SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Automated External Defibrillator

Device Trade Name: HeartStart FR3 Defibrillators Models 861388 (Text) and 861389 (ECG Display), Primary Battery (Models 989803150161, 989803150171), Rechargeable Battery (Model 989803150241), Charger for the Rechargeable Battery (Model 861394), SmartPads III (Models 989803149981, 989803149991), DP pads (Models 989803158211, 989803158221), and Pediatric Key (Model 989803150031)

Device Procode: MKJ

Applicant's Name and Address: Philips Medical Systems
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Bothell, WA 98021

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P160028

Date of FDA Notice of Approval: May 11, 2020

The HeartStart FR3 Defibrillator has been commercially available since 2011, when it was first cleared by FDA under K111693. P160028 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 HeartStart FR3 Defibrillator. 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 HeartStart FR3 defibrillator.

II. INDICATIONS FOR USE

The models 861388 and 861389 are indicated for use by trained responders to treat ventricular fibrillation (VF), the most common cause of sudden cardiac arrest (SCA), and pulseless ventricular tachycardias (VTs). The models 861388 and 861389 are used with the SmartPads III or DP defibrillator pads applied to potential victims of SCA with the following symptoms:

- Unconsciousness

- Absence of normal breathing
- Absence of pulse or signs of circulation

The models 861388 and 861389 are indicated for adults and children over 55 pounds (25 kg) or greater than 8 years old. The models 861388 and 861389 are also indicated for children under 55 pounds (25 kg) or 0-8 years old when used with the optional Infant/Child Key. If the Infant/Child Key is not available, or you are uncertain of the child's age or weight, do not delay treatment.

III. CONTRAINDICATIONS

The HeartStart FR3 Defibrillator should not be used when a patient is conscious, breathing normally, or has a detectable pulse or other signs of circulation.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the FR3 Instructions for Adminstrators labeling.

V. DEVICE DESCRIPTION

The Philips HeartStart FR3 Defibrillator (FR3) is a compact, light-weight, battery-powered, automated external defibrillator (AED). It is indicated to treat suspected victims of ventricular fibrillation (VF), a common cause of sudden cardiac arrest (SCA), and certain ventricular tachycardias (VTs). This device is designated prescription-use only. The use environment of this AED is in pre-hospital emergency response settings. The intended user is trained in Basic Life Support (BLS), Advanced Life Support (ALS), or another physician-authorized training program (e.g., the user is accustomed to CPR and AED operation). The device can be used in adults, infants, and children. The FR3 prompts the user to take specific actions if a potentially shockable rhythm is detected. The FR3 uses defibrillation pads placed on the victim's skin to deliver a shock. Once the defibrillation pads are placed on the patient, it analyzes the heart rhythm, determines whether or not a shock is required, charges the capacitor, and indicates to deliver a shock. The FR3 is able to provide verbal instructions to the user, detect where the user is in the event response, and provide general CPR coaching. Lastly, the device can display incident information.

The FR3 AED uses a proprietary shock advisory algorithm (Patient Analysis System [PAS]) and a biphasic shock waveform (non-escalating, impedance compensating SMART Biphasic waveform) to deliver a 150 J nominal shock to adults and 50 J nominal shock to infants/children to achieve its indicated use.

The SmartPads III and DP pads are non-sterile, multi-functional disposable single-use defibrillation pads are used to collect the ECG data and provide a mechanism to deliver the shock. The HeartStart FR3 AED models are shipped with SmartPads III, which are pre-connectable pads that can treat all age groups when incorporating adjustable

defibrillation energy functionality. They are designed to allow testing of the pads' readiness condition when pre-connected. The FR3 AED also accepts HeartStart DP Electrode pads which are are non-sterile, multi-function disposable single-use defibrillator pads. HeartStart DP Electrode pads are indicated for adults and SmartPads III are indicated for all age groups.

A non-rechargeable, lithium manganese dioxide battery powers the FR3 AED, with a typical capacity of 300 shocks or 12 hours of monitoring time for clinical use.

An optional pediatric Infant/Child Key is available for treatment of patients under 55 lbs (25 kg) or 0-8 years of age. When the key is inserted into the FR3 AED, the device identifies the insertion and enters into Infant/Child mode. The shock intensity of the FR3 AED is then decreased to 50 J.

The FR3 is available in two (2) models: FR3 AED ECG model 861389 (ECG display) and the FR3 AED Text model 861388 (text only display). The FR3 AED is shown in Figure 1. The FR3 features and accessories are identified in Figure 2.

