SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Automated External Defibrillator

Device Trade Name: HeartStart FRx Defibrillator (861304), Primary Battery (M5070A), Aviation FRx Battery (989803139301), SMART Pads II (989803139261), and Infant/Child Key (989803139311)

Device Procode: MKJ

Applicant's Name and Address: Philips Medical Systems
22100 Bothell Everett Hwy
Bothell, WA 98021

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P180028

Date of FDA Notice of Approval: May 11, 2020

The HeartStart FRx has been commercially available since 2005, when it was first cleared by FDA under K050004. P180028 (which was initially submitted as part of P160029, but subsequently made an independent PMA) was 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 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 FRx defibrillator.

II. INDICATIONS FOR USE

The HeartStart FRx Defibrillator (Model 861304) is indicated for use on potential victims of sudden cardiac arrest (SCA) with the following symptoms:

- Unconsciousness, and
- Absence of normal breathing

The HeartStart FRx (Model 861304) is indicated for adults over 55 pounds (25 kg). The Model 861304 is also indicated for infants and children under 55 pounds (25 kg) or 0-8 years old when used with the optional Infant/Child Key (Model 989803139311). If the

Infant/Child Key is not available, or you are uncertain of the child's age or weight, proceed using adult treatment without the infant/child key.

III. CONTRAINDICATIONS

The HeartStart FRx Defibrillator should not be used when a patient is conscious or breathing normally.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the FRx Owner's Manual.

V. DEVICE DESCRIPTION

The Philips HeartStart FRx Defibrillator (861304) is a small, lightweight, portable, rugged, battery powered automated external defibrillator (AED) indicated to treat victims of sudden cardiac arrest (SCA).

The FRx prompts the user to take specific actions if a potentially shockable rhythm is detected. The FRx 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 FRx is able to provide verbal instructions to the user, detect where the user is in the event response, and provide general CPR coaching.

The FRx is a public access AED. Users should have received training in basic life support/AED, or a physician-authorized emergency medical response training program.

The FRx necessary accessories include a lithium manganese dioxide battery and HeartStart SmartPads II defibrillation pads. The HeartStart SmartPads is single patient use only electrode indicated for all ages with an optional reusable Infant/Child Key available to treat infants and children 0-8 years old or less than 55 lbs. When the Key is installed in the Infant/Child Key slot at the top of the FRx front panel, the software in the FRx attenuates the energy delivered by the FRx. The FRx uses a proprietary shock advisory algorithm (Patient Analysis System [PAS]) and a truncated exponential biphasic shock waveform (impedance compensating SMART Biphasic waveform) to deliver a 150 J nominal shock to adults and 50 J nominal shock to infants/children (pediatric defibrillation) to achieve its indicated use. The FRx AED is shown in Figure 1. The FRx features are identified in Figure 2.

