SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. General Information

Device Common Name:	Wearable Cardioverter Defibrillator
Device Trade Name:	ASSURE Wearable Cardioverter Defibrillator (WCD) System (ASSURE system)
Product Code:	MVK
Applicant's Name and Address:	Kestra Medical Technologies, Inc. 3933 Lake Washington Blvd. NE, Suite 200 Kirkland, WA 98033
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P200037
Date of FDA Notice of Approval:	July 28, 2021

II. INDICATIONS FOR USE

The ASSURE system is indicated for adult patients who are at risk for sudden cardiac arrest and are not candidates for, or refuse, an implantable defibrillator.

III. CONTRAINDICATIONS

The ASSURE system is contraindicated for use on patients with an active implantable defibrillator.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the ASSURE system labeling.

V. DEVICE DESCRIPTION

The ASSURE Wearable Cardioverter Defibrillator (WCD) System (ASSURE system) is a non-invasive, external, patient-worn device designed to automatically assess an electrocardiogram (ECG) for life-threatening ventricular arrhythmias and deliver a defibrillation shock to the heart to restore an effective rhythm without further interaction from the patient or bystander. The system is available to patients by prescription only and typical length of use is anticipated to be 2–3 months.

The primary use environment of the ASSURE system is the home healthcare setting, but the device may be worn in a clinical environment. The ASSURE system is intended to be worn 24 hours a day during normal activities except while bathing or swimming. The device can be worn at home, in outdoor environments, office environments, retail environments, schools, vehicles, emergency shelters, and independent living retirement homes.

The ASSURE system includes the WCD and accessories. The WCD is comprised ofwearable components including the Garment, Monitor, Battery, and Therapy Cable. The Carry Pack is a wearable accessory designed to hold the Monitor and provide a method for the patient to wear the Monitor around the waist or over the shoulder. Non-wearable components of the ASSURE system include the Charger and a Tablet for programming the Monitor. Components of the ASSURE system are illustrated in Figure 1 and further described in Table 1.

The ASSURE system communicates its status to the patient through alerts, which may consist of voice messages, display icons, audio tones, and vibration. When the device detects a ventricular arrhythmia, it issues an alert to notify the patient that they are about to receive a shock. The ASSURE system automatically delivers a defibrillation shock within approximately 40 seconds from the onset of VF (approximately 80 seconds for VT), unless a conscious patient diverts the shock by pressing the Alert Button. The ASSURE system can deliver up to five shocks during an arrhythmic episode. The heart rate threshold above which an arrhythmia is detected and treated is set using the Tablet per the physician prescription during the device fitting process. Information about detected rhythms are stored in the form of episodes including four channels of electrogram data and a marker channel that identifies algorithm detection decisions.

Episodes are retrievable from the Monitor over a Bluetooth link and can be transmitted to a remote Medical Device Data System (MDDS) for viewing and printing. Refer to the Instructions for Use for additional details.

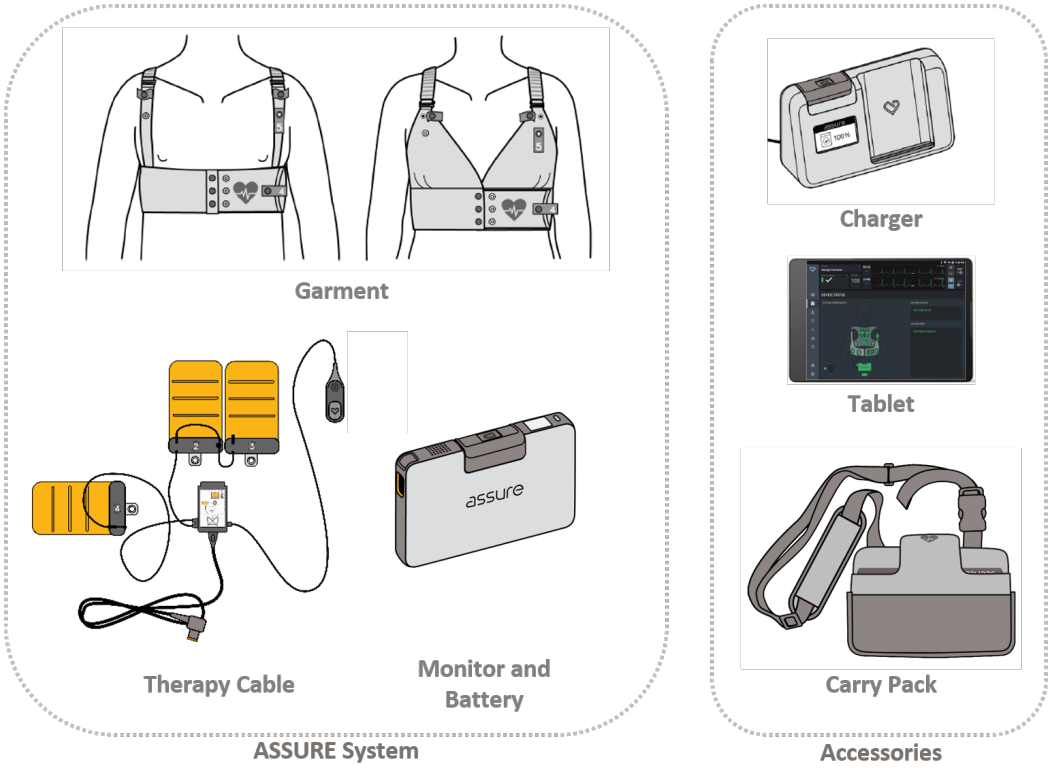

Figure 1: ASSURE System

Table 1: ASSURE System Component Descriptions

ASSURE System Component	Description
Garment	A fabric top that contains the ECG sensors that track heart rhythm. It is worn directly on the body against bare skin.
Therapy Cable	A group of connected parts consisting of the Hub, Alert Button, Therapy Pads, and a Cable that connects to the Monitor. The front and back Therapy Pads are inserted into the Garment and dispense gel prior to delivering an electrical shock to the heart when needed.
Monitor (with Battery)	The part of the ASSURE system that provides power and displays system status information (a rechargeable Battery powers the Monitor).
Charger	A separate device that charges the Battery.
Tablet	An electronic device used to program the ASSURE system and assist in patient fitting and training.
Carry Pack	A portable case that holds the Monitor while patient is wearing the ASSURE system.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for adult patients who are at risk for sudden cardiac arrest and are not candidates for, or refuse, an implantable defibrillator. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle. The alternatives include:

- *Antiarrhythmic medication for reduction or suppression of certain ventricular arrhythmias.* Some drugs such as amiodarone and beta-blockers have been shown to decrease the number of ventricular arrhythmias and thus reduce the incidence of sudden cardiac arrest (SCA). However, they are limited in use to patients who have already experienced ventricular tachyarrhythmias and have documented morbidity and even mortality impact.
- *Sudden Cardiac Arrest Treatment by Emergency Medical Services, EMS, or Calling 911.* Paramedics are trained to diagnose defibrillation-reversible conditions and apply such therapy if needed, but paramedics may not always be available in a timely manner to treat someone who arrests.
- *Automatic External Defibrillators (AEDs) in the community.* Bystander use of an AED is an option; however, a bystander with an AED may not always be available in a timely mannerto treat an arrested patient.
- *AEDs in the Home.* AEDs may be prescribed for use within the home, however, a caregiverin the home with an AED may not always be available in a timely manner to treat an arrested patient.
- *Implantable Cardioverter Defibrillators (ICDs).* ICDs are surgically implanted in patients shown to have long term risk of SCA to protect them from sudden cardiac death. In general, patients having uncertain or temporary SCA risk are not indicated for ICD implantation. ICDs

also impose risks of infection, inappropriate therapy, and require a waiting period during which the patient is vulnerable to a repeat cardiac arrest.

- *Telemetry monitoring within a Hospital Environment.* Hospitalization with telemetry monitoring for arrhythmias and rapid response for external defibrillation can be effective but requires extended hospitalization for monitoring and also attention by staff for arrhythmia notifications.
- *Use of other commercially available WCD products.*

VII. MARKETING HISTORY

The ASSURE system has not been marketed in the United States or any foreign country. The system has no approvals for sale outside of the U.S. There have been no sales or payments for these devices to date. The ASSURE system has not been withdrawn from the market in any country for any reason.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of potential adverse effects (e.g., complications) associated with the use of a Wearable Cardioverter Defibrillator:

- Failure to sense and detect a treatable ventricular arrhythmia resulting in death.
- Unsuccessful cardioversion or defibrillation resulting in death or disability.
- Inappropriate shock causing abnormal heart rhythms, including fatal rhythms.
- Improper, ineffective, or non-operation of the device due to external causes such as electromagnetic interference.
- Failure resulting from random component failure.
- Damage to or reset of a pacemaker due to a shock.
- Superficial skin burns resulting from defibrillation.
- Pain from conscious shock.
- Mild to moderate skin irritation or allergic dermatitis due to sensitivity to the materials used in the construction of the Garment.
- Skin infection (bacterial or yeast) secondary to continuous skin contact by electrodes or Garment.
- Bystander shock from patient contact during a treatment event.
- Fire hazard in the presence of a high oxygen concentration.
- Muscle strain or shoulder discomfort.
- Bruising from monitor striking a body part.
- Trip hazard or fall

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

The ASSURE system underwent laboratory-based testing that included bench testing summarized in Table 2, biocompatibility evaluations, electrical and EMC testing, and software verification and validation. Testing was conducted on key device subassemblies and the complete system.