Figure 1: FR3 Model 861388 and 861389

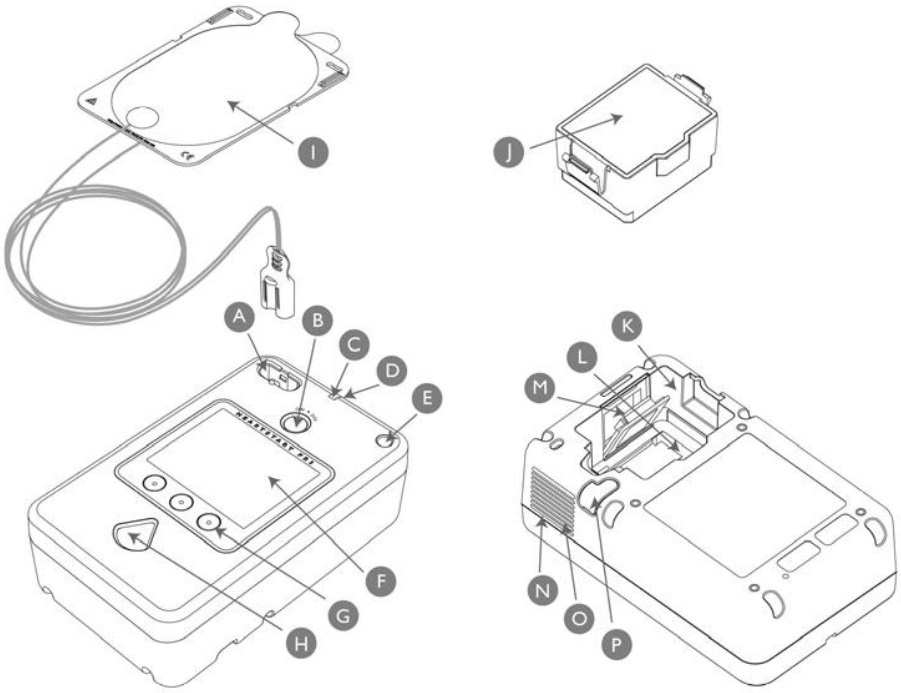

Figure 2: FR3 Features and Accessories

A. Defibrillator pads connector socket. Receptacle for the defibrillator pads cable connector (optionally can attach 3-Lead ECG). A light on the socket flashes when the HeartStart FR3 AED is turned on to show socket location.

B. Green On/Off button. Turns on HeartStart FR3 AED and starts voice and text prompts. A second press brings up the status screen then turns off the HeartStart FR3 AED.

C. Green Ready light. Shows the readiness status of the HeartStart FR3 AED.

D. Microphone. Can be configured to optionally record audio during an incident.

E. Infant/Child Key port. Accommodates the optional Infant/Child Key accessory for the HeartStart FR3 AED to enable pediatric treatment protocols for patients under 55 lbs (25 kg) or 0-8 years old.

F. Screen. Displays text prompts, graphics, and incident data. The 861389 ECG model also displays the patient's ECG, if enabled.

G. Option buttons (three). When pressed, activates the function identified on the screen.

H. Orange Shock button. Controls shock delivery. The button flashes when the FR3 AED is ready to deliver a shock.

I. SmartPads III. Self-adhesive pads supplied with attached cable and connector.

J. Battery. Long-life battery used to power the AED.

K. Battery compartment. Provides electrical connection for the installed battery and contains the data card slot and optional Bluetooth wireless technology transceiver module compartment.

L. Data card slot. Receptacle for optional data card accessory. Located beneath the battery in the battery compartment.

M. Bluetooth wireless technology transceiver module compartment. Accommodates the optional module accessory. Located behind a removable door in battery compartment.

N. Speaker. Broadcasts the AED's voice prompts and alert tones when appropriate.

O. Beeper. Broadcasts the AED's alert chirps when appropriate.

P. Accessory port. Connection port for accessories.

The two (2) FR3 AEDs models (861388 and 861389) share the same basic features, with both having manual analysis capability. The 861389, which has the ECG display on the text screen, also has the additional capability of manual charge and manual shock delivery in Advanced Mode. In contrast, the 861388 text model does not have ECG display capability and, therefore, does not have the manual charge or manual shock capability.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Defibrillation is the only currently available treatment for termination of ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT).

VII. MARKETING HISTORY

The FR3 AED was first marketed in the United States in 2011. The FR3 AED is currently marketed in numerous other countries including Canada, Australia, European Union countries requiring CE Mark, and over 20 other countries in South America, the Middle East, and Asia. It has not been withdrawn from marketing for any reason related to its safety or effectiveness.

VIII. PROBABLE ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the probable adverse effects (e.g., complications) associated with the use of the device.

- Failure to identify shockable arrhythmia;
- Failure to deliver a defibrillation shock in the presence of ventricular fibrillaton (VF) or pulseless ventricular tachycardia (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 defibrillation pads placement area;
- Allergic dermatitis due to sensitivity to the materials used in the defibrillation pads construction; and
- Minor skin rash.

IX. SUMMARY OF NONCLINICAL STUDIES

1. Laboratory Studies

The FR3 AED and accessories underwent laboratory-based studies that included bench testing (summarized in Table 1), biocompatibility evaluations, electrical and EMC testing, and software verification and validation. Testing was conducted on key device subassemblies and the complete systems.

