

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Automated External Defibrillator

Device Trade Name: AED Plus® and Fully Automatic AED Plus®

Device Procode: MKJ

Applicant's Name and Address: ZOLL Medical Corporation
269 & 271 Mill Rd
Chelmsford, MA – 01824

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P160015

Date of FDA Notice of Approval: May 26, 2017

The AED Plus automated external defibrillator (AED) has been commercially available since March 25, 2002, when the Semi-Automatic model was first cleared by FDA under K011388. The Fully-Automatic model of the AED Plus has been commercially available since October 26, 2012, when it was first cleared by FDA under K120406. P160015 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. A product affected by this Order is the AED Plus device. 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 AED Plus.

II. INDICATIONS FOR USE

AED Plus® and Fully Automatic AED Plus® are used when a suspected cardiac arrest victim has an apparent lack of circulation as indicated by:

- Unconsciousness and
- Absence of normal breathing and
- Absence of a pulse or signs of circulation.

The devices are intended for use by personnel who have been trained in their operation. Users should have received training in basic life support/AED, advanced life support or a physician-authorized emergency medical response training program.

When a victim is less than 8 years of age, or weighs less than 55 lbs. (25kg), the ZOLL AED Plus® and Fully Automatic AED Plus® should be used with the ZOLL AED Plus Pediatric Electrodes. Therapy should not be delayed to determine the patient's exact age or weight.

III. CONTRAINDICATIONS

Do NOT use the AED Plus and Fully Automatic AED Plus when the victim:

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

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

The ZOLL AED Plus and Fully Automatic AED Plus devices are lightweight, portable, battery-powered automated external defibrillators that uses voice prompts and visual icons to guide a user through a resuscitation sequence that may include defibrillation and/or cardiopulmonary resuscitation (CPR). The devices utilize the ZOLL Rectilinear Bi-Phasic defibrillation waveform, and operate in either adult or pediatric mode. The AED Plus and Fully Automatic AED Plus support both adult and pediatric defibrillation electrode pads, and automatically adjusts the defibrillation energy based on the type of electrode pads connected to it. The devices are designed to be used by trained responders for the treatment of cardiac arrest. The AED Plus and the Fully Automatic AED Plus are the same in physical design and visually in the labeling of the top cover; however, the Fully Automatic AED Plus is further labeled as "Automatic" near the on/off switch of that device. See Figures 1 and 2.

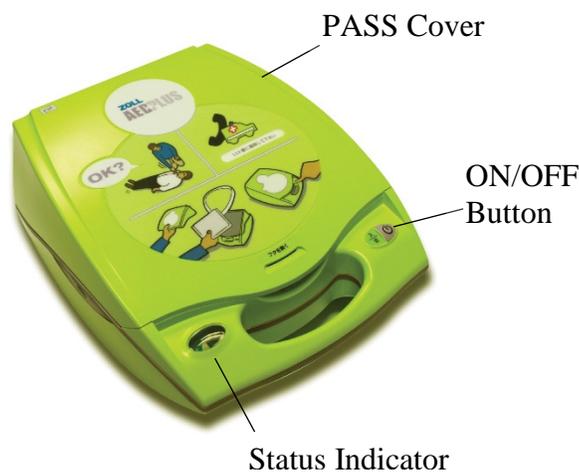


Figure 1: AED Plus and Fully Automatic AED Plus Top View



Figure 2: Fully Automatic AED Plus (ON/OFF Button)

There are also differences in the User Interface label which are discussed on Page 6.