Figure 1: FRx AED

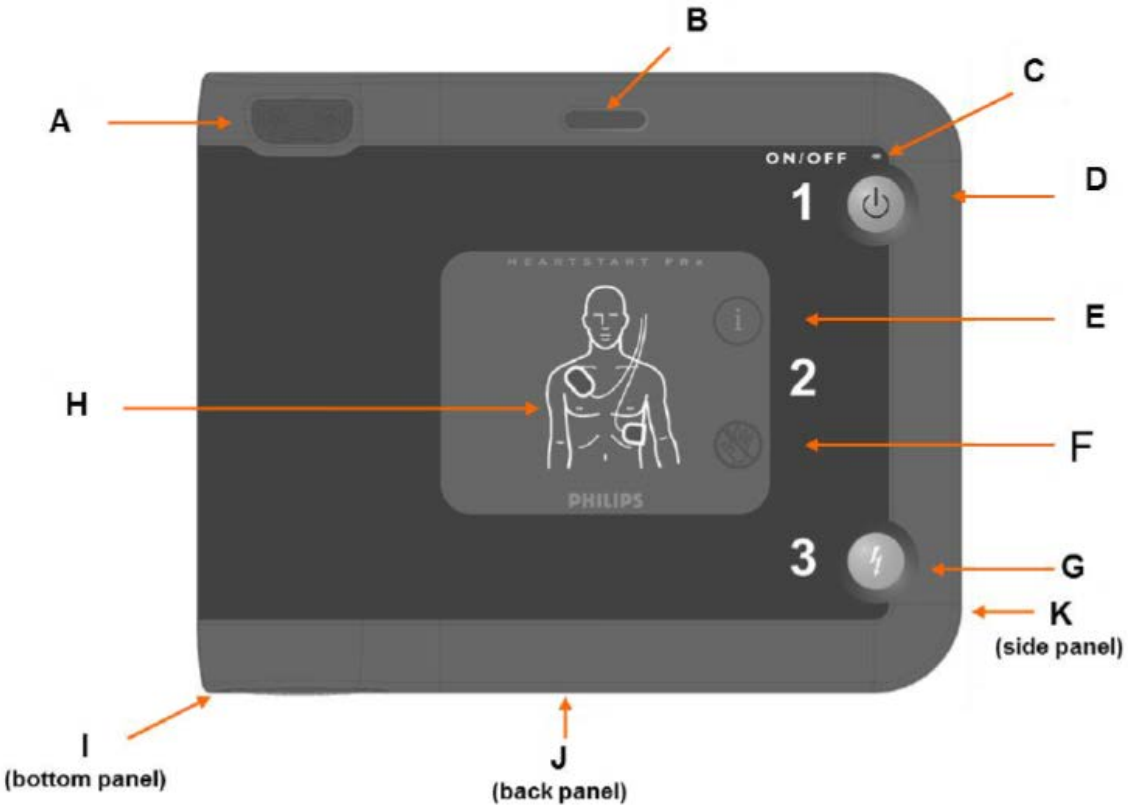

Figure 2: FRx Features

A. Pads Connector Port. Receptacle for the defibrillator pads connector.

B. Infant/Child Key Port. Accomodates the Infant/Child Key for the HeartStart FRx AED to enable pediatric treatment protocols for patients under 55 lbs (25 kg) or 0-8 years old.

C. Readiness indicator LED. The FRx Readiness Indicator LED is used to indicate the device's status.

D. On/Off button. The green On/Off button is a push button used to activate the device from stand-by mode or deactivate it to stand-by mode.

E. Information button (or i-button). The FRx blue i-button is used to provide information to the user.

F. Caution indicator LED. The indicator blinks or is on when no one should be touching the patient, such as when ECG analysis is being performed or a shock is about to be delivered.

G. Shock button. Controls shock delivery. The button flashes when the FRx AED is ready to deliver a shock.

H. Pads Placement Graphic and LEDs. When the pads cartridge is installed (M071A or M5072A), the FRx has a pads placement graphic on the front panel to provide the user with a guide to correct pad placement. The FRx pads placement graphic also incorporates LEDs indicating when the pads have been placed on the patient.

I. Speaker. Voice instructions and information are provided through the speaker.

J. Beeper. The FRx beeper provides chirps and warning tones.

K. Infrared (IR) port. The FRx IR port facilitates communication between the FRx internal circuitry and external devices.

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 FRx was first marketed in the United States in 2005. The device has not been withdrawn from marketing for any reason related to its safety or effectiveness. FRx is currently sold in Australia, Canada, European Union countries requiring CE Mark, and over 50 countries in Central and South America, Asia, and Africa. 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 VF or pulseless VT, which may result in death or permanent injury;
- Inappropriate energy, which could cause failed defibrillation or post-shock dysfunction;
- Myocardial damage;
- Fire hazard in the presence of high oxygen concentration or flammable anesthetic agents;
- Incorrectly shocking a pulse sustaining rhythm and inducing VF or cardiac arrest;
- Bystander shock from patient contact during defibrillation shock;
- Interaction with pacemakers;
- Skin burns around the 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

A. Laboratory Studies

The FRx 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. HeartStart FRx Bench Tests