Bench Testing

Table 1: Bench Tests for FR3 AED

Test	Purpose	Acceptance Criteria	Results
Sealing/Moisture Resistance	Verify the FR3 meets the requirements for IPX5 rating	The device shall resist jetting water per EN60529 Class IPx5	Pass
Mechanical Crush	Verify the device continues to meet all performance requirements after receiving a 1100 lb. load distributed across the AED	The device shall have no damage which could result in electrical shock, fire, or injury to persons, remains functional throughout the test, and delivers 10 shocks (all exceeding 128 J) following the crush test following application of a 499 kg (1100 lb.) load distributed across 65+/-6.5 square cm. (10+/- square inches) to any location on its top surface	Pass
Dielectric Withstand	Verify the device complies with the requirements of	The device shall comply with the requirements of 60601-2-4 paragraphs 20.3 test 1 for	Pass

Test	Purpose	Acceptance Criteria	Results
	60601-2-4 paragraphs 20.3 test 1	Operator Access, Between Defibrillator Electrodes and Across Defibrillator Switches	
Drop Test	Verify the device complies with IEC 60601-1: *21.5 Free Fall	The device shall withstand a drop from 1.0 m onto a 50 mm thick hardwood board over concrete on each of its three (3) axes without producing a safety risk	Pass
Therapy Delivery Endurance	Verify the device complies with IEC 60601-2-4: *103 Endurance	The therapy delivery subsystem will be capable of delivering 2500 charge and discharge cyces at rated energy into a load of 50 Ohms	Pass
Primary Battery Stand-By Life	Verify primary battery will last a minimum of 3 years	The Primary Battery will be capable of lasting 3 years	Pass
Infant/Child Key Identification	Verify the insertion of the infant/child key is identified	The insertion of the infant/child key is identified by the system and the shock is reduced to 50 J	Pass

Biocompatibility

The FR3 AED is not intended for patient contact, but the pads will contact the patient. Biocompatibility testing was performed per AAMI ANSI ISO 10993-5:2009/(R) 2014 and ISO 10993-10:2010 for the SmartPads III and DP pads, as well as the 3-Lead ECG cable. All testing was performed under good laboratory practices (GLP) conditions using Cytotoxicity and Sensitization protocols. All tests passed for biocompatibility.

Electrical Safety and EMC

The FR3 AED hardware was validated and found to meet the performance criteria in the following standards (Table 2).

Table 2: Electrical Safety and EMC Standards for FR3 AED

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 3: 2007-03	Medical Electrical Equipment - Part 1-2: General Requirements For Basic Safety And Essential Performance - Collateral Standard: Electromagnetic Compatibility - Requirements And Tests

Software Testing

The software for the FR3 AED was verified/validated and documented as a Major Level of Concern device according to the FDA guidance document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The 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, report of unresolved anomalies, and cybersecurity documentation, as applicable. Unit, integration, and system-level testing were documented and demonstrated that the software for the FR3 AED performs as intended.

2. **Animal Studies**

The animal studies summarized in Table 3 were conducted in support of the adult and pediatric biphasic waveforms used with the FR3 AED device.

Table 3. Animal Studies for FR3 AED

Study	Reference	Study Summary
Comparison of biphasic to monophasic defibrillation in swine	1. Gliner et al. Transthoracic defibrillation of swine with monophasic and biphasic waveforms. *Circulation* 1995, 92(6):1634-1643.	Three (3) interrelated studies were performed to evaluate the transthoracic defibrillation effectiveness of two (2) biphasic waveforms in comparison to monophasic shocks in 19 swine. The study demonstrated the superiority of truncated biphasic waveforms over monophasic waveforms for transthoracic defibrillation of swine.
Energy attenuation for	2. Jorgenson D et al. Energy attenuator for pediatric application of an automated	An animal study was conducted on 29 swine to evaluate 50 J fixed-energy, impedance-compensating biphasic truncated exponential

Study	Reference	Study Summary
pediatric AED treatment	external defibrillator. Critical care medicine 2002, 30(Suppl):S145-147. 3. Tang W et al. Fixed-energy biphasic waveform defibrillation in a pediatric model of cardiac arrest and resuscitation. Critical care medicine 2002, 30:2736-2741.	(ICBTE) shocks. In the first experiment, four (4) different weight groups (3.8, 7.5, 15, and 25 kg) of piglets were induced to VF and defibrillated with a modified AED designed to deliver 50 J shocks. In the second experiment, three (3) weight groups of three (3) piglets each were induced to VF and resuscitated using an adult AED with pediatric pads. All piglets were resuscitated and total energy delivered was not weight dependent.

Tang et al.[3] conducted an evaluation of a 50 J biphasic waveform in a porcine model using a custom Codemaster ICBTE device. The device used in Phase I is equiavlent to the SMART biphasic waveform as implemented on the FR3 AED, demonstrated by waveform characterization data provided by Philips.

In Phase 1 of the Tang et al. study, four (4) groups of five (5) anesthetized mechanically ventilated piglets weighing 3.8, 7.5, 15, and 25 kg were evaluated for a total of 20 animals. Ventricular fibrillation was induced with an AC current delivered to the right ventricular endocardium. After 7 minutes of untreated VF, defibrillations were attempted with an impedance-compensated biphasic waveform defibrillator modified to deliver shocks with a nominal energy level of 50 J.

All animals were successfully resuscitated. The average total number of shocks (range 1.8-5.2) and total delivered energy (96 J – 290 J) was not weight dependent ($p < 0.05$). Post-resuscitation hemodynamic and myocardial function quickly returned to baseline values in both experimental groups; 100% of the animals survived. Animals were monitored for survival at 24, 48, and 72 hours; all animals survived through the last time-point. In conclusion, in Phase 1 of Philips' animal study, defibrillation was successfully delivered in 20/20 (100%) of the animals, with successful return of spontaneous circulation (ROSC) and survival in 20/20 (100%) of the animals.

