a rate consistent with AHA/ERC recommended guidelines | + | + |
| ***FULLY RELEASE* Prompt**<br><br>Display the text prompt FULLY RELEASE, which instructs rescuers to lift (fully release) their hands from the patient's chest after compressions to allow full recoil. | + | |
| ***CPR Dashboard***<br><br>  | | |
| • CPR Rate and Depth Measurements<br>Displays the CPR rate and depth measurements. For adult only, if the unit detects CPR Performance (compression rate and/or rate) is below the AHA/ERC recommended value, the corresponding value(s) will be highlighted and displayed in red (needs improvement). | + | + |
| • CPR Release Indicator<br>The CPR Release Indicator is intended to provide feedback on the rescuer's ability to fully lift his hands off the sternum during the upstroke of the compression. | + | |

| CPR Feature | Adult CPR Features (Available when Adult CPR Electrodes are attached) | Pediatric CPR Features (Available when Pediatric CPR Electrodes are attached.) |
|---|---|---|
| The release indicator is filled when rescuers release compressions more quickly, whereas the indicator will only fill partially if chest compression release is slow. | | |
| • Chest Compression Indicator<br>This diamond-shaped figure provides a quick, overall indicator of how well the rescuer's combined rate and depth of chest compressions match the AHA/ERC recommendations for adult CPR. | + | |
| **CPR Depth Idle Time Display**<br>This display indicates the elapsed time in minutes and seconds since the last detected chest compression. | + | + |
| **CPR Compression Bar Graph**<br>display a CPR compression bar graph next to the dashboard that is computed from the CPR sensor signals | + | |

**Table 4: Listing of CPR features with Adult CPR Electrode vs. Pediatric CPR Electrode when used with R Series device**

When used with ZOLL electrodes with built-in CPR Sensor, See-Thru CPR functionality allows the rescuer to see a close approximation of the patient's underlying ECG rhythm while performing CPR by removing not all, but much of the CPR artifact from the ECG signal.

The R Series can perform ECG monitoring through ECG electrodes connected to the 3- or 5-Lead ECG patient cables or through Multi-Function electrodes, or standard defibrillation paddles.

The R Series device incorporates features such as SpO2 Monitoring, CO2 Monitoring, and Non-Invasive Blood Pressure Monitoring which are cleared OEM technology.

R Series units can support data transfer through Wi-Fi (when used with R Series Data COMM Card or R Series Data COMM II Card), USB device connector and compact flash card slot. The R Series defibrillator automatically records defibrillation and cardioversion events, PACER mode information, heart rate alarms, and segments of ECG when the recorder is activated. Associated event information including device control settings, time, and date are also recorded.

A wide-format 80 mm printer option is available in the R Series. The printing option allows user to print the following patient information:

- Waveforms;
- Reports; and
- Trends.

### C. AED Pro

The ZOLL AED Pro® is a portable device designed to be used by trained emergency care personnel in both the hospital and pre-hospital arenas. The ZOLL AED Pro is designed for all emergent care situations and provides ECG and CPR monitoring of patients in critical care and transport. The AED Pro provides an ECG monitoring feature and manual override capabilities for physicians and appropriately trained rescue personnel. An Alternate configuration of AED Pro, the AED Pro AW (Air Worthy), was created by making non-significant changes to the device and accessories to improve the EMC performance. Changes included:

- EMI suppression coating to the enclosure (for Device only); and
- Addition of EMI/EMC suppression ferrite (Device and accessories).

**Figure 9: AED Pro Front Panel**

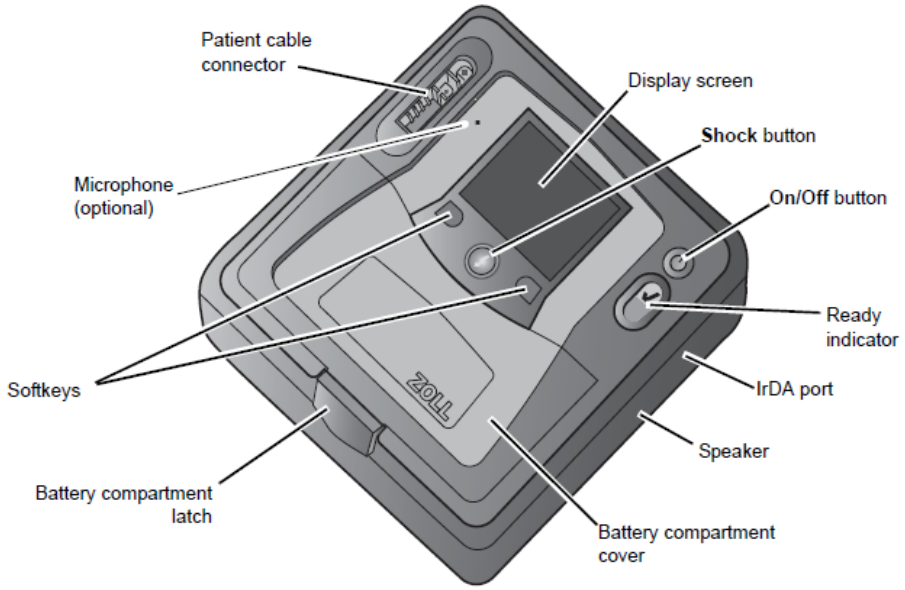



**Figure 10: AED Pro Front Panel**

The AED Pro device is an automated external defibrillator with manual override capabilities for physicians and appropriately trained rescue personnel. The device may be configured to operate in Manual or Semiautomatic mode.

The currently marketed AED Pro device utilizes a biphasic defibrillation waveform with a shape that varies slightly depending upon selected energy and patient impedance.

When used with ZOLL electrodes with built-in CPR Sensor, the CPR monitoring function of the AED Pro device assists caregivers during cardiopulmonary resuscitation (CPR) by evaluating the rate and depth of chest compressions and providing audio and visual feedback to encourage rescuers to perform chest compressions at the AHA/ERC recommended rate and depth. The following CPR monitoring features are offered with AED Pro.

- **CPR Metronome**
  Used to encourage rescuers to perform chest compressions at a rate consistent with AHA/ERC recommended guidelines.

- **CPR Compression Depth Gauge**
  AED Pro displays a gauge, which shows the depth of compression. Compression depth is correct when the bar extends downwards between the lower two lines which represent 2.0 and 2.4 inches (5 or 6 cm).

- **CPR Prompts**
  When the detected compression depth is consistently less than 2 inches (5 cm), the unit issues the voice and text prompt PUSH HARDER. If the rescuer responds by increasing compression depth to 2 inches (5 cm) or more, the unit issues the voice and text message GOOD COMPRESSIONS.