Test	Purpose	Acceptance Criteria	Results
Sealing/Moisture Resistance	Verify the FRx 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 comply with all of its performance requirements following application of a 500 kg (1100 lb.) load distributed across 65+/-6.5 square cm (10+/- square inches) to any location on its top surface.	Pass
Dielectric Withstand – Operator Access	Verify the device complies with the requirements of 60601-2-	The device shall comply with the requirements of 60601-2-4 Edition 3.0 section 201.8.8.3 test 1 when 3000V DC is applied	Pass

Test	Purpose	Acceptance Criteria	Results
	4 Edition 3.0 section 201.8.8.3 test 1.	between the patient end of the electrode cable with the electrodes shorted together and metal foil in intimate contact with non-conductive parts liable to be handled in NORMAL USE.	
Dielectric Withstand – Between Defibrillator Electrodes	Verify the device complies with the requirements of IEC60601-2-4 Edition 3.0 section 201.8.8.3 test 2.	The device shall comply with the requirements of IEC60601-2-4 Edition 3.0 section 201.8.8.3 test 2 when 3000V DC is applied between the defibrillator electrodes.	Pass
Dielectric Withstand – Across Defibrillator Switches	Verify the device complies with the requirements of IEC60601-2-4 Edition 3.0 section 201.8.8.3 test 3.	The device shall comply with the requirements of IEC60601-2-4 Edition 3.0 section 201.8.8.3 test 3 when 3000V DC is applied across each switching device.	Pass
Drop Test	Verify the device complies with IEC 60601-1:15.3.4.2 and IEC 60601-1-12.	The device shall maintain basic safety and essential performance after being dropped from 0.5 meters onto a concrete or tile-over-concrete surface on each of its three (3) axes without producing a safety risk to the device.	Pass
Therapy Delivery Endurance	Verify the device complies with IEC 60601-2-4: *103 Endurance and IEC 60601-2-4:201.103 * Endurance.	The therapy delivery subsystem shall meet all of its performance requirements after being charged and discharged no less than 2500 times at rated energy into a 50 Ω load.	Pass
Primary Battery Stand-By Life	Verify the installed primary battery will last a minimum of 3 years.	After being installed into a device kept in standby mode for the periods specified below, the primary battery shall be able to supply power according to specification “Low Battery, Remaining Capacity.” Typical: 4 years, assumes new battery, device with typical standby and self-test currents Minimum: 3 years	Pass
Infant/Child Key Identification	Verify the insertion of the infant/child key is identified.	The insertion of the infant/child key initiates the pediatric mode of the FRx.	Pass

Biocompatibility

The FRx AED is not intended for patient contact, but the pads will contact the patient. Biocompatibility testing complies with ISO 10993-5:2009 and ISO 10993-10:2010 for the FRx SMART Pads II and infant/child SMART Pads cartridge. All testing was performed under GLP conditions utilizing Cytotoxicity and Sensitization protocols. All tests passed for biocompatibility.

Electrical Safety and EMC

The FRx 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 FRx

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
IEC 60601-1-12 Edition 1.0 2014-06	Medical Electrical Equipment -- Part 1-12: General Requirements for Basic Safety and Essential Performance -- Collateral Standard: Requirements for medical electrical equipment and medical electrical systems intended for use in the emergency medical services environment

Software Testing

The software for the FRx 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 FRx AED performs as intended.

B. **Animal Studies**

Animal studies summarized in Table 3 were conducted in support of the adult and pediatric biphasic waveforms used with the FRx AED.

Table 3. Animal Studies on Waveform

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 pediatric AED treatment	2. Jorgenson D et al. Energy attenuator for pediatric application of an automated 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.	An animal study was conducted on 29 swine to evaluate 50 J fixed-energy, impedance-compensating, biphasic truncated exponential (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 equivalent to the SMART biphasic waveform as implemented on the FRx, 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.