3. **Additional Studies**

Shock Advisory Algorithm Validation

The Patient Analysis System (PAS) shock advisory algorithm used in FR3 AED was validated using ECG Databases intended to provide a representative sample of rhythms from patients who were in-hospital, out of hospital, and with or without emergency care. The rhythms represented cardiac states ranging from normal sinus rhythms (NSR) to cardiac arrest. Data sources were the Massachusetts Institute of Technology-Beth Israel Hospital (MIT-BIH) Arrhythmia Database, MIT-BIH Malignant Ventricular Arrhythmia Database, MIT-BIH Supraventricular Arrhythmia Database, Creighton University

Ventricular Tachyarrhythmia Database, American Heart Association ECG Database, Ohio State-Michigan Instruments Database, Philadelphia Heart Institute Database, Arntz Database, and the Heartstream Gemini II External Defibrillator Study Database.

The device meets the recommendations of the American Heart Association (AHA) for performance goals of arrhythmia analysis algorithms, as summarized in Table 4 Shock Advisory Algorithm Performance.

Table 4. FR3 AED Shock Advisory Algorithm Performance

Rhythms	Test Sample Size (Minimum Required)	Performance Goal	Observed Performance[1]	90% One-sided LCL (Minimum LCL)
Shockable				
Coarse Ventricular Fibrillation	300 (200)	>90% sensitivity	98.7%	97.3% (87%)
Ventricular Tachycardia (poly/flutter)	100 (50)	>75% sensitivity	78%	71.7% (67%)
Non-shockable: minimum 300 total				
Normal Sinus Rhythm	300 (100)	>99% specificity	100%	99.2% (97%)
Atrial Fibrillation, Sinus Bradycardia, Supraventricular Tachycardia, heart block, idioventricular, Premature Ventricular Contraction, Bundle Branch Block	450 (30)	>95% specificity	100%	99.49% (88%)
Asystole	100 (100)	>95% specificity	100%	97.7 (92%)

Intermediate	Test Sample Size (Minimum Required)	Specificity Results[2]	Sensitivity Results[2]	Physician Disagreement[3]
VF (low rate/ amplitude)	100 (25)	(3/3) 100%	(52/97) 56.3%	17%
VT (unspecified)	115 (25)	(58/60) 96.7%	(13/55) 23.6%	71%

[1]These results are scored against a unanimous consensus from all three (3) physicians as to the recommended shock/no-shock response. Performance goals, minimum sample size, and minimum LCL were established by the AHA Scientific Statement (external reference 1).
[2]These result are scored against the majority recommendation from at least two out of three physicians as to the recommended shock/no-shock response.
[3]Physician Disagreement: this percentage represents the percentage of data files that generated a disagreement among the three annotating physicians as to the recommended shock/no-shock response (i.e., the cases where a unanimous consensus was not obtained).

Usability Studies

Usability studies have been performed on the FR3 AED to demonstrate the AED's usability in the indicated user population and to demonstrate an adequate user interface and labeling materials for profession responders.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

Philips, or its predecessor Heartstream using the same devices, was directly responsible for the conduct of clinical trials related to the safety and effectiveness of the Philips family of AEDs. One of these trials, the Gemini Trial, had a feasibility study (Gemini I), a pivotal study (Gemini II), and a safety substudy. All trials were conducted under local Institutional Review Board (IRB) or ethics committee approval and oversight.

Table 5. Summary of Clinical Studies

Study Name	Reference	Study Summary
Gemini I Feasibility Study	4. Bardy et al. Truncated biphasic pulses for transthoracic defibrillation. Circulation 1995, 91(6):1768-1774.	Randomized, controlled trial (RCT), single-center, 30 patients. Feasibility study to evaluate the effectiveness of two (2) different low-energy (115 J and 130 J), biphasic, truncated waveforms compared to a standard, damped sine waveform for transthoracic defibrillation. The biphasic truncated transthoracic shocks of low energy (115 J and 130 J) were as effective in the tested group as 200 J damped sine wave shocks used in transthoracic defibrillators.