- **Fully Release prompt**
  Display the text prompt FULLY RELEASE, which instructs rescuers to lift (fully release) their hands from the patient's chest after compressions to allow full recoil.

When used with ZOLL electrodes with built-in CPR Sensor, See-Thru CPR functionality allows the rescuer to see a close approximation of the patient's underlying ECG rhythm while performing CPR by removing not all, but much of the CPR artifact from the ECG signal.

The AED Pro can perform ECG monitoring through ECG electrodes connected to the AED Pro ECG patient cable or through Multi-Function electrodes.

The AED Pro incorporates recording/memory capabilities which include recording ECG rhythms, event data, device identification, and, optionally, voice recording of rescuer and ambient sounds. Data exchange between the AED Pro and a personal computer is via IrDA (infrared interface standard) ports.

The AED Pro utilizes an easily replaced rechargeable lithium-ion battery pack marketed as SurePower Battery Pack, or the non-rechargeable lithium-ion battery packet marketed as AED Pro Non-Rechargeable Lithium Battery Pack.

## D. AED 3 BLS

The AED 3 BLS device is an automated external defibrillator (AED) that is designed to be used for both adult and child victims of sudden cardiac arrest. The AED 3 BLS defibrillator incorporates a sequence of audio and visual prompts to help rescuers follow established AHA/ERC Guidelines for use of AEDs.

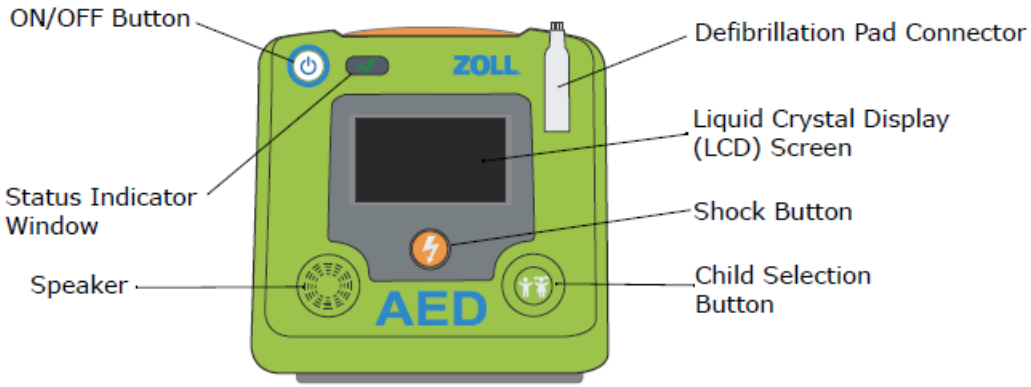



**Figure 11: Operating Controls and Indicators (Front Panel of device)**

**Figure 12: Operating Controls and Indicators (Rear Panel of device)**

***Graphical Display Area:***

The AED 3 supports the following device modes: AED Management Mode and Rescue Mode. In Rescue Mode, the LCD screen displays graphics that are coordinated with audio prompts to guide the rescuer through a rescue (see figure 11 and 12). In AED Management Mode, the icons on the touch screen allow the administrator to change configuration settings and upload files. The information displayed on the device LCD in each of these modes is identified below:

- **AED Management Mode**

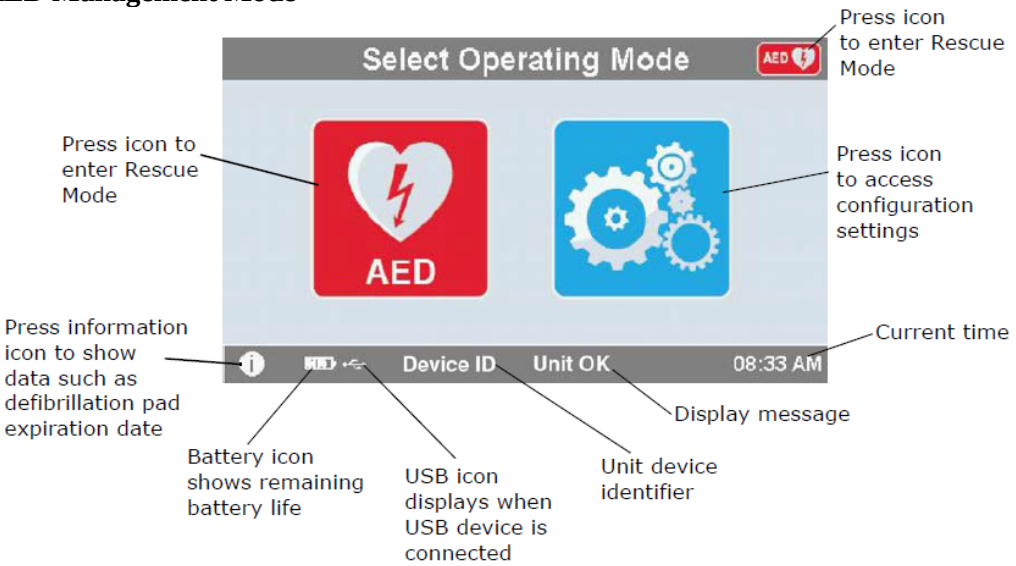



**Figure 13: Information displayed on device LCD in AED Management Mode**

- **Rescue Mode**

The ZOLL AED 3 BLS model can be configured to show the Lay Rescuer display, CPR only display, or CPR and ECG display.

**Lay Rescuer Display**

**Figure 14: Information displayed when configured for Lay Rescuer Mode**

| Display Parameter | Description |
|---|---|
| **CPR Countdown Timer** | Indicates the amount of time remaining in the CPR interval. |
| **CPR Depth of Compression Indicator** | A bar graph that displays the depth of chest compressions measured while the rescuer is performing CPR. Indicator lines are displayed in the bar graph at 2 and 2.4 inches (5 and 6 centimeters) of compression depth and provide reference points for rescuers performing CPR. |
| **User Prompt** | Indicates the amount of time that has elapsed since the start of the rescue. |
| **Elapsed Event Time** | Indicates the amount of time that has elapsed since the start of the rescue. |
| **Number of Shocks** | Indicates the total number of defibrillation shocks during the rescue. |