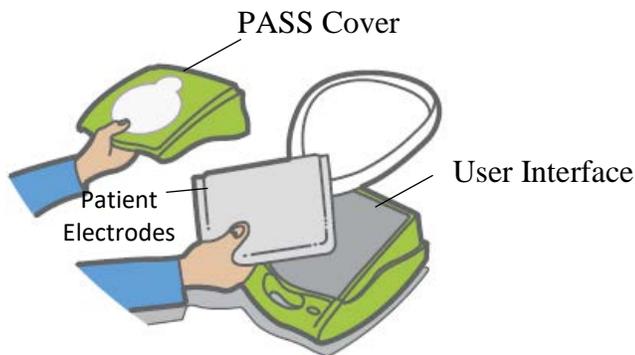


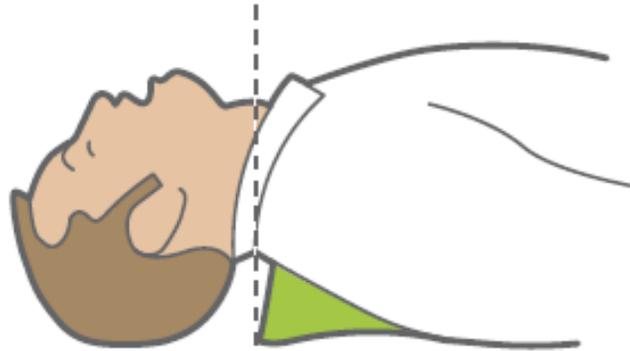
Figure 3: AED Plus Top View
(with Passive Airway Support System Cover Lifted).

The defibrillation function of the AED Plus and Fully Automatic AED Plus devices is indicated for use on both adult and child victims of sudden cardiac arrest. The AED Plus and Fully Automatic AED Plus support both adult and pediatric defibrillation electrode pads, and automatically adjust the defibrillation energy based on the type of electrode pads connected to the device. When the victim is less than 8 years of age, or weighs less than 55 lbs (25 kg), the ZOLL AED Plus and Fully Automatic AED Plus should be used with the ZOLL AED Plus Pediatric Electrodes.

The AED Plus and Fully Automatic AED Plus units utilize 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 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. CPR monitoring feature is only available with the adult defibrillation electrodes.

If there is no evidence of head or neck trauma, the head tilt chin lift method is the recommended maneuver for opening the airway. The PASS cover (identified in Figure 3 above) may be placed under the victim's shoulders to help maintain head tilt. The shape of the PASS cover, when placed under the shoulders of the victim, can be used to help maintain an open airway. See Figure 4 below.



Place the PASS under the victim to lift his/her shoulders. Do not use the PASS if there is a suspected head or neck injury.

Figure 4: Using the PASS Cover

The AED Plus and the Fully Automatic AED Plus incorporate recording/memory capabilities to allow medical control authorities to review a rescuer's use of the device. Recording includes electrocardiogram (ECG) rhythms, event data, device identification, and optionally, voice recording of rescuer and ambient sounds. This information is available via an upload capability to a personal computer for event review and archiving.

Data exchange between the AED Plus/Fully Automatic AED Plus and a personal computer is via IrDA (infrared interface standard) ports. One port is located on the side of the unit and the other is located on a personal computer or another IrDA equipped device.

Fully Automatic Protocol (Fully Automatic AED Plus)

The only difference in the treatment protocol for semi-automated defibrillation and Fully Automated Protocol is that in the Fully Automated Protocol when a shockable rhythm has been detected defibrillation energy is delivered by the device without the need for the user (rescuer) to depress the shock button following a sequence of appropriate prompts and a warning tone. This configuration of the AED Plus device is marketed as Fully Automatic AED Plus.

The software in a Fully Automatic AED Plus is functionally identical to the Semi-Automatic AED Plus except for the following:

1. When the Fully Automatic AED Plus unit is turned on it announces that it is a Fully Automatic AED Plus, before it announces “Unit OK” or “Unit Failed” message.
2. The shock delivery protocol is changed to the following:
 - a. When a shockable rhythm is detected during the analysis, the Fully Automatic protocol described in the right column of Table 1 is implemented in the software. A Semi-Automatic AED Plus will have the protocol described in the left column.