Study Name	Reference	Study Summary
Gemini II Pivotal Study	5. Bardy GH et al. Multicenter comparison of truncated biphasic shocks and standard damped sine wave monophasic shocks for transthoracic ventricular defibrillation. Circulation 1996, 94(10):2507-2514.	RCT, 14 sites (US, CAN), 318 patients (electrophysiology laboratory). Low-energy truncated biphasic and high-energy damped sine monophasic were "not significantly different." This study of a 115 J and 130 J biphasic waveform contributed to the development of the 150 J, nominal, shock energy that is used in the Philips AEDs.
Gemini II Safety Substudy	6. Reddy RK et al. Biphasic transthoracic defibrillation causes fewer ECG ST-segment changes after shock. Annals of emergency medicine 1997, 30(2):127-134.	Prospective, randomized, single-center sub-study, 30 patients. Twelve (12)-lead ECGs were collected from the patients that received either monophasic or biphasic defibrillation shocks. Independent, blinded clinicians determined the presence and severity of any ST-segment changes, a surrogate marker of cardiac injury. The high-energy monophasic waveform was associated with significantly more post-shock ST-segment changes on ECG than either of the two (2) biphasic waveform, suggesting that the biphasic waveform had a lower preponderance to cause cardiac injury.
ORCA Trial	7. Schneider T et al. Multicenter, randomized, controlled trial of 150-J biphasic shocks compared with 200- to 360-J monophasic shocks in the resuscitation of out-of-hospital cardiac arrest victims. *Circulation* 2000, 102(15):1780-1787	European RCT at four (4) Emergency Medical Centers in 338 patients (115 patients with VF and emergency resuscitation). Study demonstrated superior defibrillation performance of the low-energy, impedance-compensating, biphasic waveform (SMART waveform) in comparison with escalating, high-energy, monophasic shocks in out-of hospital cardiac arrest (average time from call to first shock was 8.9 minutes). SMART biphasic waveform defibrillated at higher rates than monophasic truncated exponential and monophasic damped sine (96% first-shock effectiveness vs. 59%), with more patients achieving return of spontaneous circulation (ROSC). Survivors of SMART Biphasic resuscitation were more likely to have good cerebral performance at discharge, and none had coma (vs. 21% for monophasic survivors).
Pediatric AED Trial	8. Atkins DL and Jorgenson DB. Attenuated pediatric electrode pads for automated external	Prospective surveillance study analyzed pediatric patients (age 0-23 years, median 2) who had been treated with an AED with attenuated, lower energy pads. There were 26 confirmed pediatric-use cases, 23 of which could be analyzed. VF was reported

Study Name	Reference	Study Summary
	defibrillator use in children. *Resuscitation* 2005, 66(1):31-37.	and shocks were delivered in seven (7) cases with successful termination. Of the seven (7), five (5) survived to hospital discharge. In the 16 patients without VF, the device appropriately detected the rhythm as non-shockable and appropriately withheld shock delivery.
SMART CPR Trial	9. Freese JP et al. Waveform analysis-guided treatment versus a standard shock-first protocol for the treatment of out-of-hospital cardiac arrest presenting in ventricular fibrillation: results of an international randomized, controlled trial. *Circulation* 2013, 128(9):995-1002.	RCT at two (2) sites (The London Ambulance Service (LAS) and the Fire Department of New York (FDNY), 6738 patients enrolled (987 evaluable patients). Comparison of standard shock-first protocol to a waveform-analysis of VF which then guided therapy. There was no long-term survival benefit associated with VF waveform analysis (ROSC, survival to admission or survival to hospital discharge).

A. Adult Defibrillation Waveform

The pivotal clinical trial supporting the Philips SMART biphasic waveform was comprised of three (3) studies. The first was a single center feasibility trial (Gemini I), followed by a prospective randomized clinical trial (Gemini II), and finally a safety sub-study (Gemini Safety). These studies supported the safety and effectiveness of the SMART Biphasic defibrillation waveform.

1. *Gemini I Feasibility Study*[13]

   Objective: Gemini I was a clinical evaluation of the transthoracic defibrillation effectiveness of two (2) different biphasic truncated exponential waveforms (115 J and 130 J), with that of a then standard 200 J monophasic damped sine waveform.

   Study Design: The study was a single site, prospective, randomized and blinded study involving patients undergoing transvenous implantable cardioverter defibrillator (ICD) surgery. Transthoracic ventricular defibrillation rescue shocks were tested after a failed transvenous defibrillation shock was delivered in the course of ICD testing. Each of the three (3) different rescue shocks was tested in random order in each patient. All shocks were delivered at end expiration. The shock was considered a success if it defibrillated a patient. The biphasic waveforms were generated using a custom, experimental defibrillation

(Heartstream) system. The damped sine wave was from the Physio-Control Lifepack 6's defibrillator.

Results: Thirty-three (33) patients were enrolled and 30 completed the protocol. Of the 30 patients, 22 were men. All were undergoing a planned procedure for ICD implantation and consented to inclusion in the clinical study. All three (3) waveforms were equally effective at 97%, with 1 patient failing to be defibrillated with each waveform. The defibrillation data are shown in Table 6 below.

Table 6. Delivered Waveform Variables

Waveform	Energy, J	Current, A*	Voltage, V*	Duration, ms**	Resistance
Standard	212 ± 6 (196-222)	33.8 ± 5.2 (23.7-44.9)	2497 ± 175 (2067-2842)	6.1 ± 1.0 (4.5-8.5)	76 ± 17 (46-120)
Biphasic Energy (J)	113 ± 2 (110-116)	25.1 ± 5.7 (14.9-39.5)	1857 ± 14 (1816-1885)	8.3 ± 0.4 (8.0-9.9)	78 ± 18 (46-127)
Biphasic Energy (J)	126 ± 3 (118-130)	21.9 ± 5.1 (13.6-34.4)	1611 ± 13 (1583-1637)	12.0 ± 0.0 (11.9-12.1)	78 ± 18 (46-120)
P, ANOVA	<.0001	<.0001	<.0001	<.0001	NS

Values are mean = SD and range.

*Leading edge for biphasic waveform: peak for standard waveforms.

**Sum of the durations of first and second phases for biphasic waveforms: durations after decay to 20% of peak for standard waveforms.

The defibrillation energy for the two (2) biphasic waveforms was significantly lower as compared to the damped sine wave ($p < 0.001$), as was the peak current and voltage.