**Table 5: Description of display parameters for Lay Rescuer display.**

**CPR Only/CPR and ECG Displays**

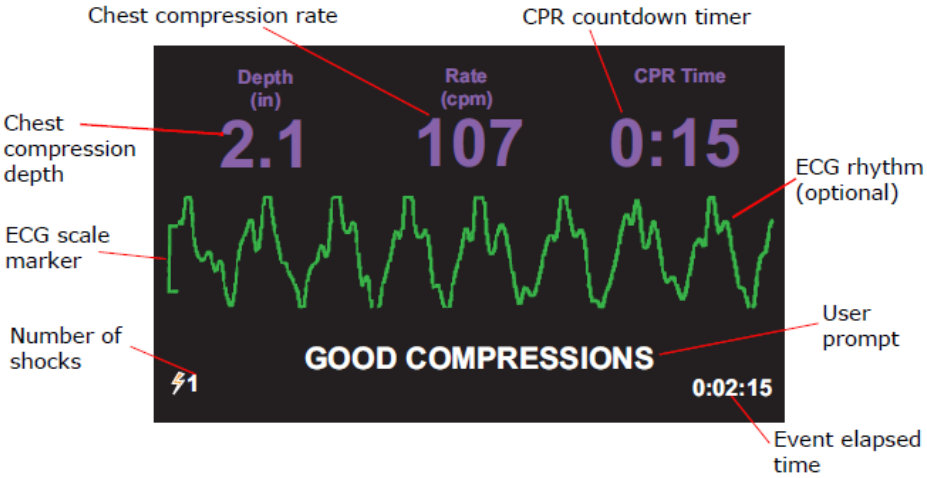



**Figure 15: Information displayed when configured for CPR Only/CPR and ECG Displays**

| Display Parameter | Description |
|---|---|
| **Chest Compression Depth** | Indicates the depth of the current CPR compressions. |
| **Chest Compression Rate** | Indicates the rate of the current CPR compressions. |
| **CPR Countdown Timer** | Indicates the amount of time remaining in the CPR interval. |
| **ECG Rhythm (optional)** | Displays the current ECG waveform. |
| **User Prompt** | Displays a visual message on the screen while simultaneously issuing an audio prompt. |
| **Event Elapsed Time** | The amount of time that has elapsed since the start of the rescue. |
| **Number of Shocks** | Indicates the total number of defibrillation shocks during the rescue. |

**Table 6: Description of display parameters for CPR Only/CPR and ECG Displays.**

## VI. ALTERNATIVE PRACTICES AND PROCEDURES

Defibrillation is the only currently available treatment for termination of ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT). Public access defibrillation is designed to provide potentially lifesaving treatment prior to the arrival of emergency personnel.

## VII. MARKETING HISTORY

The X Series device has been marketed in the U.S. since March 2012 and is commercially available in over 60 countries, including the United States, Canada, and countries in the European Union, Asia, and South America. As of December 2017, approximately 25,093 devices have been distributed in and outside the United States. It has not been withdrawn from marketing for any reason related to its safety or effectiveness.

The R Series device has been marketed in the U.S. since August 2006 and is commercially available in over 95 countries, including the United States, Canada, and countries in the European Union, Asia, and South America. As of December 2017, approximately 67,932 devices have been distributed in and outside the United States. It has not been withdrawn from marketing for any reason related to its safety or effectiveness.

The AED Pro device has been marketed in the U.S. since June 2004 and is commercially available in over 100 countries, including the United States, Canada, and countries in the European Union, Asia, and South America. As of December 2017, approximately 39,048 devices have been distributed in and outside the United States. It has not been withdrawn from marketing for any reason related to its safety or effectiveness.

The AED 3 BLS has not been marketed in the U.S. It has been marketed outside the US since March 2016 and is commercially available in over 30 countries including Canada and countries in the European Union, Asia, and South America. As of December 2017, approximately 2,045 devices have been distributed outside the United States. It has not been withdrawn from marketing for any reason related to its safety or effectiveness.

## VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device. The potential adverse events listed below are in order of seriousness:

- Failure to identify shockable arrhythmia;
- Failure to deliver a defibrillation shock in the presence of VF or pulseless VT, which may result in death or permanent injury;
- Inappropriate energy which could cause failed defibrillation or post-shock dysfunction;
- Myocardial damage;
- Fire hazard in the presence of high oxygen concentration or flammable anesthetic agents;
- Incorrectly shocking a pulse sustaining rhythm and inducing VF or cardiac arrest;
- Bystander shock from patient contact during defibrillation shock;
- Interaction with pacemakers;
- Skin burns around the electrode placement area;
- Allergic dermatitis due to sensitivity to materials used in electrode construction; and
- Minor skin rash.

## IX. SUMMARY OF NONCLINICAL STUDIES

### A. Laboratory Studies

The X Series, R Series, AED Pro, and AED 3 BLS and their accessories underwent bench testing, animal testing, biocompatibility evaluation and human factors and usability testing, as well as software verification and validation appropriate for devices having major level of concern. Testing was conducted on key device subassemblies and the complete systems.

Bench Testing:

Table 7 below summarizes the major bench testing conducted to demonstrate proper performance of all the four (4) defibrillator devices, including conformance with applicable consensus performance standards.

| Test Title | Results |
|---|---|
| Electrical Safety Testing (IEC 60601-1 and IEC 60601-2- 4) | Pass |
| Electromagnetic Compatibility Testing (IEC 60601-1-2) | Pass |
| Integrated System Testing (Combined Hardware and Software Testing) | Pass |
| Device Software Testing | Pass |
| Shock and Vibration Testing | Pass |
| Battery Testing | Pass |
| Maximum Temperature Testing | Pass |
| Printed Circuit Board Assembly Testing | Pass |
| ECG Arrhythmia Analysis Algorithm Performance Testing | Pass |

**Table 7: Bench Testing**

The ECG arrhythmia analysis algorithm performance for the devices listed above has been evaluated by using ZOLL's ECG Rhythm Database. The devices meet the recommendations of the AHA for performance goals of arrhythmias analysis algorithms[1].

The performance of the arrhythmia analysis algorithm is summarized below in Table 8 and Table 9 for adult and pediatric patients.