Table 2: Functional and Environmental Tests for the ASSURE System

Test	Purpose	Acceptance Criteria	Results
Accuracy of energy delivery	Verify the ASSURE system energy delivery meets its specified requirements across a range of impedances.	The device shall meet or exceed the requirements of IEC 60601-2-4: 2010 clause 201.12.1 for delivered energy accuracy.	Met
Sealing/Moisture Resistance	Verify the ASSURE system meets the requirements for IP22 rating per specifications.	The device shall meet EN60529 Class IP22 as appropriate per specification.	Met
Random vibration	Demonstrate reliable operation after being subjected to the Vibration test according to IEC 60601-1-11 clause 10.1.3 c) for a Transit Operable Body Worn device.	The device shall maintain Basic Safety and Essential Performance after being subjected to the Vibration test.	Met
Drop test	Demonstrate reliable operation after being subjected to drop testing per IEC 60601-1:15.3.4.1 and IEC 60601-1-11.	The device shall maintain basic safety and essential performance after being dropped from 1 meter onto a hardwood board on a concrete surface on each of its three (3) axes without producing a safety risk to the device.	Met
Push test	Demonstrate reliable operation after enclosure parts are subjected to push test per IEC 60601-1 clause 15.3.2.	ASSURE Monitor meets basic safety and essential performance requirements after enclosure parts are subjected to push test.	Met

Table 2: Functional and Environmental Tests for the ASSURE System (Continued)

Test	Purpose	Acceptance Criteria	Results
Mechanical Shock	Demonstrate reliable operation following shock test according to IEC 60601-1-11 clause 10.1.3 a.	ASSURE Monitor meets basic safety and essential performance requirements following shock test. The enclosure parts shall have no rough surfaces, sharp edges or corners that could result in injury or damage.	Met
Impact test	Demonstrate ability of ASSURE Monitor to withstand impact testing per IEC 60601-1 clause 15.3.3 while powered on.	System meets basic safety and essential performance requirements following impact test. The enclosure parts shall have no rough surfaces, sharp edges or corners that could result in injury or damage.	Met
Transport and storage environment conditions	Verify the system withstands storage and transport conditions as defined in IEC 60601-1-11 clause 4.2.2.	The device shall meet the requirements for Basic Safety and Essential Performance during and after being subjected to specified storage requirements.	Met
Operating environment conditions	Verification of device performance over ranges of temperature, altitude, and humidity.	The device shall meet the requirements for Basic Safety and Essential Performance while being subjected to specified storage requirements per 60601-1-11 clause 4.4.3.	Met
RF Performance	Verify the ASSURE system and data collection client, together, shall not exceed the limits for maximum permissible exposure to RF Electromagnetic Fields.	47 CFR Part 2, Subpart J Section 2.1093 for portable devices and per FCC Office of Engineering & Technology Bulletin 65 (Edition 97-01).	Met
Wireless Coexistence	Demonstrate ability of system to withstand expected levels of wireless transmission from external sources.	No observations at the applied levels and no latent effects resulting from exposure– system must pass operate as specified test.	Met

Table 2: Functional and Environmental Tests for the ASSURE System (Continued)

Test	Purpose	Acceptance Criteria	Results
Dielectric strength	Verify the device complies with the requirements of IEC60601-2-4 Edition 3.0 section 201.8.8.3 test 2 and test 3.	IEC 60601-2-4 clause 201.8.8.3 with an applicable highest working voltage of 1680 VDC.	Met
Therapy Cable durability	Verify the Therapy Cable's ability to comply with the requirements of IEC60601-2-4 Edition 3.0 section 201.15.4.101.	After being subjected to the stresses specified in IEC 60601-2-4 clause 201.15.4.101, the Therapy Cable shall not have worked loose from its connectors nor shall the cable show visible damage beyond that specified in the standard.	Met
Electrode Active Area	Verify the Therapy Pads shall comply with the Electrode Active Area requirement in IEC 60601- 2-4 for adult transthoracic electrodes after gel release.	After gel release, the Therapy Pads shall comply with the active area requirement in IEC 60601- 2-4 clause 201.108.1.7	Met
Battery	Verify device compliance with IEC 60602-2-4 clause 201.102.3.2 for an infrequent use device.	Using a new and fully charged Battery, the ASSURE system shall deliver 20 defibrillation discharges of 170J.	Met
Therapy Delivery Endurance	Verify device compliance with IEC 60602-2-4 clause 201.103 for an infrequent use device.	The device shall meet its performance requirements for therapy delivery after being charged and discharged no less than 100 times into a 50Ω load per the requirements of IEC 60601-2-4 clause 201.103.	Met
Battery Life	Verify a newly charged Battery can power the ASSURE system for a minimum of 24 hours.	With new and fully charged Battery installed in the Monitor, the WCD shall be able to operate for a minimum of 24 hours according to typical runtime scenarios	Met

Test	Purpose	Acceptance Criteria	Results
Simulated use of overall system	Demonstrate system functionality	The system shall successfully complete rhythm detection and shock decisions for various database rhythms. When a shock is required, the device shall activate shock alarms and deliver a shock.	Met

All protocols, test reports, and acceptance criteria have been reviewed and found to be acceptable. All devices met all pre-determined acceptance criteria during testing.

Biocompatibility Testing

Biocompatibility evaluation for the Garment and Therapy Cable components of the ASSURE system was performed in accordance with the recommendations of CDRH's biocompatibility guidance document, Use of International Standard ISO 10993-1, "Biological Evaluation of Medical Devices-Part 1: Evaluation and Testing within a risk management process". Direct patient contact materials underwent cytotoxicity, intracutaneous reactivity, and sensitization testing and were found to adequately demonstrate biocompatibility.

Electrical Safety and EMC

The ASSURE system hardware was tested and found to meet the performance criteria in the following standards (Table 3).

Table 3: Electrical Safety and EMC Standards for the ASSURE System

Standard	Title
ANSI/AAMI ES60601-1:2005/(R)2012 and A1:2012 C1:2009/(R)2012 and A2:2010/(R)2012 (Consolidated Text)	Medical electrical equipment - Part 1: General requirements for basic safety and essential performance (IEC 60601-1:2005, MOD)
IEC 60601-2-4: 2010 (Third Edition) for use in conjunction with IEC 60601-1 (2005)	Medical electrical equipment Part 2: Particular requirements for the safety of cardiac defibrillators
IEC 60601-1-2 Edition 4.0: 2014-02	Medical Electrical Equipment - Part 1-2: General Requirements For Basic Safety And Essential Performance - Collateral Standard: Electromagnetic Disturbances - Requirements and Tests

Further, comprehensive risk management was performed for the risks of electromagnetic disturbance to the wearable AED, which are not adequately addressed by the specifications of the above-mentioned standards. The risk management considered the relevant recommendations of FDA's "Design Considerations for Devices Intended for Home Use" guidance document (https://www.fda.gov/media/84830/download). The risk management resulted in an EMC test protocol based on the relevant gap analysis with the following.

- Section 20 of the "RTCA DO-160G:2010, Environmental conditions and test procedures for

airborne Equipment" to demonstrate aircraft immunity per Category R.

- All the information in the "ISO 14117 Second edition 2019-09, Active implantable medical devices - Electromagnetic compatibility - EMC test protocols for implantable cardiac pacemakers, implantable cardioverter defibrillators and cardiac resynchronization devices" standard.
- The specifications of the "AIM Standard 7351731 Rev. 2.00 2017-02-23 Medical Electrical Equipment and System Electromagnetic Immunity Test for Exposure to Radio Frequency Identification Readers" standard.

Finally, the EMC test was performed based on the recommendations of the "Information to Support a Claim of Electromagnetic Compatibility (EMC) of Electrically-Powered Medical Devices" guidance document (https://www.fda.gov/media/94758/download).

Packaging and Shelf Life

Packaging/Shipping Test

The packaging of the ASSURE system was subject to and has met the requirements for international shipping and handling using procedures and methods defined in ISTA Procedure 2A, Performance Test Procedure for Individual Packaged Products Weighing 150 Lbs. (68 Kg) or less. The shipping and storage temperature of the ASSURE System Kit is from -20°C to 50°C with a relative humidity up to 90%.

Shelf-Life

The shelf-life of the ASSURE system is limited by the shelf-life of the Battery and Therapy Pads. Testing has been completed that supports a shelf life of 24 months. The ASSURE system may be stored at temperatures of -20ºC (-4ºF) to 50ºC (122ºF) and up to 95% humidity with no condensation.

Software

Comprehensive verification and validation testing were conducted to confirm that the software used in the ASSURE system meets all specified requirements and that the software will operate reliably and safely under normal or abnormal use conditions.

The software for the ASSURE system was verified/validated and documented as Major Level of Concern software according to the FDA Guidance Document, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices: Guidance for Industry and FDA Staff" issues on May 11, 2005. Software development activities included establishing detailed software requirements, tracing requirements to associated verification tests, software code reviews, unit testing, system level testing and defect tracking, and dispositioning to ensure the software conforms to user needs and intended uses. Unit, integration, and system level testing was documented and demonstrated that the software for the ASSURE system performs as intended.

Cybersecurity was verified and documented according to FDA Guidance Document, "Content of Premarket Submissions for Management of Cybersecurity in Medical Devices Guidance for Industry and Food and Drug Administration Staff" issued on October 2, 2014.

B. Animal Studies

Kestra performed a series of pre-clinical studies to test the safety and effectiveness of the ASSURE WCD shock waveform. Swine were used as the animal model for these studies because their thoracic anatomy, coronary arteries, and thoracic impedance are similar to humans and they have been used in

numerous other defibrillation studies. Animal care complied with the Guide for Animal Care and Use of Laboratory Animals (NIH), the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals, the USDA Animal Welfare Act and Regulations, and IACUC Standard Operating Procedures and the facility animal care program.

The ASSURE waveform was developed and tested through nine pre-clinical studies, seven specifically evaluating effectiveness and two evaluating safety. The following table provides a chronological listing of the seven effectiveness studies. Initial studies (studies 1-5) with prototype waveforms facilitated selection of the final pulse widths and energy. Studies 6 and 7 were statistical studies to evaluate the final ASSURE waveform. Study 6 tested the waveform shape at three different impedance levels using an energy level near the estimated 50% defibrillation threshold. Study 7 tested the waveform at full energy. Two additional studies were performed to establish waveform safety.

Effectiveness Study Descriptions

Effectiveness Study 1: Original Pilot Study

Background: This study compared the effectiveness of two prototype ASSURE waveforms with the V waveform. The purpose of this study was to compare the effectiveness of the prototype ASSURE shock waveforms to the V shock waveform in swine.

Methods: A programmable waveform generator was used to generate attenuated shock waveforms that simulated the waveshape that was delivered into 25Ω, 50Ω, and 100Ω. Shock success rates were recorded for each waveform at each impedance level in ten swine. The tested prototype waveforms were considered non-inferior to V waveform at a given impedance if the lower 95% confidence bound for the difference in success rate (i.e. ASSURE – V) was greater than -10%.

Results: The prototype ASSURE wave forms were non-inferior to the V shock waveform at all three impedances. Prototype ASSURE2 success rates were numerically greater than prototype ASSURE1 but the difference was not statistically significant.

Conclusions: The prototype ASSURE2 shock waveform was chosen for further study.