Table 1: Comparison of Shock Delivery Protocol in Fully Automatic and Semi-Automatic Models of AED Plus

Semi-Automatic Protocol	Fully Automatic Protocol
Semi-Automatic (current configuration) shock prompt sequence	Fully Automatic shock prompt sequence
SHOCK ADVISED	DON'T TOUCH PATIENT
DON'T TOUCH PATIENT	SHOCK WILL BE DELIVERED IN THREE
PRESS THE FLASHING SHOCK BUTTON	TWO
	ONE

- b. After announcing “ONE” the unit blinks the Shock indicator and plays a warning tone before delivering the shock to the patient.

Operating Controls and Indicators are the same for the AED Plus and the Fully Automatic AED Plus except for the following:

- The shock button now functions as a Shock Indicator which Illuminates when the Fully Automatic AED Plus is charged and in the process of delivering a shock to the victim.
- The Fully Automatic AED Plus uses a revised user interface label compared to the AED Plus (Figures 5 and 6, respectively). The revised user interface label on the Fully Automatic AED Plus is consistent with its operation (i.e., the device delivers shock automatically without the need for the user to press the shock button). The

only differences between the two (2) interface labels is the presence of the hand graphic on the shock button in the center of the user interface for the AED Plus only and the addition of the “Automatic” label near the on/off switch for the Fully Automatic AED Plus only. (The “Automatic” label is seen more clearly in Figure 2).



Figure 5: User Interface label on the AED Plus



Figure 6: User Interface label on the Fully Automatic AED Plus

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 AED Plus has received its CE Mark in the European Union (EU) as well as an approval in Canada. In the U.S., AED Plus was first cleared for sale via premarket notification K011388. The Indications for Use were expanded for defibrillation function to include patients less than 8 years of age in 2004 via premarket notification K033474. The Fully Automatic AED Plus was cleared for sale in 2012 via premarket notification K120406.

As of December 2015, approximately 462,275 devices have been distributed in and outside the United States. The AED Plus and Fully Automatic AED Plus are available in over 100 countries and territories.

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 AED Plus and 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 3 below summarizes the major bench testing conducted to demonstrate proper performance of the AED Plus and Fully Automatic AED Plus, including conformance with applicable consensus performance standards.

Table 3: Bench Testing

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

The ECG arrhythmia analysis algorithm performance 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 4 for adult patients and Table 5 for pediatric patients.

Table 4: Clinical Performance Results (Adult Patients)^{2,3}

Rhythms	Test Sample Size	Performance Goal	Observed Performance	90% One-sided Lower Confidence Limit
<i>Shockable</i>				
Coarse VF	536	>90% sensitivity	100% sensitivity	99.44%
Rapid VT	80	>75% sensitivity	98.75% sensitivity	94.21%
<i>Non-shockable</i>				
NSR	2210	>99% specificity	99.95% specificity	99.79%
AF, SB, SVT, heart block, idioventricular, PVCs	819	>95% specificity	100% specificity	99.63%
Asystole	115	>95% specificity	100% specificity	97.43%
<i>Intermediate</i>				
Fine VF	69	Report only	94.20% sensitivity	87.22%
Other VT	28	Report only	100% specificity	89.85%

Table 5: Clinical Performance Results (Pediatric Patients)^{2,3}

Rhythms	Test Sample Size	Performance Goal	Observed Performance	90% One-sided Lower Confidence Limit
<i>Shockable</i>				
Coarse VF	42	>90% sensitivity	100% sensitivity	99.44%
Rapid VT	79	>75% sensitivity	100% sensitivity	94.21%
<i>Non-shockable</i>				
NSR	208	>99% specificity	100% specificity	99.79%
AF, SB, SVT, heart block, idioventricular, PVCs	348	>95% specificity	99.43% specificity	99.63%
Asystole	29	>95% specificity	100% specificity	97.43%
<i>Intermediate</i>				
Fine VF	0	Report only	N/A	N/A
Other VT	44	Report only	81.82% specificity	69.58%

Biocompatibility Testing:

The only patient contacting portions of the AED Plus and Fully Automatic AED Plus systems are the electrodes used with the device, and the plastic cover of the AED Plus which is used for passive airway support. 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 AED Plus and Fully Automatic AED Plus software 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 AED Plus software perform as intended.