**Table 8: Clinical Performance Results (Adult Patients) [1]**

| Rhythms | Sample Size | Performance Goal | Observed Performance | 90% Lower Confidence Limit |
|---|---|---|---|---|
| **Shockable** | | **Sensitivity** | | |
| Coarse VF | 536 | >90% | >99% | >99% |
| Rapid VT | 80 | >75% | >98% | >94% |
| **Non-shockable** | | **Specificity** | | |
| NSR | 2210 | >99% | >99% | >99% |
| AF, SB, SVT, Heart block, idioventricular, PVCs | 819 | >95% | >99% | >99% |
| Asystole | 115 | >95% | >99% | >97% |
| **Intermediate** | | | **Sensitivity** | |
| Fine VF | 69 | Report Only | >90% | >85% |
| Other VT | 28 | Report Only | >98% | >85% |

| | Shockable | Non-shockable |
|---|---|---|
| Shock | 680 | 3 |
| No Shock | 5 | 3169 |

**Table 9: Clinical Performance Results (Pediatric Patients) [1]**

| Rhythms | Sample Size | Performance Goal | Observed Performance | 90% Lower Confidence Limit |
|---|---|---|---|---|
| **Shockable** | | **Sensitivity** | | |
| Coarse VF | 42 | >90% | >99% | >93% |
| Rapid VT | 79 | >75% | >99% | >96% |
| **Non-shockable** | | **Specificity** | | |
| NSR | 208 | >99% | >99% | >98% |
| AF, SB, SVT, Heart block, idioventricular, PVCs | 348 | >95% | >99% | >98% |
| Asystole | 29 | >95% | >99% | >90% |

| | | | | |
|---|---|---|---|---|
| **Intermediate** | | | **Sensitivity** | |
| Fine VF | 0 | Report Only | NA | NA |
| Other VT | 44 | Report Only | >80% | >69% |

| | **Shockable** | **Non-shockable** |
|---|---|---|
| Shock | 121 | 10 |
| No Shock | 0 | 619 |

Biocompatibility Testing:

The only patient contacting portions of the X Series, R Series, AED Pro, and AED 3 BLS systems are the electrodes used with the device. These accessories were tested in accordance with ISO 10993 for cytotoxicity, irritation, and sensitization testing, and passed all testing to adequately demonstrate biocompatibility.

Software Documentation and Validation:

The software for the X Series, R Series, AED Pro, and AED 3 BLS systems was documented and validated according to the FDA guidance document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" for a major level of concern device. Software documentation included level of concern, software description, device hazard analysis, software requirements specification, software architecture diagrams, software design specifications, requirements traceability matrix, software development environment description, verification and validation documentation, revision level history, unresolved anomaly report, discussion of tools to detect run-time errors, and cybersecurity documentation. Software verification and validation testing conducted on each model included unit, integration, and system- level protocols and test reports with pre-defined pass/fail criteria. This testing demonstrated that the software in all the four (4) models of the defibrillator perform as intended.

## B. Animal Studies

To support a pediatric Indication for Use for the ZOLL Rectilinear Biphasic Waveform, ZOLL submitted pre-clinical data to the FDA as part of a 510(k) submission for its AED Plus device (K033474). The protocol for this pre-clinical study, along with a summary of the results, are included in this PMA application. A summary of this study is presented below.

To demonstrate the safety and effectiveness of the Rectilinear Biphasic Waveform when used to treat pediatric VF patients, ZOLL conducted a study using a porcine model of pediatric patients less than 8 years of age. This study included 18 piglets in three (3) size groups (two (2) animals weighing 4 kg, eight (8) animals weighing 8 kg, and eight (8) animals weighing 16 kg) and compared the defibrillation dose/response curves observed using the Rectilinear Biphasic Waveform with those observed using a standard monophasic damped sine wave (DSW) defibrillator to treat short duration (~30 seconds) ventricular fibrillation. The study demonstrated that the biphasic waveform defibrillates pediatric pigs with equal efficacy but lower energy (on a Joules/kg basis) than traditional monophasic damped sine wave defibrillators. To confirm the safety of the proposed biphasic waveform in pediatric patients,

we studied and compared measures of cardiac function before and after both DSW and Rectilinear Biphasic Waveform defibrillation shocks over a range of relevant energies. The study demonstrated that the biphasic defibrillation produced equivalent or milder disturbances of cardiac function when compared to traditional DSW defibrillation at the same energies.

Another animal study compared the ZOLL rectilinear biphasic (RLB) waveform to a biphasic truncated exponential (BTE) waveform. The study, using an immature porcine model (n=21), was a prospective, randomized, controlled design to determine the dose response curves for the RLB and BTE defibrillation waveforms. A weight range from 4 to 24 kg for an animal represented a pediatric patient. The weight ranging from 4 to 8 kg represented a patient less than 1 year old (infant subgroup), and the weight range from 16 to 24 kg represented a pediatric patient between the ages of 2 and 8 years (young children subgroup).

The Zoll RLB waveform demonstrated a statistically superior capability to defibrillate a porcine pediatric model with < 90% of the D50 energy required for a BTE waveform (D50 energy: RLB 25.6 ± 15.7 J, BTE 28.6 ±17.0 J, $P \leq 0.0232$; D90 energy: RLB 32.6 ± 19.1 J, BTE 37.8 ± 23.2 J, $P \leq 0.0228$).

The ECG ST segment changes (mV) and LV pressure changes (dP/dt) following a defibrillation shock were compared between the RLB waveform to the BTE waveform. The RLB waveform had an average ST segment increase above baseline of 0.138 ± 0.136 mV (N=401 shocks) compared to the BTE waveform's average increase of 0.146 ± 0.148 mV (N=396 shocks). The RLB waveform had an average dP/dt at the 40 mmHg threshold (the point in time when an animal's blood pressure exceeded 40 mmHg spontaneously) of 1987 ± 411 mmHg/s (N=496 shocks) compared to the BTE waveform's average dP/dt of 2034 ± 425 mmHg/s (N=496 shocks).

The RLB waveform demonstrated a safe dosing level of 4 J/Kg to achieve a 100% probability of defibrillation success (D100). The D100 dosing level was consistent for both the infant subgroup and the young child subgroup.

## X. SUMMARY OF PRIMARY CLINICAL STUDIES

The ZOLL X Series (cleared by the FDA under K142915), R Series (cleared by the FDA under K160556), AED Pro (cleared by the FDA under K110526) and AED 3 BLS all utilize the ZOLL Rectilinear Biphasic Waveform, which is the same waveform as ZOLL's previously cleared M Series Biphasic Defibrillator (cleared by the FDA under K990762). It was in this earlier 510(k) submission for ZOLL's M Series Biphasic Defibrillator (K990762) that the clinical data supporting the safety and efficacy of ZOLL's Rectilinear Biphasic Waveform was presented to the FDA.

Effectiveness of ZOLL's rectilinear biphasic waveform has been clinically verified during various studies for defibrillation of VF/VT. Feasibility studies were performed initially for defibrillation of VF/VT (n=20) and synchronized cardioversion of AF (n=21) on two (2) separate groups of patients to ensure waveform safety and energy selection. Subsequently a multi-center, randomized clinical trial was performed to verify effectiveness of the waveform. Descriptions of these studies are provided below. All studies were performed using ZOLL defibrillation systems consisting of ZOLL defibrillators, rectilinear biphasic waveform and ZOLL Multi-Function Pads.