Effectiveness Study 2: Non-inferiority Study with prototype ASSURE Waveform

Background: The Original Pilot Study provided evidence that the prototype ASSURE2 waveform was non-inferior to the V waveform when the shocks were generated with a programmable waveform generator, this second effectiveness study sought to compare the prototype ASSURE2 shock success rate to the V shock success rate at 50Ω, 85Ω, and 125Ω using an ASSURE prototype system.

Methods: Prototype ASSURE shock waveforms were attenuated to achieve approximately 50% success rate and the V shock waveforms were attenuated by the same percentage. Prototype ASSURE2 was considered non-inferior to V at a given impedance if the lower 95% confidence bound for the difference in success rate (i.e., ASSURE – V) was greater than -10%. Thirty-six swine were planned for this study.

Results: The study was terminated after 20 swine because ASSURE2 was unlikely to meet non-inferiority objectives.

Conclusions: The prototype ASSURE2 waveform effectiveness was lower than V at all three impedance levels, especially at 125Ω. Further investigation was undertaken to improve the performance of the prototype ASSURE shock waveform.

Effectiveness Study 3: WOW 125 Ohm Study

The WOW 125 Ohm Study compared the Walcott Optimized Waveform (WOW) to the prototype ASSURE2 waveform at 125Ω. This informal study used six animals, a sample size that had previously been adequate to provide meaningful results. The results indicated that the Walcott Optimized Waveform was about 10% more effective than the original prototype ASSURE2 waveform at 125Ω.

Effectiveness Study 4: WOW 50 Ohm Study

The WOW 50 Ohm Study compared the effectiveness of the Walcott Optimized Waveform at two different charge voltages to V at 50Ω. The results from this study indicated that the WOW waveform was slightly less effective than ASSURE2 at the same charge voltage at 50Ω. If the charge voltage was increased slightly, the WOW waveform was about equivalent to ASSURE2. These results led to the development of a 'blended' waveform – a shock waveform that used the ASSURE2 waveform below 85Ω and used the WOW waveform above 85Ω.

Effectiveness Study 5: Blended Pilot Study

The Blended Pilot Study tested the Final ASSURE Waveform (the blended waveform with slightly higher charge voltage resulting in 170J) at 50Ω and 125Ω. The purpose of this final study was to gather data for sample size estimation before initiation of a formal non-inferiority study. Nine swine were tested at 50Ω and six swine at 125Ω. The results from this study suggested that this Final ASSURE Waveform was more effective than any of the previous shock waveforms.

Effectiveness Study 6: Non-inferiority Study with Attenuated Energy

Background: This study sought to provide scientifically rigorous evidence that the Final ASSURE Waveform was non-inferior to the V waveform at three impedances (50, 85, and 125Ω).

Methods: Thirty-six pigs were shocked with the Final ASSURE Waveform and the V waveform at three impedances ASSURE shock waveforms were attenuated to achieve approximately 50% success rate and V shock waveforms were attenuated by the same percentage. ASSURE was considered non-inferior to V waveform at a given impedance if the lower 95% confidence bound for the difference in success rate (i.e. ASSURE – V) was greater than -10%.

Results: A total of 2,160 ventricular fibrillation (VF) inductions were performed in 36 swine.

Table 4: Percent Differences in Success Rate (ASSURE -V)

	% Success Assure	% Success V waveform	Difference
50 ohms	56%	55%	1%
85 ohms	53%	46%	7%
125 ohms	53%	41%	12%

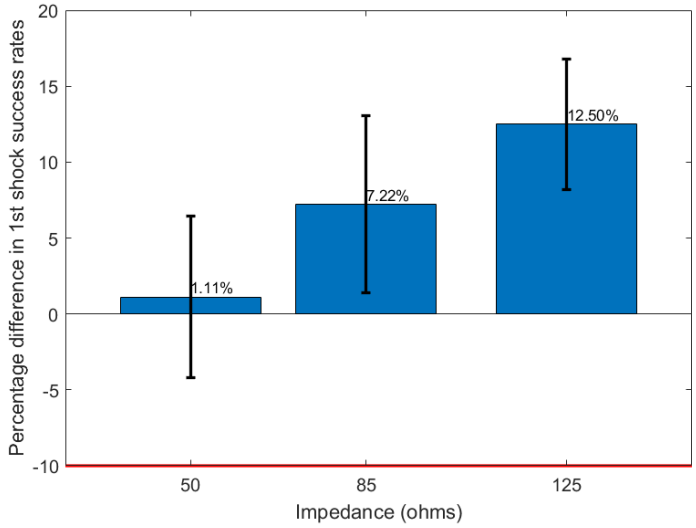

Figure 2: Differences in Success Rate (ASSURE-V)

Conclusions: This study demonstrated that an attenuated ASSURE shock waveform was non-inferior to an equally-attenuated V shock waveform.

Effectiveness Study 7: Full Energy Effectiveness Study

Background: While previous studies compared shock waveforms at reduced energy levels, the Full-Energy Effectiveness Study compared the Final ASSURE waveform at 170J to the V waveform at 150J. The goal of the study was to demonstrate that the ASSURE waveform was non-inferior to the V waveform at clinically relevant energy levels.

Methods: Six pigs 27 – 33 kg were induced into VF and shocked with either a 170J ASSURE waveform or 150J V waveform Ten shocks with each waveform were given to each pig. ASSURE was considered non-inferior to V at a given impedance if the lower 95% confidence bound for the difference in success rate (i.e. ASSURE – V) was greater than -10%.

Results: All shocks succeeded, giving 100% shock success rate for each device. Because there were no shock failures for either waveform the difference in success rates was zero. The lower 95% confidence interval of the difference was zero, which met the definition of non-inferiority.

Conclusions: This study demonstrated that a full-energy ASSURE shock waveform is non-inferior to a full-energy V shock waveform.

Safety Studies

Safety Study 1:

Background: The study aimed to show that the ASSURE WCD shock waveform does not cause more injury than another commercially available external defibrillator.

Methods: Eight 62 – 76 kg swine were split into two groups of four. One group was shocked with five 170J ASSURE shocks, while the other group was shocked with five 200J external defibrillator shocks. All shocks were delivered synchronously into a normal sinus rhythm. Pre- and post-shock values of Troponin I, CPK, CK-MM, and CK-MB were compared to look for signs of injury. Pre- and post-shock ECG recordings were also compared. Post-shock blood draws and ECG recordings were taken at 6 hours and 24 hours. In addition, tissue samples were evaluated for injury at the macro and microscopic level by a board-certified pathologist. Tissue injury was evaluated on a scale of 0 – 3, where 0 is normal and 3

represents significant injury. An injury score difference (ASSURE minus external defibrillator) of 0.4 or greater was considered significant.

Results: None of the blood tests demonstrated a significant difference between the two devices.

Table 5: Troponin I Results (mean ± std dev)				
	ASSURE	External Defibrillator	P-Value	Pass/Fail
6-hour delta	0.7275 ± 0.97	0.2725 ± 0.40	0.4522	Pass
24-hour delta	0.0875 ± 0.15	0.0750 ± 0.11	0.8893	Pass

Table 6: CK-MM Results (mean ± std dev)				
	ASSURE	External Defibrillator	P-Value	Pass/Fail
6-hour delta	40800 ± 15500	23200 ± 32000	0.1178	Pass
24-hour delta	35500 ± 7900	10500 ± 6200	0.2678	Pass

The histology results showed that the difference in injury scores were below the predetermined threshold of 0.4 in all tissue samples.

Table 7: Histology Injury Results (mean ± std dev)				
Tissue Section	ASSURE Average	External Defibrillator Average	Difference	Pass/Fail
Myocardium	0.75 ± 0.5	0.50 ± 0.6	0.25	Pass
Lung	0.0 ± 0	0.5 ± 0	-0.5	Pass
Skin and Skeletal Muscle	1.5 ± 0.5	1.5 ± 0.6	0.0	Pass

The ECG evaluation showed that although transient post-shock ECG changes were observed in both groups, no significant changes persisted at the one-hour mark or six-hour mark post-shock. Overall, there were no significant differences between the two groups.

Conclusions: The ASSURE shocks did not cause significantly more injury than External Defibrillator shocks in this study.

Safety Study 2: V and 360J External Defibrillator Safety Study

Background: While Safety Study 1 found no significant difference in the mean values of ASSURE and an external defibrillator, there were outliers in the ASSURE CPK results. This study sought to explain these outliers by gathering additional data under more controlled conditions.

Methods: Fourteen swine (38 – 52kg) were split into four groups. The 170J ASSURE group (N=5), the 150J V group (N=5), and the 360J external defibrillator group (N=3) all received five synchronous shocks in normal sinus rhythm with the corresponding defibrillator. The final group was a sham animal (N=1) to explore the effect of the test procedure on CPK values. Pre- and post-shock values of troponin I, CPK, CK-MM, and creatinine were compared to look for signs of injury. Post-shock blood draws were taken at 1 hour, 6 hours, and 24 hours. Pre-shock ECG recordings were compared to those taken at 1 hour and 6 hours.

Results: No significant ($p<.05$) differences between ASSURE and V were found in troponin I, CPK, CK-MM, and creatinine were found. Statistically significant differences between ASSURE and the external

defibrillator were found in Troponin I, CPK, and CK-MM.

Table 8: Troponin I Results (mean ± std dev)					
	ASSURE	V waveform	P-Value	EXTERNAL DEFIBRILLATOR	P-Value
1-hour delta	0.00 ± 0.01	-0.01 ± 0.01	0.51	0.03 ± 0.03	0.07
6-hour delta	0.12 ± 0.04	0.05 ± 0.06	0.06	0.46 ± 0.23	0.01
24-hour delta	0.08 ± 0.05	0.05 ± 0.04	0.27	0.29 ± 0.35	0.27

Table 9: CK-MM Results (mean ± std dev)					
	ASSURE	V waveform	P-Value	EXTERNAL DEFIBRILLATOR	P-Value
1-hour delta	1,134 ± 1,401	321 ± 147	0.23	1,532 ± 385	0.66
6-hour delta	7,508 ± 3,417	7,108 ± 5,242	0.85	13,181 ± 623	0.03
24-hour delta	14,745 ± 7,932	20,888 ± 15,698	0.45	32,860 ± 10,203	0.03

Table 10: Creatinine Results (mean ± std dev)					
	ASSURE	V waveform	P-Value	EXTERNAL DEFIBRILLATOR	P-Value
1-hour delta	0.14 ± 0.25	0.06 ± 0.11	0.57	0.10 ± 0.10	0.68
6-hour delta	0.23 ± 0.13	0.20 ± 0.19	0.13	0.53 ± 0.59	0.92
24-hour delta	0.32 ± 0.34	0.04 ± 0.21	0.15	0.23 ± 0.12	0.67

The sham animal showed no increase in troponin I and a small increase in CPK and CK-MM, as well as a creatinine change that was comparable to the shocked animals.