Shelf Life Testing:

Shelf life testing was conducted to demonstrate the claimed shelf life for the electrodes used with the AED Plus and Fully Automatic AED Plus[®]. Table 6 below lists electrode shelf life information.

Table 6: Electrode Shelf Life

Electrode	Shelf Life
CPR-D Padz Electrode	63 Months
CPR Stat-Padz Electrode	24 Months
Stat-Padz II electrode	24 Months
Pedi-padz II Electrode	24 Months

The applicant validated the shelf life for each electrode model via electrical and performance testing of samples after accelerated aging.

B. Animal Studies

To support a pediatric Indications For Use for the ZOLL Rectilinear Bi-Phasic 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 Bi-Phasic 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 proposed 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 Bi-Phasic 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).

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The ZOLL AED Plus and Fully Automatic AED Plus use the ZOLL Rectilinear Bi-Phasic Waveform, which is the same waveform as ZOLL's M Series Bi-Phasic Defibrillator (cleared by the FDA under 510(k) Premarket Notification K990762). It was in this earlier 510(k) submission for ZOLL's M Series Bi-Phasic Defibrillator that the clinical data supporting the safety and effectiveness of ZOLL's Rectilinear Bi-Phasic Waveform was presented to the FDA. A summary of this clinical data is presented below.

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 (3) consecutive 120, 150, 170J) efficacy of the rectilinear biphasic waveform with that of a monophasic waveform (three (3) 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 (2) waveforms were considered statistically significant when the 90% confidence interval between the two (2) 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 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 Bi-Phasic defibrillation waveform. The resulting clinical

paper, “Performance of a rectilinear biphasic waveform in defibrillation of presenting and recurrent ventricular fibrillation: A prospective multicenter study,”⁴ was provided as support to demonstrate 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.

As the data and studies to support use of the ZOLL Rectilinear Bi-Phasic Waveform for adult and pediatric patients were previously reviewed and cleared by the FDA under the 510(k) submissions K011388, K033474, and K120406; no new studies have been conducted or included in this PMA application. Rather, all of 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 Bi-Phasic Defibrillation Waveform technology for use in both adult and pediatric patients, are included in this PMA application.

D) Human Factors and Usability Study

Overview:

To support a fully automatic shock delivery protocol, ZOLL submitted usability testing as part of a 510(k) submission (K120406) for its AED Plus. The protocol for this usability study, along with a summary of the results, are included in this PMA application. A summary of this study is presented below.

Objectives:

The goal of this usability evaluation was to validate, using summative test methods, that the final design modifications and corresponding hazard mitigations were effective in mitigating user error with hazard and no unanticipated hazards were created.

In addition to assessing the effectiveness of the device design in mitigating specific use-related hazard of the Fully Automatic AED Plus, the applicant also assessed additional hazards wherein:

- User confuses a semi-automatic device with a fully automatic device – user does not press the shock button and treatment is not delivered.
- The Fully Automatic device order is incorrectly shipped with semiautomatic software configuration – user does not press the shock button and treatment is not delivered.

Methods:

Three (3) devices were used in this study: An AED Plus, a Fully Automatic AED Plus, and a device inaccurately labeled as a Fully Automatic AED Plus but configured with semi-automatic software. The reason the applicant used a mislabeled (semi-automatic) AED Plus was to test the additional hazards in the bulleted list above. Twenty-one (21) healthcare professionals trained in CPR and the use of an AED were recruited for this study. The subjects were asked to go through the primary use case of the device, which is a simulated victim of cardiac arrest that is unresponsive. The subjects were evaluated on the key tasks and response times for delivery of therapy and essential tasks.