### A) Randomized Multi-Center In-Hospital Clinical Trial for VF/VT Defibrillation:

*Overview:* The defibrillation efficacy of ZOLL's rectilinear biphasic waveform was compared to a monophasic damped sine waveform in a prospective, randomized, multi-center study of patients undergoing ventricular defibrillation during electrophysiological studies, implantable cardioverter defibrillator (ICD) implants, and tests. A total of 192 patients were enrolled in the study. Eight (8) patients who did not satisfy all protocol criteria were excluded from the analysis.

*Objectives:* The primary goal of this study was to compare the first shock efficacy of the 120J rectilinear biphasic waveform with a 200J monophasic waveform. The secondary goal was to compare all shock (three consecutive 120, 150, 170J) efficacy of the rectilinear biphasic waveform with that of a monophasic waveform (three consecutive 200, 300, 360J). A significance level of p=0.05 or less was considered statistically significant using Fischer Exact test. Also, differences between the two waveforms were considered statistically significant when the 90% confidence interval between the two waveforms was greater than 0%.

*Results:* The study population of 184 patients had a mean age of 63±14 years. One hundred forty-three (143) patients were males. There were no adverse events or injuries related to the study.

The first shock, first induction efficacy of biphasic shocks at 120J was 99% versus 93% for monophasic shocks at 200J (p=0.0517, 90% confidence interval of the difference of -1.01% to 15.3%).

Successful defibrillation with rectilinear biphasic shocks was achieved with 58% less delivered current than with monophasic shocks (14±1 vs. 33±7 A, p=0.0001).

The difference in efficacy between the rectilinear biphasic and the monophasic shocks was greater in patients with high transthoracic impedance (greater than 90 ohms). The first shock, first induction efficacy of biphasic shocks was 99% versus 86% for monophasic shocks for patients with high impedance (p=0.02, 90% confidence interval of the difference of 0.037% to 0.706%).

A single patient required a second biphasic shock at 150J to achieve 100% efficacy versus six (6) patients for whom monophasic shocks of up to 360J were required for 100% total defibrillation efficacy.

*Conclusion:* The data demonstrate equivalent efficacy of low energy rectilinear biphasic shocks compared to standard high energy monophasic shocks in patients with high transthoracic impedance. The data also demonstrate the superior efficacy of low energy rectilinear biphasic shocks compared to standard high energy monophasic shocks in patients with high transthoracic impedance at the 90% confidence level. There were no unsafe outcomes or adverse events due to the use of the rectilinear biphasic waveform.

## B) Published Clinical Data – Out of Hospital Use

*Overview:* Additional clinical data is included in this PMA application to support out-of-hospital use of ZOLL's Rectilinear Biphasic defibrillation waveform. The resulting clinical paper, "Performance of a rectilinear biphasic waveform in defibrillation of presenting and recurrent ventricular fibrillation: A prospective multicenter study,"[2] was provided as support to demonstrate a reasonable assurance of safety and effectiveness of the AED Plus and Fully Automatic AED Plus when used in an out-of-hospital environment. A summary of this study is presented below.

*Objectives:* ZOLL tested the hypothesis that shock success differs with initial and recurrent episodes of ventricular fibrillation (VF).

*Methods:* From September 2008 to March 2010 out-of-hospital cardiac arrest patients with VF as the initial rhythm at 9 study sites were defibrillated by paramedics using a rectilinear biphasic waveform. Shock success was defined as termination of VF within 5 seconds post-shock. We used generalized estimating equation (GEE) analysis to assess the association between shock type (initial versus defibrillation) and shock success.

*Results:* Ninety-four (94) patients presented in VF. Mean age was 65.4 years, 78.7% were male, and 80.9% were bystander-witnessed. VF recurred in 75 (79.8%). There were 338 shocks delivered for initial (n = 90) or recurrent (n = 248) VF available for analysis. Initial shocks terminated VF in 79/90 (87.8%) and subsequent shocks in 209/248 (84.3%). GEE odds ratio (OR) for shock type was 1.37 (95% CI 0.68–2.74). After adjusting for potential confounders, the OR for shock type remained insignificant (1.33, 95% CI 0.60–2.53). There was no observed significant difference in ROSC (54.7% versus 52.6%, absolute difference 2.1%, p = 0.87) or neurologically intact survival to hospital discharge (21.9% versus 33.3%, absolute difference 11.4%, p = 0.31) between those with and without VF recurrence.

*Conclusions:* Presenting VF was terminated with one shock in 87.8% of cases. There was no observed significant difference in the frequency of shock success between initial versus recurrent VF. VF recurred in the majority of patients and did not adversely affect shock success, return of spontaneous circulation (ROSC), or survival.

## C) Internal Defibrillation Study

*Overview:* To support internal defibrillation with the Rectilinear Biphasic defibrillation waveform, ZOLL submitted a clinical study to the FDA as part of a 510(k) submission for its M Series device (cleared by the FDA under K032439). As part of this study, based upon an observational comparison of the biphasic truncated exponential (BTE) and rectilinear biphasic (RLB) waveforms, it was hypothesized that the RLB waveform would have equivalent safety and efficacy when compared to the reported clinical data for open heart defibrillation using the BTE waveform.

*Objectives:* To demonstrate the safety and efficacy of the rectilinear biphasic (RLB) waveform when the waveform is applied directly to ventricular fibrillation (VF) during open heart surgery.

*Methods:* Twenty patients who were undergoing coronary artery bypass graft (CABG) surgery were eligible for inclusion in this study. Patients were excluded if their New York Heart Association (NYHA) Class for heart failure was four, their left ventricular ejection fraction was

less than 20%, or they were less than 18 years of age. One or more RLB waveform shocks were applied directly to the heart if VF occurred (VF may occur following the removal of the aortic cross-clamp during the application of warm cardioplegia). The RLB shock sequence was 5, 10, 20, 30, and 50 J. Shock energies were applied in sequence until defibrillation occurred.

Surgery data regarding aortic occlusion time, core myocardial temperature, blood chemistry, cardioplegia perfusion time, ECG changes, inotropic medication, and length of fibrillation time prior to start of defibrillation sequence were compiled at the time of aortic cross-clamp release.

Each RLB shock from the M-Series was applied using internal handles (1.5", 2.0", or 2.7" diameter). The defibrillator, when equipped with the internal handles, does not permit a defibrillation shock greater than 50 J.