Conclusions: This study found no significant differences in injury markers for swine shocked with ASSURE versus V. The ASSURE shocks caused less injury than 360J external defibrillator shocks.

C. Additional Studies

Detection Algorithm Validation

The ASSURE detection algorithm was validated using ECG databases intended to provide a representative sample of rhythms from patients who were both in-hospital and out of hospital. The device meets or exceeds the recommendations of the American Heart Association (AHA) Scientific Statement[1] performance goals of arrhythmia analysis algorithms, as summarized in Table 11.

The database contains 1,683 ECG segments from 590 patient cases. Per AHA guidelines, only the first segment obtained from each subject of a particular rhythm type was included for this analysis.

Table 11: Detection Algorithm Performance

Rhythms	Test Sample Size (Minimum required[1])	Performance Goal[1]	Observed Performance	90% One-sided LCL (Minimum LCL[1])
Shockable				
Coarse VF	204 (200)	>90% sensitivity	99.0%	97.4% (87%)
Rapid VT	62 (50)	>75% sensitivity	98.4%	93.9% (67%)
Non-Shockable				
Normal Sinus Rhythm (NSR)	132 (100)	>99% specificity	100%	98.3% (97%)
AF, Sinus Bradycardia, SVT, Heart Block, idioventricular, PVCs	219 (30)	>95% specificity	96.3%	94.1% (88%)
Asystole	169 (100)	>95% specificity	97.6%	95.3% (92%)
Intermediate				
Fine VF	28 (n/a)	Report Only	75.0% sensitivity	61.6% (n/a)
Other VT	22 (n/a)	Report Only	95.5% sensitivity	83.4% (n/a)
Slow VT	36 (n/a)	Report Only	97.2% specificity	89.6% (n/a)

1. Richard E. Kerber et al., "Automatic External Defibrillators for Public Access Defibrillation: Recommendations for Specifying and Reporting Arrhythmia Analysis Algorithm Performance, Incorporating New Waveforms, and Enhancing Safety," *Circulation* 95, no. 6 (1997): pp. 1677-1682, https://doi.org/10.1161/01.cir.95.6.1677)

Human Factors Testing

A human-factors/usability analysis was conducted in accordance with FDA's February 3, 2016 Guidance Document "Applying Human Factors and Usability Engineering to Medical Devices - Guidance for Industry and Food and Drug Administration Staff" and IEC 62366-1:2015 - Medical devices - Part 1: Application of usability engineering to medical devices.

The ASSURE system task analysis was evaluated by conducting usability studies on selected functions that were determined to be critical and essential tasks important to the effective use and safety of the ASSURE system. During the human factors validation (summative) study, 54 representative users from three user groups (17 patients, 19 caregivers, 18 bystanders) performed critical tasks associated with each

distinct user population. The three user groups were as follows:

- Patient user group. The patient is the primary user of the ASSURE system. The patient is prescribed the ASSURE system by their healthcare professional (HCP) and receives training before use. This training is provided by a Kestra patient service representative (PSR) and is standardized involving didactic and hands-on activities.

- Caregiver user group. The caregiver is the secondary user of the ASSURE system. The caregiver is someone familiar to the patient such as a spouse, significant other, or adult child who will likely know the patient wears a device for their heart condition; however, they may not be familiar with specifics of the ASSURE system. The caregiver may assist the patient in set up, assembly, and care of the ASSURE system.

- Bystander group. Bystanders may be in the environment and exposed to the ASSURE system during an out-of-hospital cardiac arrest (OHCA). Bystanders may or may not know the patient and likely will not have knowledge of the ASSURE system. During a heart alert, bystanders should follow the voice prompts and not interferewith the ASSURE system.

This device is available by prescription only, and training is provided prior to the device being dispensed. Data from the human factors validation (summative) study was analyzed to identify potential consequences of all use errors that occurred. The root cause analysis was determined based on the aggregation of observations of user performance, knowledge task data, and subjective comments from the user related to that performance. A root cause of any use error was classified as a device issue, test artifact, training issue, or use error.

For any use errors, a residual risk analysis was performed to determine the impact of the error that could potentially lead to a failure to deliver therapy.

The usability evaluations performed demonstrated that users understood the instructions provided in the patient manual and that they could use the device safely.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed two clinical studies to establish assurance of safety and effectiveness of defibrillation shock with the ASSURE Wearable Cardioverter Defibrillator (WCD) System for adult patients who are at risk for sudden cardiac arrest and are not candidates for, or refuse, an implantable defibrillator in the United States. The first of which was to evaluate ambulatory and arrhythmia detection performance and safety of the device. The second study evaluated conversion effectiveness and safety of the ASSURE defibrillation waveform, under IDE # G190232. Data from these clinical studies, supported by the animal studies, were the basis for the PMA decision.

The clinical data that demonstrate a reasonable assurance of safety and effectiveness of the ASSURE system came from the following trials:

- ACE-DETECT
- ACE-CONVERT

A summary of each study is presented in Table 12.

Table 12: Summary of Clinical Studies

	ACE-DETECT (NCT03887052)	ACE-CONVERT (NCT04132466)
Objectives	Evaluate ambulatory and arrhythmia detection performance and safety	Evaluate conversion effectiveness and safety
Study Design	Prospective, non-randomized	Prospective, non-randomized
Patient Population	Patients at risk for sudden cardiac arrest who had an active, Implantable Cardioverter Defibrillator (ICD)	Patients at risk for sudden cardiac arrest and undergoing noninvasive programmed stimulation (NIPS) or ICD pulse generator replacement
Endpoints	Primary: WCD False Positive Alarm rate calculated as False Positive Alarms per subject-day Secondary: • Summary of WCD True Positive Detections and Missed Events (False Negative Detections) • Estimated inappropriate shock rate • Summary of adverse events determined to be at least possibly related to the device	Primary effectiveness: Estimated cumulative first and second shock VT/VF conversion effectiveness ≥ 94% Secondary effectiveness: First shock VT/VF conversion effectiveness Safety: Summary of adverse events that are at least possibly related to use of the investigational Test System, including classification of Unanticipated Adverse Device Effects
Number of Patients Enrolled	130	13
Follow-up	Study complete 3,501 subject-days (9.6 years)	Study complete Acute, intra-procedural testing only

XI. ACE-DETECT

A. Study Design

Patients were enrolled between March 20, 2019 and June 18, 2019. The database for this PMA reflected data collected through June 18, 2019 and included 130 patients enrolled at 10 investigational sites in the U.S.

The study was a prospective, non-randomized, single arm, multi-center open label study in patients at risk for sudden cardiac arrest who had an active, Implantable Cardioverter Defibrillator (ICD) implanted for either primary or secondary indications.

A sample size of 105 was required to show that the False Positive Alarm rate per subject-day (primary endpoint) for the ASSURE system was statistically significantly lower than the comparator rate of 0.29 at a one-sided 0.025 significance level with at least 90% power. A total of 130 subjects, with at least 35 of each sex, were planned to be enrolled to meet the sample size requirement for the primary endpoint while also achieving the goal of recording approximately two shockable events. A Statistical Analysis Plan (SAP) for the ACE-DETECT study was generated to guide the analyses for the defined endpoints.

The ASSURE systems used in this study were production-equivalent with defibrillation therapy programmed OFF, shock alarms disabled (Shock Alarm Event Markers were recorded by the device for analysis purposes), and detection parameters at nominal settings [ventricular tachycardia (VT) rate threshold at 170 bpm and ventricular fibrillation (VF) rate threshold at 200 bpm]. As such, ventricular arrhythmias with a heart rate greater than 170bpm sustained for at least 20 seconds should be detected in this study. When initial arrhythmia detection criteria are met, the ASSURE system opens an episode and begins storage of ECG signals. If the rhythm is sustained for the confirmation period (5 seconds for VF, 45 seconds for VT), a Shock Alarm Event Marker is recorded. Any episode that is opened is retained in device memory regardless of the presence of a Shock Alarm Event Marker.

An independent panel of board-certified electrophysiologists reviewed all ventricular tachyarrhythmia episodes recorded by the ASSURE system and/or ICD. The panel was established prior to study commencement and consisted of three voting members with broad experience with clinical trials and no vested interest in the ASSURE system.

An independent Medical Monitor reviewed all adverse events. The Medical Monitor had no financial, scientific, or other conflict of interest with the study.

Clinical Inclusion and Exclusion Criteria

Enrollment in the ACE-DETECT study was limited to patients who met the following inclusion criteria:

- Males or females, age ≥ 18 years
- Patients with an active Implantable Cardioverter Defibrillator (ICD)
- Left Ventricular Ejection Fraction (LVEF) ≤ 40%, measured within the past year (12 months) by echocardiography, nuclear imaging (including MRI), or left ventricular angiography
- Able and willing to provide written informed consent before undergoing any study-related procedures

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

- Any condition that by the judgment of the physician investigator precludes thesubject's ability to comply with the study requirements, including cognitive and/or physical limitations that would prevent the subject from interacting with the device asintended
- Any known skin allergy or sensitivity to the study Garment materials that will be nextto the skin
- Any breached or compromised skin on the upper body that would be exacerbatedby wearing the study Garment
- Work with or are frequently around equipment that produces high electromagnetic fields, for example magnetic resonance imaging devices, power supply facilities, or welding equipment
- Any planned surgical or medical procedures during the participation period thatwould require the subject to remove the study device for more than 12 hours
- Any planned air travel during the participation period.
- Pregnancy
- Use of mechanical circulatory support, for example Left Ventricular Assist Device (LVAD) or Total Artificial Heart
- Implanted Cardiac Resynchronization Therapy Defibrillator (CRT-D)
- Simultaneous plan/prescription for Holter monitor, mobile cardiac outpatient telemetry (MCOT), Event Recorder, or in-hospital telemetry
- Use of any electronic medical device that is worn on or near the body requires Sponsor approval, other than continuous positive airway pressure (CPAP), continuous blood glucose monitor, or pulse oximeter oxygen saturation (SpO2) monitor
- Under bust chest circumference greater than 52 inches (132 cm) or less than 28inches (71 cm)
- Current hospital inpatient

Follow-up Schedule

After consent, a visit was performed to fit the Garment and instruct the subject on how to wear and manage the ASSURE system. Subjects were asked to wear the ASSURE system as much as possible for approximately 30 days. Weekly phone calls were conducted to address subject questions, review any potential adverse events, and review usage information.