Results:

All subjects were able to open each AED and turn it on, open the pad packaging and attach the pads to the patient, use AED analysis on a shockable rhythm (including shock delivery), and perform CPR based on the device prompts. No subjects failed to appropriately press the shock button when using the semi-automatic device or the fully-automatic device configured with the semi-automatic software, and no subjects came into contact with the patient during the delivery of the shock with the fully-automatic device. The response time between semi-automatic and fully automatic models were comparable.

Conclusions:

The design of the AED Plus and Fully Automatic AED Plus devices appropriately addressed the intended use and user needs. The design properly mitigated the use-related risks and use-related errors. No use-related errors were noted during the study which could cause a hazard.

E) Complaint Analysis

To further demonstrate the safety and effectiveness of the devices in clinical use, relevant complaint data were analyzed since the devices were launched for marketing.

Between January 1, 2014, and June 15, 2016, a total of 915 complaints (i.e., Medical Device Reports (MDRs)) have been received on the AED Plus. (Note: Prior to this PMA submission, both the AED Plus and Fully Automatic AED Plus were marketed under the same trade name. Therefore they are indistinguishable in the MDRs.)

Twenty-five (25) deaths were reported for the AED Plus, of which seven (7) devices were returned to the applicant for investigation. Four (4) of the seven (7) devices failed to charge for a “shock advised” prompt because the user pressed the shock button prior to the device prompting the user to press the flashing shock button. The other three (3) deaths were reportedly due to the device inappropriately shutting down, but the applicant was unable to duplicate the reported problem in these events. The remaining 18 devices were not returned to the applicant for investigation. In four (4) of 18 reports, the applicant described that the device gave a “no shock advised” prompt for a shockable rhythm. Five (5) other reports described that the device failed to power up during a patient event. The remaining nine (9) reports indicated that the device was unable to detect the attached electrode pads.

Of the 915 MDRs, there were 830 malfunctions reported for the AED Plus device, of which 347 were returned to the applicant for evaluation. The malfunctions in these 347 reports are grouped into the following categories.

1. Failure to Power Up and Loss of Power (211 reports)
 - Main board failures which were caused by various component issues such as a resistor, transistor, and capacitors malfunctions
2. Device Displays Error Message (98 reports)
 - Battery depletion due to fuse issues and battery board malfunctions
3. Connection Issue (3 reports)
 - Electrode pads connection failure due to pin malfunction
4. Failure to Discharge (6 reports)
 - Due to faulty connector on the LCD interface board
5. Communication Issue (2 reports)

- Language software not installed in the device

6. Device failure to power up due to user maintenance issue (27 reports)
The device failures (reflected in numerals 1 through 4 above) were confirmed by the applicant.

F) Pediatric Extrapolation

In this premarket approval application, two (2) animal studies were 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 Bi-Phasic 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 and a biphasic truncated exponential waveform. 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

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation.

The applicant submitted a signed certification of financial interests and arrangements of clinical investigators with regard to the two (2) clinical studies they sponsored. The applicant certified 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). The applicant also certified that each clinical investigator required to disclose to the applicant 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) did not disclose any such interests. The applicant further certified 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 2011⁴, 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 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 Bi-Phasic 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* (82 (2011) 685–689)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 Bi-Phasic 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 and a biphasic truncated exponential waveform.

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^{1,4}. 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 waveform⁴ 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. AEDs 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 7% to 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 will 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 for patients in cardiac arrest who are unconscious, not breathing, or without circulation the probable benefits outweigh the probable risks.

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 May 26, 2017. FDA has developed unique conditions of approval to pursue real world information and in response to panel comments from the 515i Panel discussed in Section XI above. The final conditions of approval cited in the approval order are described below.

The applicant will 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.

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. Young KD, Lewis RJ: "What is confidence? Part 2: Detailed definition and determination of confidence intervals". *Annals of Emergency Medicine*, September 1997; 30; 311-218.
3. "CRC Standard Mathematical Tables 28th Edition", William H. Beyer, Ph.D., CRC Press, Inc, Boca Raton, FL., 1981, Percentage Points, F-Distribution Table, pg 573.

4. 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.