C. **Additional Studies**

Shock Advisory Algorithm Validation

The Patient Analysis System (PAS) shock advisory algorithm used in FRx was validated using ECG Databases intended to provide a representative sample of rhythms from patients who were in-hospital, out of hospital, with and 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 AHA for performance goals of arrhythmia analysis algorithms, as summarized in the Table 4 Shock Advisory Algorithm Performance.

Table 4. FRx 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 (2) out of three (3) 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 (3) 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 conducted for FRx to demonstrate the AED's usability in the indicated user population and an adequate user interface and labeling materials for professional responders.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

Philips, or its predecessor Heartstream, 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 investigational 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.
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. Ywelve (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

Study Name	Reference	Study Summary
		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 defibrillator use in children. *Resuscitation* 2005, 66(1):31-37.	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 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.

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*[4]

   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 6s 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 below in Table 6.

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 US 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 delivery 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. and others), and 150 J is the energy dose in the SMART biphasic waveform used in the FRx 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 HeartStart FRx in out-of-hospital defibrillation. The ForeRunner device used in this study, and the FRx 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) European 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 impedance-compensated biphasic waveform AEDs (Philips ForeRunner 150 J) or standard 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 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 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 FRx 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 (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 Defibrillator and the HeartStart OnSite Defibrillator) to the FRx AED. Data from both defibrillators used in this study are applicable to the safety and effectiveness of the FRx AED.

Study Design: This prospective, observational, post-market surveillance study included the Philips FR2 AED and Pediatric Attenuated Electrodes, the HeartStart OnSite AED with attenuation pads cartridge, and the HeartStart FRx AED with its infant/child key accessory and corresponding pads. Data from the FR2 and OnSite are applicable to the consideration of the safety and effectiveness of the FRx because the FRx AED uses the same principles for its SMART biphasic therapy waveform and PAS patient analysis algorithm. The study was conducted under local IRB approval.

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 VF and received attenuated shocks, all had termination of VF 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 pads cartridge performed safely and effectively in the pediatric population, which can be applied to the pediatric use of the FRx.

D. 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.

E. Human Factors and Usability Studies

Bright - Adults and Pediatrics, 2004	Adult Study: This study involved a simulated rescue scenario with the FRx and the included Quick Reference Guide (QRG). The objective of the study was to understand whether CPR/AED trained lay users (but naïve to the FRx) could complete a successful adult rescue with the FRx AED in a way that caused no harm to the rescuer or the patient using only the QRG. All of the participants were able to achieve appropriate pads placement and press the shock button with no significant safety issues for the victim, user or a potential by-stander. Furthermore, the time to shock was consistent with those previously reported in the literature for trained responders. Pediatric Study: The infant child usability study involved a simulated child rescue scenario with the FRx and the included QRG. The objective of this study was to understand whether participants could insert the infant child key into the FRx defibrillator correctly and successfully place pads, in a way that caused no harm to the rescuer or the patient. All of the participants were able to recognize the need to use the infant/child key and achieve appropriate pads placement and all uses had no significant safety issues for the victim, user or potential bystander.

Wahoo, 2015	A usability study was completed to validate minor updates to the FRx product design. User interface usability validation included seven (7) police officers responding to simulated SCA, and replacing the device battery and pads. No participants created clinically significant hazards and all participants successfully delivered a shock, and replaced the device battery and pads.

F. 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 four (4) clinical studies relevant to support safety and effectiveness for the FRx AED.

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 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 Devices 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' FRx AED was based on the analysis of the defibrillation waveform, the arrhythmia detection algorithm, and 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 future clinical studies and in the HeartStart FRx models. The clinical study by Schneider et al[6] 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[6]. The Tang study demonstrated that the 50 J shock had successful return of ROSC and survival, without different effects on hemodynamics despite the difference in body weight, in an animal model.

A second set of experiments delivered shocks through special pediatric pads in conjunction with a conventional adult AED.

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 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 FRx 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[10]. 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[11]. 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[12] whereas for infants and children sudden cardiac arrest related to breathing is more common, although the importance of rapid AED deployment remains[13]. The role early defibrillation plays in adult and pediatric sudden cardiac arrest has been extensively documented[14] 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 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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