Detected arrhythmias were stored in the ASSURE system and/or ICD. At the end of the 30-day period, the subject returned for the exit visit and ended participation in the study.

Adverse events (at least possibly device-related) were reported at all scheduled and unscheduled visits throughout the study.

Clinical Endpoints

Primary Endpoint

The primary endpoint analysis was based on the Intent to Treat cohort and was performed as a one-sided test with 0.025 significance level of the null hypothesis (H_0) that the WCD False Positive Alarm rate per subject-day for the study device is equal to or greater than the comparator rate (0.29). The alternative hypothesis (H_1) was that the WCD False Positive Alarm rate is lower than (superior to) the comparator rate. A random effects Poisson regression model was fit with the number of false positive alarms for each subject as the outcome variable, the logarithm of days of wear as an offset term, and

random site effect. An additional random effects Poisson regression model was fit that included subject characteristics (age, sex, height, and weight) as covariates.

Secondary Endpoints

The secondary endpoint analyses were exploratory and did not have specific performance criteria requirements. No formal tests of hypotheses were planned. Summary statistics were provided for True Positive Detections, Missed Events, and Adverse Events (AE).

The estimate of the Inappropriate Shock rate was calculated as the product of the WCD False Positive Alarm rate (the primary endpoint of this study) and the Missed Shock Alarm rate. The Missed Shock Alarm rate (23.1%) was derived from the upper limit of the 95% confidence interval of the missed alarm rate observed in two prior feasibility studies during which shock alarms were delivered randomly to study subjects during sleep and normal daily activities. In those studies, a "missed shock alarm" was one during which the subject failed to respond to the shock alarm (press the Alert Button) within 20 seconds following alarm activation. The analysis assumes that detected ECG signals persist during the entire alarm period and likely over- estimates the Inappropriate Shock rate.

A summary of AEs at least possibly related to device use and by severity (as reported by the clinical investigator and reviewed by the Medical Monitor) was prepared.

B. Accountability of PMA Cohort

At the time of database lock, a total of 130 patients enrolled in the PMA study, 93% (121) patients were available for analysis at the completion of the study, the 30-day study exit visit. The disposition of all study subjects is summarized in Figure 3.

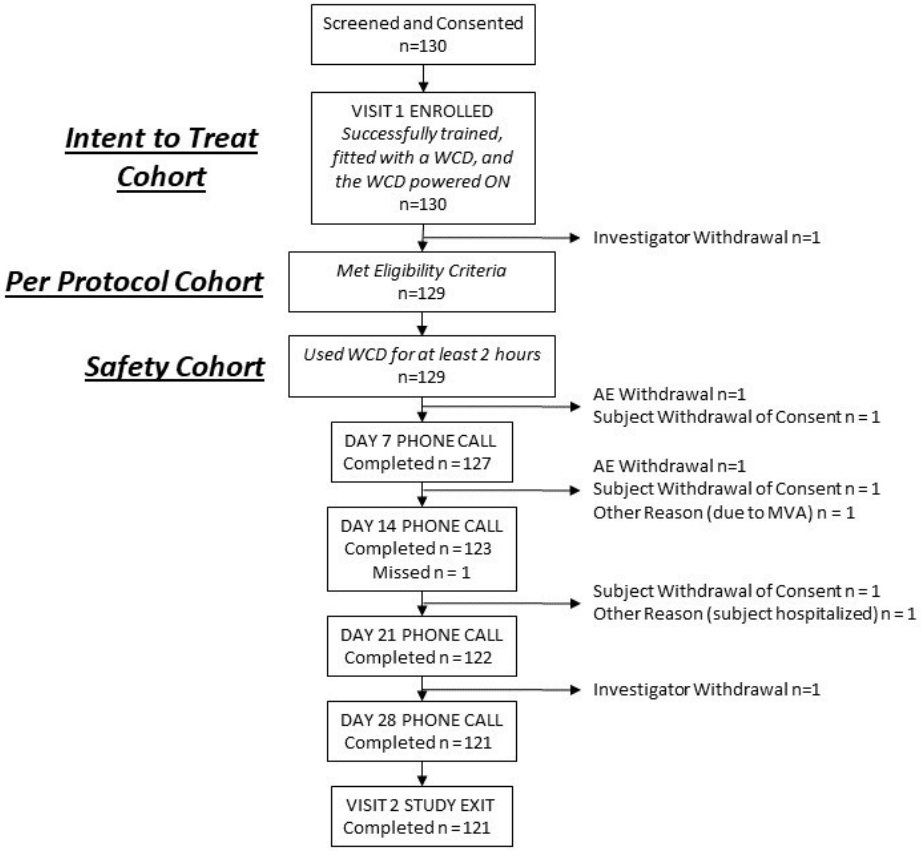

Figure 3: Study Cohort

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an ICD study performed in the U.S. This approach allowed evaluation of the ASSURE system in patients similar to those currently indicated for a WCD and in whom spontaneous occurrence of both ventricular and supraventricular arrhythmias were likely to occur.

ACE-DETECT subjects were enrolled from disparate geographic areas, were of variable body habitus, and included 30.8% female and 28% non-Caucasian participants. Subjects were reflective of a chronic heart failure population, including both an ischemic (57.7%) and non-ischemic (33.8%) etiology, with a median LVEF of 30% and mean LVEF of 28%, similar to other published studies of the commercially available WCD. Patient demographics and clinical characteristics are summarized in Table 13 and Table 14, respectively. Body habitus is shown in Figure 4.

Table 13: Baseline Demographic Characteristics

Baseline Characteristics	**Enrolled Subjects N = 130**
Age (years)	
N	130
Mean ± SD	61.2 ± 11.4
Median	62.0
IQR	15.0
Min, Max	29.0, 89.0
Sex	
Male	90 (69.2%)
Female	40 (30.8)
Race (not mutually exclusive)	
American Indian or Alaska Native	0 (0.0%)
Asian	0 (0.0%)
Black or African American	35 (26.9%)
Native Hawaiian or Other Pacific Islander	1 (0.8%)
White	83 (63.8%)
Other	0 (0.0%)
Not Reported	11 (8.5%)
Ethnicity	
Hispanic or Latino	2 (1.5%)

Not Hispanic or Latino	124 (95.4%)
Unknown or Not Reported	4 (3.1%)

Table 14: Cardiovascular and Other Medical History

Medical History	**Enrolled Subjects N = 130**
Etiology of Cardiovascular Disease (Primary)	
Ischemic	75 (57.7%)
Nonischemic (not primarily valvular)	44 (33.8%)
Mixed ischemic/nonischemic	1 (0.8%)
Primary valvular	2 (1.5%)
Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)	0 (0.0%)
Hypertrophic Cardiomyopathy	3 (2.3%)
Congenital	0 (0.0%)
Sarcoidosis	0 (0.0%)
Other	5 (3.8%)
NYHA Classification	
I	9 (6.9%)
II	52 (40.0%)
III	43 (33.1%)
IV	2 (1.5%)
Unknown	19 (14.6%)
LVEF (%)	
N	130
Mean ± SD	28.2 ± 7.1
Median	30.0
IQR	12.0
Min, Max	11.0, 40.0
Method of LVEF Determination	
Echocardiogram	122 (93.8%)

Nuclear, including SPECT and cMR	6 (4.6%)
Left Ventricular Angiography	1 (0.8%)

Table 14: Cardiovascular and Other Medical History (Continued)

Medical History	**Enrolled Subjects N = 130**
Other	1 (0.8%)
Medical History (not mutually exclusive)	
Coronary Artery Disease	95 (73.1%)
Prior Myocardial Infarction (MI)	75 (57.7%)
Prior Coronary Artery Bypass Graft (CABG)	26 (20.0%)
Prior Percutaneous Coronary Intervention (PCI)	57 (43.8%)
Heart Failure	125 (96.2%)
Diabetes	41 (31.5%)
Type I	2 (1.5%)
Type II	39 (30.0%)
Hypertension	96 (73.8%)
Chronic Obstructive Pulmonary Disease (COPD)	28 (21.5%)
Chronic Kidney Disease	31 (23.8%)
End Stage Renal Disease	4 (3.1%)
Dialysis Dependent	3 (2.3%)
Current Smoker	23 (17.7%)
Use of Concomitant Medical Devices	
Yes	32 (24.6%)
No	98 (75.4%)
Type of Concomitant Medical Devices (not mutually exclusive)	
Implantable Loop Recorder (ILR)	1 (0.8%)
Cane	5 (3.8%)
CardioMEMs	1 (0.8%)
Continuous Positive Airway Pressure (CPAP)	21 (16.2%)
Walker	3 (2.3%)

Other	3 (2.3%)
Subject Has Worn a Life Vest Previously	
Yes	21 (16.2%)
No	109 (83.8%)

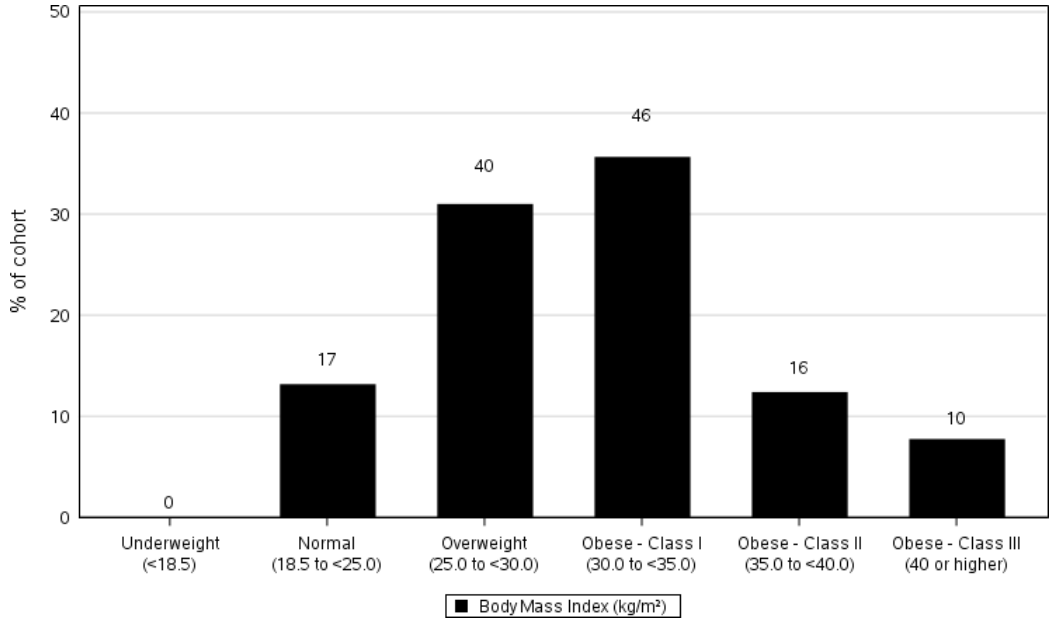

Figure 4: Body Habitus

Compliance

Enrolled subjects achieved cumulative device usage of 3,501 subject-days (9.6 years). Average usage was 29.4 ± 6.9 days and average daily usage was 22.7 ± 1.7 hours (Table 8). Most subjects (114, 88.4%) achieved an average daily use of at least 20 hours. No differences were found in usage by gender, age, or use of concomitant medical devices (Table 15).

