SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Automated External Defibrillator

Device Trade Name: HeartSine samaritan® PAD 350P (SAM 350P), HeartSine samaritan® PAD 360P (SAM 360P), and HeartSine samaritan® PAD 450P (SAM 450P)

Device Product Code: MKJ

Applicant's Name and Address: HeartSine Technologies LLC
121 Friends Lane, Suite 400
Newtown, PA 18940

Date of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P160008

Date of FDA Notice of Approval: January 12, 2017

The SAM 350P automated external defibrillator (AED), Pad-Paks™, and Saver EVO® software have been commercially available since July 11, 2013 when it was first cleared by FDA under K123881. The SAM 450P has been commercially available since March 27, 2015 when it was first cleared by FDA under K142709. The SAM 360P was never cleared as a 510(k) and has been available commercially outside the US since August 2014. P160008 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 samaritan® PAD Models SAM 350P, SAM 360P, and SAM 450P. A combination of post market experience data, relevant literature, animal testing, and in-vitro bench testing has been reviewed to demonstrate a reasonable assurance of safety and effectiveness for the samaritan® PAD Models SAM 350P, SAM 360P, and SAM 450P.

II. INDICATIONS FOR USE

The HeartSine samaritan® PAD 350P (SAM 350P), HeartSine samaritan® PAD 360P (SAM 360P), and HeartSine samaritan® PAD 450P (SAM450P) are indicated for use on victims of cardiac arrest who are exhibiting the following signs:
   • Unconscious
   • Not breathing
   • Without circulation (without a pulse)

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

The devices are indicated for use on patients greater than 8 years old or over 55 lbs. (25 kg) when used with the adult Pad-Pak (Pad-Pak-01 or Pad-Pak-07). They are indicated for use on children between 1 and 8 years of age or up to 55 lbs. (25 kg) when used with the Pediatric-Pak (Pad-Pak-02).

III. CONTRAINDICATIONS

Use of the samaritan® PAD Models SAM 350P, SAM 360P and SAM 450P is contraindicated if the patient is responsive or conscious.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the HeartSine samaritan® PAD Models SAM 350P, SAM 360P, and SAM 450P user manuals.

V. DEVICE DESCRIPTION

A. samaritan® PAD Models SAM 350P, SAM 360P and SAM 450P Defibrillators

The samaritan® PAD Models SAM 350P, SAM 360P, and SAM 450P are portable, battery operated, prescription Automated External Defibrillators (AEDs) designed to treat victims of cardiac arrest. The devices are Public Access Defibrillators (PAD) intended for use by minimally trained users. The user interface incorporates voice and text/icon prompts to guide the user in the use of the device. The devices also incorporate an audible metronome to guide the user as to the correct rate at which chest compressions should be administered in accordance with current American Heart Association (AHA) resuscitation guidelines.

The SAM 350P, SAM 360P, and SAM 450P are similar in most respects, and unless otherwise noted, the described features and performance apply to all three (3) models. The SAM 360P is the only fully automatic model. When the SAM 360P has determined that a shockable arrhythmia is present, it will advise the user to "Stand Clear of Patient – Shock Advised," followed by the voice prompt "Stand Clear of Patient – Shock Will be Delivered in 3, 2, 1". It will then automatically deliver the shock without the need for user intervention. Both the SAM 350P and SAM 450P have the same automated rhythm analysis feature, but require the user to press a Shock button for shock delivery.

Figure 1 below shows the SAM 350P (left), SAM 450P (center), and SAM 360P (right). The models 350P and 450P have an orange shock delivery button in the center of the interface. The 360P shows the lightning bolt display in the center which flashes to indicate that a shock will be delivered. The 450P also shows the CPR rate indicator bar in the center left.

Figure 1: SAM 350P (left), SAM 450P (center), and SAM 360P (right)

All three (3) models use the same proprietary electrocardiogram (ECG) analysis algorithm, which automatically determines whether a victim has a shockable or non-shockable rhythm and advises a shock when appropriate. The devices are designed to provide a "Shock Advised" decision for ventricular fibrillation (200 microvolts peak-to-peak or greater) and ventricular tachycardia (a heart rate of 180 beats-per-minute or greater and a QRS duration equivalent to greater than 120 ms). The devices are designed to provide a "No Shock Advised" decision for rhythms and arrhythmias including, but not limited to, normal sinus rhythm, supraventricular tachycardia, bradycardia, and pulseless electrical activity.

In addition to the proprietary ECG analysis algorithm used in all models, the SAM 360P and SAM 450P include functionality based on the devices' capability to record the impedance cardiogram (ICG). The SAM 350P also records the ICG; however, the data can only be accessed through data download by the manufacturer. The SAM 360P uses the ICG recording capability as input to a motion/interference detection algorithm designed to prompt the user to cease any motion (such as CPR) during ECG analysis. In addition to the voice prompts common to all three (3) models, which advise the user to stand clear of the patient during analysis and shock, for the SAM 360P, if motion is detected during the ECG analysis period at an amplitude and duration above the ICG motion/interference algorithm threshold, the device will warn the user "Motion Detected. Do Not Touch the Patient."