*Results:* The average age of a patient was 63 (± 9) years. There were 16 male patients (80%) and 4 female patients (20%). All patients were classified as NYHA class III, had significant coronary artery disease (CAD), and underwent coronary artery bypass graft (CABG) surgery as the method of treatment. The average ejection fraction for a patient was 53% (± 6%). The average time for a patient on bypass was 92 (± 21) minutes, with an average of 57 (± 14) minutes for aortic cross-clamp. The core temperature at release of the aortic cross-clamp was 34 (± 1) 0c. All patients were successfully defibrillated with a selected shock energy less than or equal to 20 J. No patient experienced abnormal left ventricular wall motion at any time and all patients were defibrillated to normal sinus rhythm. The first shock defibrillation success rate at the initial energy selection of 5 J was 90% (18/20). The threshold energy was 6 ± 4 J, the cumulative energy was 7 ± 7 J, and the average number of shocks was 1 ± 1 shocks.

*Conclusions:* The ZOLL M-Series RLB waveform is safe and efficacious for direct ventricular defibrillation during open heart surgery. The RLB waveform has a first shock success rate of 90% at 5 J and a 100% success rate ≤ 20 J. Further, the shock performance of the RLB waveform is superior when historically compared to the reported performance of the BTE waveform.

No new studies have been conducted or included in this PMA application as the data and studies to support use of the ZOLL Rectilinear Biphasic Waveform for adult and pediatric patients, and for internal defibrillation, as well as the data and studies to support use of ZOLL's non-invasive temporary pacing waveform, were previously reviewed and cleared by the FDA under the 510(k) submissions K990762, K032439 and K033474. Rather, all the clinical data and studies that were presented by ZOLL and reviewed by the FDA under previous 510(k) submissions, and that led to clearance of ZOLL's Rectilinear Biphasic Defibrillation Waveform and non-invasive temporary pacing technologies, are included in this section.

## D) Human Factors and Usability Study

### X Series

ZOLL conducted usability evaluations throughout the design and development of the X Series to assess the device form factor, user interface, system performance and use-related hazard mitigations. ZOLL also conducted a post-market complaint analysis relating to the usability of the device since the latest version was reviewed and cleared by the agency.

The objective of the usability studies was to ensure safe and effective device use by the intended user base. This was accomplished by engaging test participants from the distinct user groups and

introducing them to simulated use scenarios to assess their ability to complete the identified primary operating functions. This included having BLS and ALS trained medical personnel perform tasks associated with the typical use of device functionality such as device setup, utilization of monitoring and therapy features, interactions with the alarm system and viewing / interpretation of user interface elements. The evaluation for each user group was scoped based on the portion of functions and features they would operate based on their training level. During the testing the study moderator and observers recorded the user's ability to successfully complete the primary operating functions and recorded any failures, close calls and use errors. Any use related hazards were then evaluated through the iterative risk management process to ensure appropriate mitigations and acceptable residual risk.

After the initial product release the device was updated to support a new communication functionality which allowed the X Series to create a web page to be used as an adjunctive display. A usability study was conducted with Emergency Medical Service providers to evaluate the primary operating functions associated with the use of the feature. This included their ability to connect the secondary display to the X Series and view, understand, and navigate the display elements without the introduction of any unacceptable use related hazards.

ZOLL provided a use-related risk impact analysis for system changes implemented since the latest version of the X Series was reviewed and cleared by the agency and provided this information with the Human Factors data. ZOLL also assessed complaint data received since the latest version of the X Series was reviewed and cleared by the agency to identify any use-related items, this data was inclusive of implemented changes identified in the use-related risk impact analysis. The complaint handling system query generated a comprehensive list of complaints, which was then filtered to remove any complaints that clearly weren't related to the usability of the device (such as component failures and shipping related issues). The remaining complaints were then assessed to identify situations where safety and efficacy may have been impacted as a result of the user's expectation / misunderstanding of device operation. The usability related errors were then reviewed in light of the identified use related hazards, the implemented mitigations and the residual risk to determine if further actions were necessary. Analysis of the complaints determined that additional modifications to the user interface would not be effective in further reducing the risk. Additionally, relative to the number of devices manufactured and distributed, the prevalence of use-related issues is sufficiently low to support the fact that the device is safe and effective for use.

**R Series**

ZOLL conducted customer acceptance trials throughout the design and development of the R Series to assess the device form factor, user interface, system performance and use-related hazard mitigations. ZOLL also conducted a post-market complaint analysis relating to the usability of the device since the latest version was reviewed and cleared by the agency.

The objective of the customer acceptance trials was to ensure safe and effective device use by the intended user base. This was accomplished by engaging test participants from distinct user groups and introducing them to simulated and actual use scenarios to assess their ability to complete the frequently used functions based on the use environment. This included having ALS trained medical professionals evaluate the device by performing mock codes similar to those they would be responding to in different hospital settings. The R Series was also tested in an Electrophysiology Lab and Cardiac Operating Room by each department's clinicians as well as by biomedical/clinical engineers who provided feedback on preventive maintenance and device troubleshooting tasks.

After the initial product release the device was updated to introduce a BLS version which added AED functionality by modifying the user interface and allowing users to change from AED to manual defibrillation. A usability test plan was developed to validate that the R Series BLS option design elements facilitated the safe and effective use of the device during the intended use cases. Concept designs and prototypes elicited feedback for initial design directions. Simulated use testing was then conducted with both BLS and ALS providers to evaluate user actions introduced by the implementation of the BLS feature. These actions included initial start-up into AED mode, use of AED mode, converting the R Series BLS from AED mode to Manual mode and returning the unit to AED mode.

The R Series platform was updated to support NIBP and EtCO2 parameters by adding new hardware and software. A usability test plan was developed to allow the intended users to validate the implementation of the features by performing tasks such as locating the NIBP "hard key," taking a NIBP measurement, initiating the EtCO2 parameter, taking an EtCO2 measurement, zeroing the EtCO2 module, powering up with NIBP only and adding EtCO2 during operation. Prototype evaluations were initially performed to gather feedback from users on design concepts, followed by simulated use testing to validate the safe and effective use of the new features.

ZOLL provided a use-related risk impact analysis for system changes implemented since the latest version of the R Series was reviewed and cleared by the agency and provided this information with the Human Factors data. ZOLL also assessed complaint data received since the latest version of the R Series was reviewed and cleared by the agency to identify any use-related items, this data was inclusive of implemented changes identified in the use-related risk impact analysis. The complaint handling system query generated a comprehensive list of complaints, which was then filtered to remove any complaints that clearly were not related to the usability of the device (such as component failures and shipping related issues). The remaining complaints were then assessed to identify situations where safety and efficacy may have been impacted as a result of the user's expectation/misunderstanding of device operation. The usability related errors were then reviewed in light of the identified use related hazards, the implemented mitigations and the residual risk to determine if further actions were necessary. Analysis of the complaints determined that additional modifications to the user interface would not be effective in further reducing the risk. Additionally, relative to the number of devices manufactured and distributed, the prevalence of use-related issues is sufficiently low to support the fact that the device is safe and effective for use.