Conclusion: The results showed that biphasic truncated transthoracic shocks of low energy (115 J and 130 J) were as effective in the tested group as 200 J damped sine wave shocks used in standard transthoracic defibrillators.

2. *Gemini II Pivotal Study*[5]

Objective: The objective of this randomized, controlled, multi-center trial was to evaluate the safety and effectiveness of the investigational biphasic truncated exponential waveform vs. the control monophasic damped sinusoidal waveform from standard commercially marketed external defibrillators.

Study Design: The study was a prospective, randomized, double-blinded investigation conducted at 14 sites in the United States and Canada. The study population consisted of 318 patients undergoing testing for insertion of an implantable defibrillator or follow-up electrophysiological evaluation post-implantation. As part of the normal testing protocol for ICDs, one or more transthoracic rescue shocks were delivered if the internal defibrillation attempt was not successful. In this study rescue shocks of investigational biphasic waveforms of 115 J and 130 J were compared to monophasic waveforms of 200 J and 360 J.

Results: A total of 318 patients were enrolled in the study, and after exclusion criteria were applied there were 294 patients included in the study analyses, for a total of 513 shocks delivered during the study. Overall, for the 294 included patients analyzed, 513 transthoracic defibrillation attempts (shocks) were performed. The overall breakdown by waveform and success rates is as follows in Table 7 below.

Table 7. Successful Defibrillations by Waveform Type

Waveform	Successful Defibrillation N (%)	95% Confidence Interval (%)
115 J Biphasic	86 (89)	82-95
130 J Biphasic	144 (86)	81-92
200 J Damped Sine	143 (86)	81-91
360 J Damped Sine	80 (96)	92-100

Conclusion: For the primary hypothesis, the effectiveness of 130 J truncated biphasic waveform and 200 J monophasic waveform were not significantly different using the Pearson chi-square test ($p = 0.97$). There were no statistically significant differences among the four waveforms with respect to defibrillation effectiveness. The 115 J and 130 J biphasic waveforms both demonstrate transthoracic defibrillation effectiveness equivalent to either the 200 J or 360 J monophasic waveforms.

The energy dose increased to 150 J in later clinical studies (ORCA study by Schneider et al.[7]) and 150 J is the energy dose in the SMART biphasic waveform used in the FR3 AED.

3. *Gemini II Safety Sub-Study*[6]

A single center, prospective analysis was conducted to look at potential differences in ECG ST-segment changes when comparing the waveforms from the pivotal trial. In this study the ST-segment changes were used as a surrogate for myocardial injury. Each patient received two (2) low-energy biphasic waveform shocks at 115 J and 130 J and a 200 J monophasic shock. ECGs were reviewed by two (2) blinded, independent reviewers.

A total of 30 patients, undergoing ICD implantation, were consented and enrolled. The 30 patient sub-study showed that ST-segment elevation was significantly greater for the 200 J damped sine wave ($p < 0.001$), indicating a potential safety advantage associated with the biphasic waveform.

B. ORCA (Out of Hospital Response to Cardiac Arrest) Trial[7]

This postmarket study supports the safe and effective use of the Philips FR3 AED in out-of-hospital defibrillation. The ForeRunner device used in this study, and the FR3 device subject to PMA, both use SMART biphasic waveforms and PAS shock advisory algorithm technology.

Study Design: Four (4) European Emergency Medical Systems (EMS) located in Mainz, Germany, Hamburg, Germany, Brugge, Belgium, and Helsinki, Finland participated in the study. Patients were prospectively enrolled in the four (4) EMS systems and included a total of 338 patients. First responders, including physicians in mobile intensive care units, paramedics, and emergency medical technicians used either the SMART biphasic waveform AEDs (Philips ForeRunner 150 J) or monophasic damped sine (MDS) and monophasic truncated exponential (MTE) AEDs with an escalating energy protocol on victims of sudden collapse when defibrillator application was indicated.

The biphasic AEDs (ForeRunner) delivered 150 J impedance-compensated biphasic waveforms. The monophasic AEDs delivered either MTE or MDS defibrillation waveforms, depending on each investigational site.

If the responder suspected that the patient was in cardiac arrest, a sequence of up to three (3) defibrillation shocks was delivered. For monophasic AEDs, the shock sequence was 200 J, 200 J, then 360 J. For the biphasic AEDs, there was a single energy output of 150 J for all shocks.

Results: A total of 338 patients were enrolled. After exclusion criteria were applied, 115 patients were included in the principal analyses, 54 treated with biphasic and 61 with monophasic AED shocks. No significant differences were observed between the groups for mean age, sex, weight, primary structural heart disease, cause of cardiac arrest, by whom arrest witnessed, or duration of CPR.

Fifty-three (53) of 54 (98%) VF patients were defibrillated using 150 J biphasic shocks compared with 42 of 61 (69%) with 200-360 J monophasic shocks ($p < 0.0001$). Further, all patients treated with biphasic AEDs were defibrillated with biphasic AEDs under EMS care, while this was not true for those treated with monophasic AEDs or a combination of monophasic AEDs and backup manual monophasic defibrillators (100% compared with 84%, $P = 0.0025$). The impedance-corrected biphasic truncated exponential (ICBTE) waveform (SMART biphasic waveform) was more effective than the MDS waveform (98% vs. 77%, Fisher's exact test $p = 0.02$). Further, more patients were defibrillated with the initial biphasic shock than with the initial monophasic shock (96% compared with 59%, $p < 0.0001$). A higher percentage of patients (76%) achieved return of spontaneous circulation (ROSC) following 150 J biphasic waveform defibrillation compared with higher energy monophasic waveform defibrillation (54%) ($p = 0.01$).