Table 15: WCD Usage

	Enrolled Subjects N = 130
Total Usage (hours)[a]	
N	130
Mean ± SD	646.4 ± 164.0
Median	694.5
IQR	57.5
Min, Max	0.6, 789.5
Cumulative Usage Across All Subjects (hours)	84,028
Cumulative Usage Across All Subjects (days)	3,501
Cumulative Usage Across All Subjects (years)	9.6

WCD Use Days ≥1 Hour Per Day[b]	
N	130
Mean ± SD	29.4 ± 6.9
Median	31.0
IQR	1.0
Min, Max	0.0, 35.0
Average Daily Usage (hours)[c]	
N	128
Mean ± SD	22.7 ± 1.7
Median	23.1
IQR	1.1
Min, Max	12.4, 24.0

a. Total Usage (hours) is calculated as the sum of hours of device usage by each subject across all study days.
b. WCD Use Days with ≥1 Hour Per Day is calculated as the number of days the subject used the device for at least 1 hour.
c. Average Daily Usage (hours) is calculated as the sum of hours of device usage, excluding any days with <1 hour of use and the first and the last wear days, divided by the number of WCD use days with ≥1 hour per day, excluding the first and the last wear days.

Table 16: WCD Usage Stratified by Age, Gender, and Concomitant Device Use

	N	Mean	SD	P-value (t-test)
Sex				
Male	90	22.7	1.8	
Female	40	22.5	1.6	p = 0.47
Age				
≥62 years	66	22.7	1.8	
<62 years	64	22.7	1.7	p = 0.97
Concomitant Device				
Yes	32	22.8	1.0	
No	98	22.6	1.9	p = 0.56

Note: Average Daily Usage (hours) is calculated as the sum of hours of device usage, excluding any days with <1 hour of use and the first and the last wear days, divided by the number of WCD use days with ≥1 hour per day, excluding the first and the last wear days.

Stored Episodes

ICD Episodes Recorded as Ventricular Tachyarrhythmias

A total of 237 ICD episodes were recorded as ventricular tachyarrhythmias in 51 (39.2%) of subjects. These episodes are summarized in Table 17. 106 were adjudicated as Rhythm Type VT/VF (44.7%). The majority (91) of these VT/VF episodes were non-sustained lasting less than 20 seconds. 15 VT/VF episodes were sustained for at least 20 seconds. The remaining episodes were adjudicated as SVT (33.8%), Atrial Fibrillation (21.1%), or Sinus Rhythm (0.4%).

Table 17: Summary of ICD Episodes

Rhythm	**Subjects (n = 51)**	**Episodes (n = 237)**
VT/VF	**40**	**106 (44.7%)**
Sustained (≥ 20 seconds)	5	15 (6.3%)
Non-sustained (< 20 seconds)	38	91 (38.4%)
Other Physiologic	**23**	**131 (55.3%)**
Atrial Fibrillation	4	50 (21.1%)

Table 17: Summary of ICD Episodes (Continued)

Rhythm	**Subjects (n = 51)**	**Episodes (n = 237)**
Atrial Flutter	0	0 (0%)
Paced Rhythm	0	0 (0%)
Sinus Rhythm	1	1 (0.4%)
SVT	18	80 (33.8%)
Uncertain	**0**	**0 (0%)**

WCD Episodes Recorded as Ventricular Tachyarrhythmias

A total of 163 WCD episodes were recorded in 18 subjects (Table 18). Four (4) episodes (2.5%) in three subjects were adjudicated as Rhythm Type VT/VF. Six (6) episodes (3.7%) in a single subject were adjudicated as Atrial Flutter without artifact. The remaining 153 episodes (93.9%) in 24 subjects had noise artifact on the recorded electrogram and were adjudicated as Other Physiologic rhythms (74.2%) or Uncertain and presumed non-shockable (19.6%). Mean adjudicated heart rate for Other Physiologic rhythms was 92.2 bpm (50-172) and was Indeterminate for all Uncertain and presumed non-shockable rhythms. None of the episodes adjudicated as Other Physiologic or Uncertain and presumed non-shockable had corresponding ICD episodes.

Table 18: Summary of WCD Episodes by Adjudicated Rhythm

Rhythm	Subjects (n = 18)	Episodes (n = 163)
VT/VF	3	4 (2.5%)
Other rhythms with artifact	16	121 (74.2%)
Atrial Fibrillation	1	1 (0.6%)
Atrial Flutter	0	0 (0.0%)
Paced Rhythm	4	29 (17.8%)
Sinus Rhythm	11	85 (52.1%)
SVT	2	6 (3.7%)
Uncertain rhythm with artifact	7	32 (19.6%)
Atrial Flutter without artifact	1	6 (3.7%)

D. Safety and Effectiveness Results

Safety Results

The analysis of safety was based on the Intent to Treat cohort of 130 patients available for evaluation. The key safety outcomes for this study are presented below in Table 19 and Table 20. Adverse effects are reported in Table 21.

The False Alarm Rate (primary endpoint) was 0.00075 per subject-day and the upper bound of the 95% confidence interval was 0.00361 per subject-day (Table 19), well below the prespecified objective performance goal of 0.29 per subject-day (ZOLL LifeVest). The null hypothesis associated with the primary endpoint was rejected. The observed False Positive Alarm rate per subject-day is equivalent to one False Positive Alarm every 1,333 days.

A total of four (4) WCD episodes were sustained long enough that a shock alarm event marker was recorded. One of these episodes was adjudicated as VT/VF and was therefore a True Positive Alarm and a True Positive Detection. The other three episodes, which occurred in two subjects (1.5%), were adjudicated as Other Physiologic rhythms with noise artifact, and were therefore False Positive Alarms.

Table 19: Results of Primary Endpoint Poisson Regression Analysis

Coefficient	Value	95% CI	t	p-Value
Intercept	0.00075	0.00015, 0.00361	-10.33	< 0.001

The Estimated Inappropriate Shock Rate (secondary endpoint) was based on the Intent-to-Treat cohort of 130 subjects. The incidence of inappropriate shocks is estimated to be 0.00017 per subject-day, or 0.00527 per subject-month (Table 20), based on a Missed Shock Alarm rate of 23.1% as prespecified in the Statistical Analysis Plan. In the worst-case scenario, assuming either that all False Positive Alarms result in a shock if not diverted by a patient or the arrhythmia spontaneously terminated, the incidence of inappropriate shocks equals the False Positive Alarm rate (0.00075 per subject-day).

Table 20: Estimated Inappropriate Shock Rate

	Enrolled Subjects (n = 130)
Estimated Inappropriate Shock Rate (assuming 23.1% Missed Shock Alarm Rate)	0.00017 per subject-day 0.00527 per subject-month
Worst Case Estimated Inappropriate Shock Rate (assuming 100% Missed Shock Alarm Rate)	0.00075 per subject-day 0.02283 per subject-month

Adverse effects that occurred in the PMA clinical study:

Adverse Events (AE) determined to be at least possibly related to the device (secondary endpoint) were based on the Safety cohort of 129 subjects. A total of 55 AEs occurred in 44 subjects (34.1%). None of the AEs were determined to be Serious by the Medical Monitor and none were classified as Unanticipated Adverse Device Effects. A summary of AEs is presented in Table 21. The average time to onset for skin-related AEs was 11.8 days and 14.7 days for musculoskeletal AEs. All adverse events were noted as either recovered/resolved (42 events) or recovering/resolving (13 events) at the end of study participation.

Table 21: Adverse Events by Severity

	Mild		**Moderate**		**Severe**	
	Events n	**Subjects (N=129*) n (%)**	**Events n**	**Subjects (N=129*) n (%)**	**Events n**	**Subjects (N=129*) n (%)**
All Adverse Events	**44**	**35 (27.1%)**	**10**	**10 (7.8%)**	**1**	**1 (0.8%)**
Skin-related	29	25 (19.4%)	7	7 (5.4%)	0	0 (0.0%)
Skin Infection (bacterial or yeast)	0	0 (0.0%)	2	2 (1.6%)	0	0 (0.0%)
Mild to moderate skin irritation	29	25 (19.4%)	5	5 (3.9%)	0	0 (0.0%)
Musculoskeletal- related	14	11 (8.5%)	2	2 (1.6%)	1	1 (0.8%)
Muscle Strain	4	4 (3.1%)	0	0 (0.0%)	0	0 (0.0%)
Bruising	3	3 (2.3%)	0	0 (0.0%)	0	0 (0.0%)
Other Musculoskeletal-related	7	5 (3.9%)	2	2 (1.6%)	1	1 (0.8%)
Other	1	1 (0.8%)	1	1 (0.8%)	0	0 (0.0%)
Fall	0	0 (0.0%)	1	1 (0.8%)	0	0 (0.0%)

Device hit ankle	1	1 (0.8%)	0	0 (0.0%)	0	0 (0.0%)

Effectiveness Results

The analysis of effectiveness of the ASSURE system was assessed by arrhythmia detection performance (True Positive Detections and Missed Events) and was based on the Intent-to-Treat Cohort of 130 evaluable patients at the 30-day time point. Of the 15 sustained (≥ 20 seconds) VT/VF episodes detected by the ICD, four were also detected by the WCD (True Positive Detections). There were no Missed Events.