**AED Pro**

ZOLL conducted a Customer Acceptance Trial to assess the usability, safety, and effectiveness of the device prior to release in 2005. ZOLL has also conducted post-market research on customer complaints to assess the usability of the system since the device was reviewed and cleared by the agency.

The goal of the Customer Acceptance Testing was to test the usability of the device with the intended users and demonstrate that it was easy and intuitive to use, as well as being safe and effective. Two different tests were run to validate usability of the product: ECG monitoring in ambulance settings with human volunteer simulated patients, and rescue defibrillation scenarios performed on pigs.

For ECG Monitoring, emergency medical technicians monitored ECG data of volunteer patients in short ambulance rides. Participants were asked to monitor patients and perform all the primary

operating functions associated with powering the device on, connecting the device to patients, and monitoring patients. Participants rated the ease and intuitiveness of completing each task with the device. They were also asked to rate the acceptability of other interface-related characteristics.

For the rescue defibrillation scenarios, participants were asked to attempt to rescue pigs using the device in different scenarios, including unconscious but not under cardiac arrest, unconscious in ventricular fibrillation, and asystole. In some cases, participants were asked to deliberately perform incorrect actions in order to determine that the AED Pro's responses to use errors were clear and effective. Participants also rated the acceptability and intuitiveness of the tasks of the scenario and other interface characteristics.

During both types of testing, the study moderators and observers recorded the user's ability to successfully complete the primary operating functions. Any use related hazards were then evaluated through an iterative risk management process to ensure appropriate mitigations and acceptable residual risk. Results from both tests indicated that average subjective participant ratings ranged from "acceptable" to "better than expected." Recorded observations and data collected also supported the conclusion that the device supports safe and effective use.

ZOLL assessed complaint data received since the latest version of the AED Pro was reviewed and cleared by the agency to identify any use-related items. The complaint list was filtered to remove any complaints that clearly were not related to the usability of the device (such as component failures and shipping related issues). The filtered list was then assessed to identify situations where safety and efficacy may have been impacted as a result of the user's expectation/misunderstanding of device operation. These usability related errors were reviewed in light of the identified use related hazards, the implemented mitigations and the residual risk to determine if further actions were necessary. Analysis of the complaints determined that additional modifications to the user interface would not be effective in further reducing the risk. Additionally, relative to the number of devices manufactured and distributed, the prevalence of use-related issues is sufficiently low to support the fact that the device is safe and effective for use.

**AED 3 BLS**

ZOLL conducted usability evaluations throughout the design and development of the AED 3 to assess the device form factor, user interface, system performance and use-related hazard mitigations.

The objective of the usability studies was to ensure that the device was easy and intuitive, and that it was safe and effective for the intended user base, namely individuals trained in CPR and in the use of an AED. Participants in the usability studies completed rescue scenarios that included all primary operating functions of the device, such as powering on the device, selecting patient type, placing pads, and delivering therapy. The rescue scenario involved either an adult or child manikin as a simulated patient in ventricular fibrillation. Data was collected on participants' ability and efficiency in completion of all of the primary operating functions of the device as they attempted to resuscitate the simulated patient. Subjective data on ease and intuitiveness of use was also collected. Participants were able to complete all tasks within the timing and accuracy constraints specified by the test protocol. In addition, participants expressed overall satisfaction with the ease of use and intuitiveness of the user interface. No new use-related hazards were identified during the usability validation studies and an analysis of existing use-related hazards (created and maintained throughout the iterative risk management process) indicated acceptable residual risk.

The design of the AED 3 BLS device appropriately addressed the intended use and user needs. The design properly mitigated the use-related risks and errors and supports safe and effective use of the device.

## E) Complaint Analysis

To further demonstrate the safety and effectiveness of the devices in clinical use, relevant adverse event data were analyzed over the past three years.

Between December 1, 2014, and December 8, 2017, a total of sixty-five (65) adverse events were reported for X Series of which no adverse events are related to the device. A total of twenty-seven (27) adverse events were reported for the R Series of which 26 are not related to the device and 1 is undetermined/unknown. A total of eleven (11) adverse events were reported for the AED Pro device of which 10 are not related to the device and 1 is undetermined/unknown. No adverse events have been reported for the AED 3 BLS device since its launch, outside the US, in March 2016.

## F) Pediatric Extrapolation

In this premarket approval application, one (1) animal study was submitted to support the reasonable assurance of safety and effectiveness of the ZOLL RLB Waveform in pediatric patients. The pre-clinical study of the safety and efficacy of ZOLL's Rectilinear Biphasic Waveform when used to treat pediatric VF patients demonstrated that the RLB waveform defibrillates pediatric pigs with equal efficacy but lower energy than a traditional monophasic damped sine wave. These studies also demonstrated that the biphasic defibrillation produced equivalent or milder disturbances of cardiac function when compared to traditional DSW defibrillation at the same energies.

## G) Financial Disclosure

ZOLL submitted the Financial Disclosure information, to the Agency, required by Clinical Investigators regulation (21 CFR 54). These financial disclosures include information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation.

ZOLL submitted a signed certification of financial interests and arrangements of clinical investigators with regard to the four (4) clinical studies that ZOLL sponsored. ZOLL certifies that they did not enter into any financial arrangement with the clinical investigators whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). ZOLL also certifies that each clinical investigator was required to disclose to ZOLL whether the investigator had a proprietary interest in the product or a significant equity in the sponsor as defined in 21 CFR 54.2(b). Pursuant to this regulation the investigators did not disclose any such interests. ZOLL further certifies that no investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f) as defined in 21 CFR 54.2(c).

The principal investigator (Erik P. Hess) of the clinical study conducted by Hess et al., published in Resuscitation in 2011[4], was supported in part by a grant from the American Heart Association, the Society for Academic Emergency Medicine, and the Emergency Medicine Foundation.

It is for these above reasons that we believe that none of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

## XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Cardiovascular Device Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel on January 25, 2011 as part of the 515(i) process. The majority of the panel recommended that AEDs be regulated as Class III PMAs to have better oversight of device manufacturing and postmarket performance.

## XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

### A. Effectiveness Conclusions

The data presented to the FDA for ZOLL's M Series Biphasic Defibrillator (K990762) demonstrated equivalent efficacy of low energy rectilinear biphasic shocks compared to standard high energy monophasic shocks in patients with high transthoracic impedance.