Conclusion: The high defibrillation effectiveness of the 150 J impedance-compensating biphasic waveform observed in this study was consistent with the Gemini I and II studies and strengthened the safety and effectiveness evidence base by providing randomized data from out-of-hospital emergency care. The concurrent controls substantiated the magnitude of the improvement in defibrillation effectiveness obtained with this biphasic waveform compared with conventional escalating-energy

monophasic-waveform methods. The 150 J biphasic waveform defibrillated at higher rates, resulting in more patients who achieved ROSC. Although survival rates to hospital admission and discharge did not differ, discharged patients who had been resuscitated with biphasic shocks were more likely to have good cerebral performance. In summary, the study demonstrated that an appropriately dosed low-energy impedance-compensating biphasic waveform (identical to the FR3 waveform) strategy results in superior defibrillation performance when compared with escalating, high-energy monophasic shocks in out-of-hospital cardiac arrest.

C. Pediatric Defibrillation

Pediatric defibrillation is supported in this submission with an animal study[3] (discussed in the Pre-Clinical section above) for the biphasic waveform energy of 50 J[3] and a postmarket surveillance study for Pediatric AED use[8].

Postmarket Surveillance Study of Pediatric AED Use[8]

The objective of the post-market surveillance study was to confirm that certain adult AEDs with shock intensity attenuation could be used safely and effectively in the pediatric population. The study population was infants and children less than 8 years of age or under 55 lbs. This study was conducted on predecessor devices (the HeartStart FR2 and OnSite Defibrillator) to the FR3 AED that are applicable to the safety and effectiveness of the FR3 AED.

Study Design: This prospective, observational, post-market surveillance study included the Philips FR2 AED with Pediatric Attenuated Electrodes and the HeartStart OnSite AED with the infant/child SMART pads cartridge. Data from the FR2 and OnSite AEDs are applicable to the consideration of the safety and effectiveness of the FR3 because they share the same principles of operation, SMART biphasic waveform and patient analysis algorithm.

Results: Through September 2004, there were 26 confirmed pediatric-use cases: 25 uses of the FR2 and 1 use of the OnSite. There were 18 US uses and eight (8) uses outside the US. There were 12 males, 11 females, and in three (3) cases the gender was not reported. The median age was 2 years. The users were predominately EMS personnel or health care professionals (n=24). Most arrests occurred at home (n=16).

Most patients to whom the device was applied had non-shockable rhythms (16, of which 13 were confirmed with AED data). Of seven (7) patients who had ventricular fibrillation and received attenuated shocks, all had termination of ventricular fibrillation and five (5) survived to hospital discharge. The median age of the seven (7) patients was 3 years (range 18 months to 10 years). These patients received on average two (2) shocks (range 1-4).

Conclusion: Based on the post market surveillance data available at time of study closure, the FR2 AED used with the FR2 infant/child attenuated pads and the

HeartStart OnSite AED used with infant/child SMART pads cartridge performed safely and effectively in the pediatric population, which can be applied to the pediatric use of the FR3.

D. SMART CPR Clinical Data

The SMART CPR algorithm was validated on a database collected from mult-center, multi-national out-of-hospital and in-hospital adult sudden cardiac arrest rhythms that were collected during a study carried out by Laerdal Medical, Stavanger, Norway. This database contained a total of 575 defibrillation shocks for 132 patients that were assessed for ROSC after each shock.[10]

Philips extracted 5-second pre-shock segments to evaluate the SMART CPR algorithm prediction of ROSC status after each shock for each of two (2) selectable thresholds: AUTO1 and AUTO2. SMART CPR performance is in the following table:

AUTO1 sensitivity	AUTO1 specificity	AUTO2 sensitivity	AUTO2 specificity
90.2%	55.3%	83.6%	69.8%

Snyder et al. 2007[11] published data on all cardiac arrests for which a ForeRunner or FR2 AED was deployed occurring from December 1996 through December 2005 in Rochester, Minnesota and the surrounding public service area were reviewed. Eighty-seven (87) VF patients were identified, all of whom were treated with a 'shock first' protocol. In this study 'CPR first' is considered, post hoc, as a potential alternate treatment. Study results showed that for the AUTO2-based SMART CPR protocol, 94% of neurologically intact survivors would retain successful shock-first treatment, and 48% of non-survivors would receive alternate CPR-first treatment.

Freese et al.[9] conducted a randomized controlled trial at at two (2) sites (The London Ambulance Service (LAS) and the Fire Department of New York (FDNY)), with 6738 patients enrolled (987 evaluable patients). Standard shock-first protocol was compared to a waveform-analysis of VF which then guided therapy (SMART CPR). While there was no long-term survival benefit associated with VF waveform analysis (ROSC, survival to admission or survival to hospital discharge), further subgroup analyses were performed for the waveform analysis arm, comparing those patients for whom the VF score increased after the CPR interval with those for whom the score declined. Electrocardiogram (ECG) data were available for 204 of 262 patients, and a total of 105 of these patients (51.5%) experienced an increase in VF score before the first defibrillatory shock.