The four True Positive Detections occurred in three subjects and were all adjudicated as VT/VF with heart rates above the WCD nominal VT threshold of 170 bpm. The ASSURE system did not detect any of the remaining 11 episodes because either the rate of the arrhythmia was below the nominal VT threshold of 170 bpm or the ASSURE system was not being worn.

Subgroup Analyses

Subgroup analysis was not feasible due to the low incidence of False Positive Alarms.

Pediatric Extrapolation

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

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 13 investigators. 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.

XII. ACE-CONVERT

A. Study Design

Patients were enrolled between November 25, 2019 and March 3, 2019. The database for this PMA reflected data collected through March 3, 2019 and included 13 patients enrolled at two investigational sites in the U.S.

The study was a prospective, non-randomized, single arm, multi-center open label study in patients undergoing any of the medically necessary electrophysiology procedures in Inclusion Criterion 3.

After consent, subjects had two pairs of commercially available disposable adhesive defibrillation pads applied. One pair was placed in defined locations and used to deliver the ASSURE defibrillation waveform using a Test System. The other pair was located on the subject's torso according to physician preference and was attached to a commercially available external defibrillator for backup rescue defibrillation. Commercially available ECG monitoring electrodes were positioned as needed. The ASSURE Monitor was configured to Manual Shock mode, which allowed the experimental shock to be delivered on command of the physician investigator.

A single sustained episode of rapid VT or VF was induced during an electrophysiologic study from a catheter or an implanted defibrillator. If the arrhythmia was > 150bpm, then a 170J shock was delivered

from the Test System to convert the arrhythmia. A second shock at 170J was delivered from the Test System if the first shock was unsuccessful. Further rescue shocks could be delivered via an internal or external defibrillator at the investigator's discretion.

An independent Medical Monitor reviewed all AEs. The Medical Monitor had no financial, scientific, or other conflict of interest with the study.

Clinical Inclusion and Exclusion Criteria

Enrollment in the ACE-CONVERT study was limited to patients who met the following inclusion criteria:

- Males or females, age ≥ 18 years
- Able and willing to provide written informed consent before undergoing any study- related procedures
- Scheduled for any of the following procedures:
    - Electrophysiology study for induction of ventricular arrhythmias
    - Non-invasive electrophysiology testing using an existing implantable defibrillator
    - ICD replacement procedure during which induction of a ventricular arrhythmia is planned
    - Ablation of ventricular tachycardia (patients undergoing ventricular tachycardia ablation in which ONLY a substrate modification approach is planned, with no intention of inducing a ventricular arrhythmia, should not be included)

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

- Any condition that by the judgment of the physician investigator precludes the subject's ability to comply with the study requirements
- Pregnancy
- Use of mechanical circulatory support (e.g. LVAD, Total Artificial Heart, intra-aortic balloon pump or Impella)
- Documented nonchronic cardiac thrombus
- Atrial fibrillation or atrial flutter without therapeutic systemic anticoagulation
- Critical aortic stenosis
- Unstable coronary artery disease (CAD)
- Recent stroke or transient ischemic attack (TIA)
- Hemodynamic instability
- Currently implanted Boston Scientific S-ICD (due to location of implant relative to test system)
- Unstable angina
- New York Heart Association (NYHA) Class IV
- Left Ventricular Ejection Fraction (LVEF) < 20%
- Any medical condition that by the judgment of the physician investigator, patient participation in this study is not in the best interest of the patient
- History of difficulty of ventricular arrhythmia induction
- Amiodarone use within 3 months before the study procedure

Follow-up Schedule

Individual subject participation was during acute intra-procedural testing only.

Adverse events that persisted at the time of the subject's study exit were followed by the investigator until the event was resolved or otherwise explained.

Clinical Endpoints

Primary Effectiveness Endpoint

The primary endpoint analysis was based on the Per Protocol cohort. The primary endpoint was calculated as the ratio of the number of subjects with successful (first or second shock) arrhythmia conversion using the Test System to the number of total inductions attempted with shocks delivered by the Test System in the respective data set. A successful arrhythmia conversion was defined as termination of an induced ventricular rhythm (>150 bpm) by first or second shock from the Test System to a non-shockable rhythm (rhythms other than VT or VF). Performance criteria were based on comparison to the published conversion effectiveness point estimate of 94% reported for a commercially available WCD.

Secondary Effectiveness Endpoint

The secondary endpoint analysis was exploratory and did not have prespecified performance criteria. Data was summarized for both the Intention-to-Treat and Per-Protocol cohorts.

Safety Endpoint

Safety was analyzed based on the Intention-to-Treat cohort. The assessment of safety was based on the summary of AEs, vital signs, physical examination findings, and ECGs. The Medical Monitor's assessment of seriousness and relatedness was used for summarizing and analyzing safety data. The Medical Monitor also evaluated AEs to determine if they were Unanticipated Adverse Device Effects. Separate summaries of AEs related to use of the Test System and by severity were prepared. Continuous variables were summarized by descriptive statistics, and categorical variables were summarized using the count and percentage of subjects in each category.

B. Accountability of PMA Cohort

At the time of database lock, a total of 13 patients enrolled in the PMA study, 100% (13) patients were available for analysis at the completion of the study, the medically necessary electrophysiology procedure. The disposition of all study subjects is summarized in Figure 5.

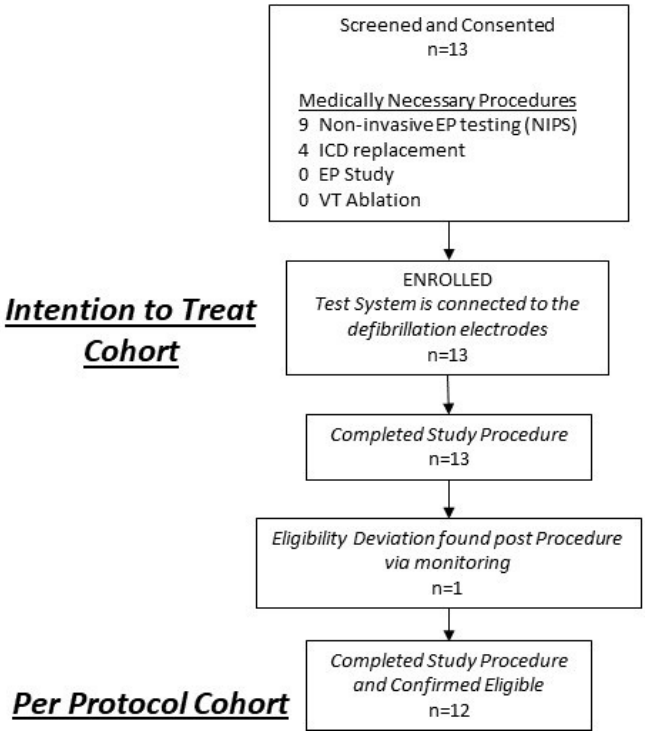

Figure 5: Study Cohort

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for patients at high risk of sudden cardiac arrest and undergoing noninvasive programmed stimulation (NIPS) or ICD pulse generator replacement in the U.S. (Table 22).

ACE-CONVERT subjects had differing primary etiologies of cardiovascular disease including ischemic (2), non-ischemic (3), mixed ischemic/nonischemic (1), congenital (3), sarcoidosis (3) and long QT syndrome (1). The mean LVEF was 46.8% ranging from 24% to 62%, and all but one had a history of heart failure (New York Heart Association class I to III). All 13 subjects had comorbidities including heart failure (11), hypertension (9), coronary artery disease (7), hyperlipidemia (7), diabetes (4), COPD (4), and kidney disease (2). Three subjects were current smokers (Table 23).

Most study subjects were on guideline-directed heart failure medical therapy, including angiotensin-converting enzyme (ACE) inhibitors (5), angiotensin II receptor blocker (3) or sacubitril-valsartan (Entresto) (2), beta blockers (11), and aldosterone antagonists (4). None of the subjects was taking antiarrhythmic drugs (Table 24).

The mean BMI in this study population was 31.5 (range 23.7–46.1). Most subjects were obese (53.8%) or overweight (38.5%) as shown in Figure 6.

Table 22: Baseline Demographic Characteristics

Baseline Characteristics	**Enrolled Subjects N = 13**
Age (years)	
N	13

Mean ± SD	55.3 ± 11.3
Median	57
IQR	15
Min, Max	37, 71
Sex	
Male	7 (53.8%)
Female	6 (46.2%)
Race (not mutually exclusive)	
American Indian or Alaska Native	0 (0.0%)
Asian	0 (0.0%)
Black or African American	3 (23.1%)
Native Hawaiian or Other Pacific Islander	0 (0.0%)
White	10 (76.9%)
Other	0 (0.0%)
Not Reported	0 (0.0%)
Ethnicity	
Hispanic or Latino	0 (0.0%)
Not Hispanic or Latino	13 (100.0%)
Unknown or Not Reported	0 (0.0%)

Table 23: Cardiovascular and Other Medical History

Medical History	**Enrolled Subjects N = 13**
Etiology of Cardiovascular Disease (Primary)	
Ischemic	2 (15.4%)
Nonischemic (not primarily valvular)	3 (23.1%)
Mixed ischemic/nonischemic	1 (7.7%)
Primary valvular	0 (0.0%)
Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)	0 (0.0%)
Hypertrophic Cardiomyopathy	0 (0.0%)

Congenital	3 (23.1%)
Sarcoidosis	3 (23.1%)
Other	1 (7.7%)
NYHA Classification	
I	1 (7.7%)
II	7 (53.8%)
III	3 (23.1%)
IV	0 (0.0%)
Unknown	0 (0.0%)
LVEF (%)	
N	13
Mean ± SD	46.8+/-11.7
Median	49
IQR	18
Min, Max	24.0, 62.0
Method of LVEF Determination	
Echocardiogram	10 (76.9%)
Nuclear, including SPECT and cMR	3 (23.1%)
Left Ventricular Angiography	0 (0.0%)

Table 23: Cardiovascular and Other Medical History (Continued)