The study by Hess et al. in Resuscitation[4] concluded that presenting VF was terminated with one shock in 87.8% of cases, and found no significant difference in the frequency of shock success between initial versus recurrent VF. Return of spontaneous circulation was 54.7% for the Zoll defibrillation (RLB) shock.

The pre-clinical study of the safety and efficacy of ZOLL's Rectilinear Biphasic Waveform when used to treat pediatric VF patients demonstrated that the RLB waveform defibrillates pediatric pigs with equal efficacy but lower energy than a traditional monophasic damped sine wave.

### B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies, a randomized multi-center clinical trial, and data reported in published literature[2]The results from the preclinical laboratory testing performed on the ZOLL AED Plus and Fully Automatic AED Plus devices demonstrated appropriate electrical safety, electromagnetic compatibility, biocompatibility, mechanical integrity, and overall performance. The preclinical animal studies demonstrated that the biphasic defibrillation produced equivalent or milder disturbances of cardiac function when compared to traditional DSW defibrillation at the same energies. The clinical data, including a published clinical study on the out-of-hospital use of the RLB waveform[2], internal defibrillation study, and a usability study, further demonstrate the safety of the device.

### C. Benefit-Risk Determination

The probable benefits of the device are based on a randomized multi-center clinical trial, published literature, and postmarket clinical data, which was collected after 510(k) clearance, described above. The benefit of early defibrillation therapy is survival of patients in cardiac arrest. Defibrillators are life-saving devices used in emergency situations. They have been shown to have a high benefit for patients with underlying diseases that remain undetected until sudden cardiac

arrest occurs. The time from collapse to defibrillation is critical in patient survival. For every minute that passes between collapse and defibrillation, survival rates from VF SCA decrease by 7-10%.

The magnitude of this benefit is either life or death. The published literature and postmarket clinical data have no ability to predict which patients will experience a benefit or determine probability of benefit because of the differing pathophysiology of underlying cardiac arrest. The subpopulations have a high degree of heterogeneity of etiologies of cardiac arrest; therefore, variation in public health benefit cannot be determined. Likewise, the duration of effect is dependent on underlying etiology and, though valuable to the patient, is highly dependent on subsequent treatment of the underlying disease. Duration of effect is not related to the device.

Patients put a high value on this treatment because it has the potential to save their lives. Patients are therefore willing to accept the risks of this treatment to achieve the benefit. If the treatment provides timely successful defibrillation, the patient may survive a life threatening cardiac arrest situation and will be able to seek further treatment.

Patient Perspectives: This submission did not include specific information on patient perspectives for the device.

In conclusion, given the available information above, the data support that the benefits outweigh the risks for patients in cardiac arrest who are unconscious, not breathing, or without circulation.

### D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

## XIII. CDRH DECISION

CDRH issued an approval order on December 27, 2017. The final conditions of approval cited in the approval order are described below.

The applicant has agreed to provide the following non-clinical information as part of the annual report, which may be followed by a PMA supplement where applicable.

1. The number of devices returned to the applicant for cause from domestic sources, with a breakdown into:

    a. Those returned for normal end-of-life.

    b. Those returned with any alleged failures or malfunctions, including a summary of root causes and the frequency of occurrence for each identified root cause.

2. The number of replacement defibrillation pads and replacement batteries issued to customers domestically for all causes.

3. A summary of information available to you related to individual domestic uses of your device that may include, but is not limited to:

    a. Defibrillation success and the number of shocks required for success.

b. Identification of any error codes or malfunctions during use and their related MDR number.

4. A listing of any safety alerts, technical service bulletins, user communications, or recalls for devices under this PMA.

In addition to the Annual Report requirements, the applicant must provide the following data in post-approval study (PAS) reports for each PAS listed below. Separate PAS Progress Reports must be submitted for each study every six (6) months during the first two (2) years of the study and annually thereafter, unless otherwise specified by FDA. Two (2) copies of each report, identified as an "OSB Lead PMA Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

OSB Lead PMA Post-Approval Study – Reconfirmation Analysis Mode Algorithm: The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. This PAS will be conducted as per protocol dated December 4, 2017, Version 0.6. This is a prospective, observational study with newly enrolled patients with a study objective to prospectively validate the Reconfirmation Analysis Mode (RAM) algorithm by comparing the performance of the RAM algorithm to the performance goals recommended by the American Heart Association.

The applicant will enroll subjects who are found in cardiac arrest and receive attempted resuscitation by participating EMS agencies and treatment with the ZOLL X-Series defibrillator and who meet the inclusion and exclusion criteria per protocol. The minimum required total number of subjects is 2,500 to provide adequate data for all rhythm categories in the final analysis. Based on Kerber's sample size and performance goals (Circulation 1997 Mar 18; 95(6):1677-1682), the following minimum sample sizes for the five different categories of rhythm will be required: 200, 50, 100, 30, and 100 subjects, respectively, for the coarse ventricular fibrillation (VF); rapid ventricular tachycardia (VT); non-shockable rhythm; other non-shockable rhythms (such as NSR (Normal Sinus Rhythm), AF (atrial fibrillation), SB (sinus bradycardia), SVT (supraventricular tachycardia), PVC (premature ventricular contraction)); and Asystole.

The applicant will measure the primary endpoint, i.e., the accuracy of the RAM algorithm, as sensitivity for shockable rhythms and specificity for non-shockable rhythms for the algorithm when compared to manual annotations provided by three experts. For hypothesis testing for each rhythm category, you will calculate a single-sided 90% lower confidence limit of either sensitivity or specificity and compare that to the performance goal (Circulation 1997 Mar 18; 95(6):1677-1682). Successful validation of the algorithm will be considered complete when the performance goal is met or exceeded as outlined in the study hypotheses (Table 1) of the protocol.
The applicant has been advised that the description of the Analysis Plan, interim (per agreed plan), and final study results will be published per protocol on the FDA Post-Approval Study Webpage http://www.fda.gov/devicepostapproval.

In addition, the results from this post-approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2).

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

## XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

## XV. REFERENCES


1. RE Kerber, LB Becker, JD Bourland, RO Cummins, AP Hallstrom, MB Michos, G Nichol, JP Ornato, WH Thies, RD White, BD Zuckerman, "Automated External Defibrillators for Public Access Defibrillation: Recommendations for Specifying and Reporting Arrhythmia Analysis Algorithm Performance, Incorporation New Waveforms, and Enhancing Safety", Circulation 1997, Vol 95, No 6, 1677-1681.

2. Hess EP, Agarwal D, Myers LA, et. al., Performance of a rectilinear biphasic waveform in defibrillation of presenting and recurrent ventricular fibrillation: a prospective multicenter study. Resuscitation. 2011;82(6):685-9.