Those whose VF scores had increased after the CPR interval had higher survival rates for all secondary survival end points (ROSC, 41.90% vs. 19.19%, $P<0.001$; sustained ROSC, 33.65% vs. 13.13%, $P<0.001$; survival to admission, 36.89% vs. 11.11%, $P<0.001$), although there was no difference in survival to hospital discharge (11.65% vs. 5.05%; $P=0.13$). There was no ability to measure CPR performance during the

study, allowing the possibility that the lack of any benefit in the waveform analysis group was the result of poor CPR performance rather than a failure of the analysis.

E. Pediatric Extapolation

In this premarket application, the applicant provided a postmarket surveillance study for pediatric AED use (Atkins et al[8]). In addition, the applicant also provided supporting animal data (Tang et al.[3]) to further support the use of the pediatric waveform.

F. Human Factors and Usability Studies

A usability study was conducted to evaluate device usability, device interfaces, and other human factors pertaining to the FR3 AED. The study included 89 patients across three (3) different user groups. The use case scenarios were designed to mimic the situations that EMS professionals may encounter and were performed in a simulated environment. All participants were able to successfully deliver a shock without causing harm to themselves, a bystander, or the patient.

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. There were three (3) clinical studies relevant to support safety and effectiveness for the FR3.

The GEMINI II study had 12 clinical investigators who contributed data. 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.

The ORCA post-market study was conducted prior to 1999 by HeartStream, Inc. Philips acted with due diligence to obtain financial disclosure information for this clinical study, but was unable to do so on the basis of the age of the studies.

The Pediatric HeartStart AED study had one external clinical investigator, who did not have 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 post-market performance.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness data provided for the Philips' FR3 AED was based on the analysis of the defibrillation waveform, the arrhythmia detection algorithm, and clinical data collected from published literature.

The pivotal clinical study by Bardy et al.[5] for in-hospital defibrillation confirmed that both the 115 J and 130 J biphasic waveforms demonstrated transthoracic defibrillation effectiveness equivalence to either the 200 J or 360 J monophasic waveforms. The energy dose increased to 150 J in subsequent clinical studies and in the HeartStart FR3 models[7]. The clinical study by Schneider et al.[7] for out-of-hospital defibrillation showed that more patients were defibrillated with the initial biphasic shock (96%) than with the initial monophasic shock (59%) and a higher percentage of patients achieved restoration of spontaneous circulation after 150 J biphasic waveform defibrillation (76%) compared with higher energy monophasic waveform defibrillation (54%).

Pediatric defibrillation was supported by a prospective, randomized animal study by Tang et al.[3] performed on swine with the biphasic waveform energy of 50 J and a post-market surveillance study for pediatric use by Atkins et al.[8] The Tang study demonstrated that the 50 J shock had successful ROSC and survival, without different effects on hemodynamics despite the difference in body weight, in an animal model.

The Atkins clinical study[8] sponsored by Philips confirmed that the Philips SMART defibrillation waveform with 50 J energy could be used safely and effectively in the pediatric population.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in a clinical studies conducted to support PMA approval and published literature as described above. The results from the nonclinical testing performed on the AEDs demonstrated appropriate electrical safety, electromagnetic compatibility, environmental conditions, biocompatibility, mechanical performance, and overall performance. The preclinical animal study demonstrated the superiority of truncated biphasic waveforms over truncated monophasic waveforms for transthoracic defibrillation of swine. The clinical data, including published clinical studies for in-hospital and out-of-hospital use, as well as pediatric use, and usability/human factor reports, further demonstrate the safety of the device.

C. Benefit-Risk Determination

The probable benefits of the FR3 AED are based on published literature and post-market clinical data collected after the device initially received 510(k) clearance, as 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 shown to have a high benefit for patients with underlying diseases that remain undetected until sudden cardiac arrest occurs. The benefit of early defibrillation is providing the sudden cardiac arrest victim a chance at surviving the arrest since the chances of surviving a sudden cardiac arrest decreases by 7-10% for each minute without defibrillation.[12] Sudden cardiac arrest is a leading cause of out of hospital death in the US, claiming approximately 326,000 lives each year, with only about a 10% survival rate.[13] Sudden cardiac arrest is the unexpected loss of the heart's ability to effectively pump blood to the body and the victim is unconscious and unresponsive. The most common rhythm of adult sudden cardiac arrest resulting in ventricular fibrillation[14] whereas for infants and children sudden cardiac arrest related to breathing is more common, although the importance of rapid AED deployment remains.[15] The role early defibrillation plays in adult and pediatric sudden cardiac arrest has been extensively documented[16] and access to an AED provides a sudden cardiac arrest victim a chance of surviving the event.

The magnitude of this benefit is either life or death. The published literature[3, 5, 7, 8] and post-market 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 of the treatment is not related to the device.

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

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

In conclusion, given the available information above, the data supports that for patients with VF and pulseless VT, both the most common cause of sudden cardiac arrest, 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 11, 2020. The final conditions of approval cited in the approval order are described below.

The applicant will provide the following non-clinincal 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; 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. 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; and
    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.

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