Medical History	**Enrolled Subjects N = 13**
Other	0 (0.0%)
Right Ventricular Function	
Normal	8 (61.5%)
Mildly reduced	1 (7.7%)
Moderately reduced	2 (15.4%)
Severely reduced	2 (15.4%)
Medical History (not mutually exclusive)	
Coronary Artery Disease	7 (53.8%)

Prior Myocardial Infarction (MI)	3 (23.1%)
Prior Coronary Artery Bypass Graft (CABG)	1 (7.7%)
Prior Percutaneous Coronary Intervention (PCI)	3 (23.1%)
Heart Failure	11 (84.6%)
Diabetes	4 (30.8%)
Type I	0 (0.0%)
Type II	4 (30.8%)
Hypertension	9 (69.2%)
Hyperlipidemia	7 (53.8%)
Prior Stroke/TIA	1 (7.7%)
Chronic Obstructive Pulmonary Disease (COPD)	4 (30.8% 53.8%)
Chronic Kidney Disease	2 (15.4%)
End Stage Renal Disease	0 (0.0% %)
Dialysis Dependent	0 (0.0%)
Current Smoker	3 (23.1%)

Table 24: Baseline Medications

Baseline Medications	**Enrolled Subjects N = 13**
ACE Inhibitors	5 (38.5%)
Beta Blockers	11 (84.6%)
Angiotensin II Receptor Blocker (ARB)	3 (23.1%)
Aldosterone Antagonist	4 (30.8%)
Combination Drug (Sacubitril-Valsartan)	2 (15.4%)
Digoxin	1 (7.7%)
Antiarrhythmic Drugs	0 (0.0%)

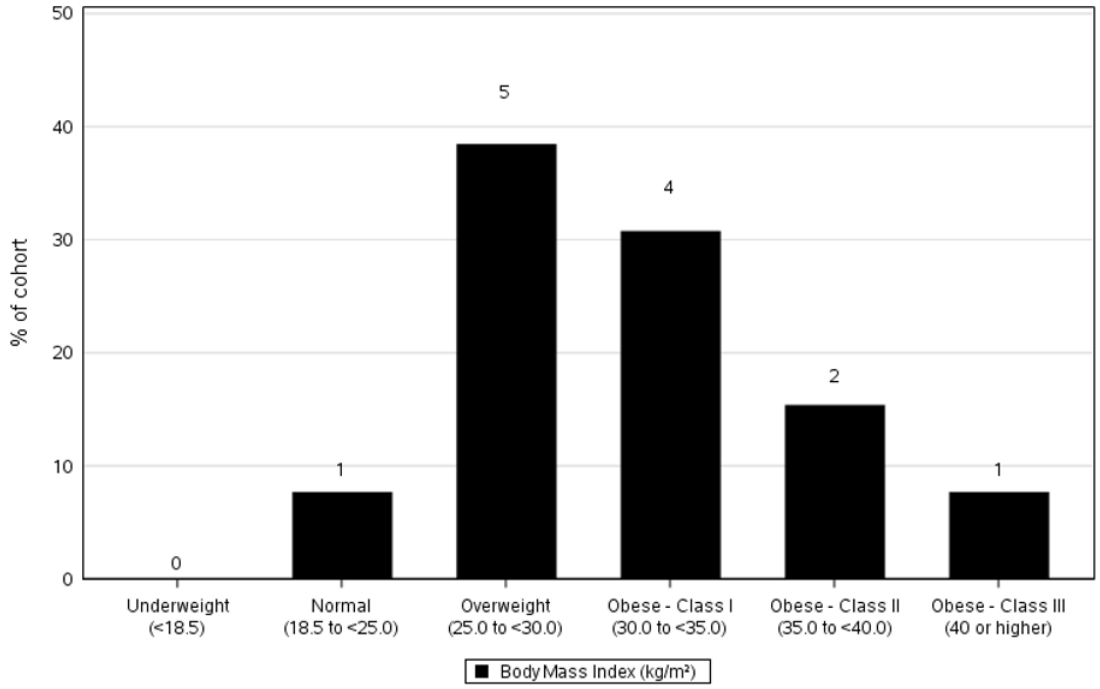

Figure 6: Body Habitus

D. Safety and Effectiveness Results

Safety Results

The analysis of safety was based on the Intent to Treat cohort of 13 patients available for evaluation. The key safety outcomes for this study are presented in Table 25 as a summary of Adverse Events (AE).

A total of three AEs occurred in three subjects (23.1%). All three were mild irritation to the skin under the adhesive defibrillation pads. None were determined to be Serious by the Medical Monitor nor were any classified as Unanticipated Adverse Device Effects. The AEs were noted as either recovered/resolved (2) or recovering/resolving (1) at the end of study participation.

Table 25: Adverse Events

AE ID	AE Description	Serious	Severity	Time from Enrollment to Event Onset (days)	Description
1	Skin irritation	No	Mild	0	Skin irritation on back, left side, square patch mark, noticed the following day after the procedure.
2	Redness of skin	No	Mild	1	Faint red outline at the edge of anterior and posterior patch

Table 25: Adverse Events (Continued)

AE ID	AE Description	Serious	Severity	Time from Enrollment to Event Onset (days)	Description
3	Skin irritation	No	Mild	1	Subject developed skin irritation and redness where the patches were placed for the defibrillation threshold test.

Effectiveness Results

The analysis of primary effectiveness endpoint using both the Intention-to-Treat cohort (13 subjects) and Per-Protocol cohort (12 subjects) was met. Key effectiveness outcomes are presented in Table 19. The cumulative first and second shock VT/VF conversion effectiveness was 100% exceeding the performance criteria point estimate of 94% (Table 26). For the Per Protocol cohort, the lower bound of the 95% confidence interval was 73.5%, which exceeded the 95% lower bound of the lowest passing criteria (71.3%) specified in the statistical analysis plan.

The secondary endpoint, first shock VT/VF conversion effectiveness, was 83.3% and 84.6% determined using the Per Protocol and Intention to Treat cohorts, respectively.

Table 26: ASSURE Defibrillation Waveform Conversion Effectiveness

	Per Protocol Analysis Population (n = 12)	Intention-to-Treat Analysis Population (n = 13)
Primary Effectiveness Endpoint: Cumulative first and second shock VT/VF conversion effectiveness	12 out of 12 100.0% (73.5%, 100.0%)	13 out of 13 100.0% (75.3%, 100.0%)
Secondary Effectiveness Endpoint: First shock VT/VF conversion effectiveness	10 out of 12 83.3% (51.6%, 97.9%)	11 out of 13 84.6% (54.6%, 98.1%)

Subgroup Analyses

No subgroup analyses were planned or performed.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 12 investigators. 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 RECOMMENDATION

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 Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel. The risk to health in external defibrillation is clearly characterized and well known by the medical community and no new clinical issues related to safety and effectiveness were identified.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The ACE-CONVERT study demonstrated that the ASSURE defibrillation waveform was highly effective at terminating VF; the primary effectiveness endpoint was met. The cumulative first and second shock VT/VF conversion effectiveness in this study was 100% exceeding the performance criteria point estimate of 94%. The lower confidence bound of the success rate in 13 subjects was 75.3%. Additionally, first shock conversion effectiveness was 84.6%.

The ACE-DETECT study demonstrated successful detection of spontaneous VT/VF events (four events in three subjects). The only sustained VT/VF events not detected were below the programmable VT threshold (170 bpm nominal) or occurred when the ASSURE system was not being worn. The ASSURE system is capable of programmable rate thresholds to address each patient's unique clinical needs.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in clinical studies conducted to support PMA approval as described above. Results from the nonclinical laboratory (e.g., biocompatibility), animal studies, and clinical studies performed on the ASSURE system demonstrate that this device is suitable for the temporary protection from risk of sudden cardiac death.

The ACE-DETECT study demonstrated a very low risk of False Positive Alarms and Inappropriate Shock. The False Positive Alarm rate was 0.00075 per subject-day with an 95% upper confidence bound of 0.000361 per subject-day, well below the prespecified performance goal of 0.29 per subject-day which was derived from the performance of the alternative commercially available WCD. The Estimated Inappropriate Shock Rate was very low at 0.0051 per subject-month. The adverse event most reported was mild skin irritation. The only severe adverse event reported was musculoskeletal pain. Overall, the ASSURE system was well tolerated in a broad range of adult patients at risk for sudden cardiac arrest with only a small portion (3.8%) who withdrew from the study due to dissatisfaction or discomfort associated with the ASSURE system. The ACE-CONVERT identified no additional risks.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in clinical studies and non- clinical studies conducted to support PMA approval as described above. The probable benefits include accurate ventricular tachyarrhythmia detection with a very low rate of false alarms, and high effectiveness for terminating induced ventricular tachyarrhythmias and restoration of a non-shockable rhythm.

The probable risks of the device are also based on data collected in clinical studies conducted to support PMA approval as described above. The probable risks include morbidity associated with wear including minor skin irritation (rash, redness, itching, irritation, abrasion), skin infection and musculoskeletal-

related events (back/shoulder pain, muscle strain, bruising, chest discomfort) and a very low rate of inappropriate shocks.

Additional factors to be considered in determining probable risks and benefits for the ASSURE system included premarket prospective studies which enrolled subjects with a broad range of ages, body habitus, and cardiac etiologies at risk for sudden cardiac arrest. One of the benefits of the ASSURE system is the availability of an additional Garment style designed for women, which may contribute to increased comfort and compliance.

Patient perspectives considered during the review included supporting evidence from the ACE-DETECT study that indicates the ASSURE system is comfortable and easy to use offering an opportunity for increased WCD compliance.

In conclusion, given the available information above, the data supports that for adult patients at risk for sudden cardiac arrest and are not immediate candidates for, or refuse, an implantable defibrillator the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application supports the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. FDA found that the application contains sufficient clinical data and information to support approval of the device for the proposed intended use.

XIII. CDRH DECISION

CDRH issued an approval order on July 28, 2021. The final clinical conditions of approval cited in the approval order are described below.

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

3. 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. Kerber, Richard E., Lance B. Becker, Joseph D. Bourland, Richard O. Cummins, Alfred P. Hallstrom, Mary B. Michos, Graham Nichol, et al. “Automatic External Defibrillators for Public Access Defibrillation: Recommendations for Specifying and Reporting Arrhythmia Analysis Algorithm Performance, Incorporating New Waveforms, and Enhancing Safety.” *Circulation* 95, no. 6 (1997): 1677–82. https://doi.org/10.1161/01.cir.95.6.1677.