The SAM 450P uses the ICG recording capability to assess the rate at which CPR is being administered. The calculated CPR compression rate prompts audio-visual feedback to be provided to the operator. Depending on the CPR rate being administered, audio feedback is emitted by the SAM 450P resulting in the following voice instructions

to the user: "push faster," "good speed," or "push slower." CPR rate feedback is provided by the SAM 450P only when an Adult (or Technical Standard Order (TSO)) Pad-Pak™ is installed. When a Pediatric-Pak™ is detected, the CPR rate feedback capability is disabled.

If a shock is required, the AED will automatically charge to the appropriate energy level and (for the SAM 350P and SAM 450P) prompt the user to press the illuminated shock button to deliver the shock. The shock waveform is an escalating, truncated exponential biphasic waveform pulse known as the SCOPE® (Self-Compensating Output Pulse Envelope) waveform, and is delivered to the patient via two (2) disposable defibrillator electrodes. For adult patients, a pre-configured 150 Joule, 150 Joule, 200 Joule escalating energy sequence is used in accordance with current AHA resuscitation guidelines. For pediatric patients, a fixed 50 Joule shock is used. All three (3) models use the identical defibrillation waveform and energy sequence.

After initial analysis and shock delivery (if appropriate), all three (3) models will advise the user to resume CPR as guided by a number of voice prompts. All three (3) devices also record the patient's ECG and the patient's ICG (Impedance Cardiogram). The ECG can be viewed/downloaded using HeartSine's Saver EVO® software (see Section V.C. below), which is an optional accessory to the devices.

B. Pad-Pak™ (Electrode and Battery Pack)

The Pad-Pak™ is a combined, single use, battery and electrode unit. The electrodes are two (2) non-sterile, single-use, self-adhesive, conductive gelled defibrillation electrodes. All three (3) AED devices are compatible with all 3 Pad-Pak versions. The three (3) versions of the Pad-Pak™ are: (1) a standard adult version (Pad-Pak™-01), (2) a pediatric version (Pediatric-Pak™-02), and (3) a standard adult version meeting US Federal Aviation Administration standards for use on commercial aircraft (Pad-Pak™-07). The pediatric version is for use on patients between the ages of 1 and 8 years or less than 55 lbs. (25 kg). When inserted into the AED, the Pediatric Pad-Pak enables delivery of 50 Joule non-escalating shocks in accordance with the AHA Resuscitation guidelines.

A device with a new Pad-Pak™ charges to 150 Joules in less than 8 seconds and to 200 Joules in less than 12 seconds, and is capable of providing at least 60 shocks at 200 Joules or 6 hours of continuous monitoring. The Pad-Pak™ has a shelf life of 4.25 years.

C. Saver EVO® Software

The Saver EVO® software is an optional accessory for use with the SAM 350P, SAM 360P, and SAM 450P defibrillators. The Saver EVO® software can be used to view and/or download the patient's recorded ECG, adjust audio and visual device outputs, run diagnostic tests on the devices, and check for upgrades to the latest Saver EVO® software version. All other settings such as energy protocol, CPR duration, and the metronome rate are not user configurable.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

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

VII. MARKETING HISTORY

HeartSine first marketed an Automated External Defibrillator in the U.S. in 2003. The current PAD design, HeartSine Samaritan® PAD, with automated voice and text prompts was first cleared for U.S. distribution on May 25, 2004. The design was updated in 2013 and became the SAM 350P to comply with AHA 2010 CPR guidelines, add CPR coaching prompts, improve the arrhythmia analysis algorithm, and introduce the TSO Pad-Pak. The SAM 350P has been marketed in the U.S. since November 2013 and is commercially available in over 50 countries, including the United States, Canada, and countries in the European Union, Asia, and South America. It has not been withdrawn from marketing for any reason related to its safety or effectiveness.

The SAM 360P was designed with a fully automated shock delivery sequence but has not been marketed in the U.S. It has been marketed outside the US since August 2014 and is commercially available in over 30 countries including Canada and countries in the European Union, Asia, and South America. It has not been withdrawn from marketing for any reason related to its safety or effectiveness.

The SAM 450P was introduced in 2015 with an updated user interface to provide feedback on the rate of chest compressions during CPR. It has been marketed in the United States since June 2015 and has not been withdrawn from marketing for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The potential adverse effects (e.g., complications) associated with use of an automated external defibrillator include, but are not limited to, the following:

- Failure to identify shockable arrhythmia.
- Failure to deliver a defibrillation shock in the presence of VF or pulseless VT, which may result in death or permanent injury.
- Inappropriate energy which could cause failed defibrillation or post-shock dysfunction.
- Myocardial damage.
- Fire hazard in the presence of high oxygen concentration or flammable anesthetic agents.
- Incorrectly shocking a pulse sustaining rhythm and inducing VF or cardiac arrest.
- Bystander shock from patient contact during defibrillation shock.
- Interaction with pacemakers.

- Skin burns around the electrode placement area.
- Allergic dermatitis due to sensitivity to materials used in electrode construction.
- Minor skin rash.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Testing

The SAM 350P, SAM 360P, and SAM 450P and their accessories (Pad-Paks™ and Saver EVO® software) underwent bench, animal, and biocompatibility evaluation, as well as software verification and validation appropriate for major level of concern devices. Testing was conducted on key device subassemblies and the complete systems.

Bench Testing

Table 1 below summarizes the bench testing conducted to demonstrate proper performance of all three (3) models of defibrillators and the Pad-Pak and Saver EVO® accessory devices, including conformance with applicable consensus performance standards.

Test Title	Results
Electrical Safety Testing (IEC 60601-1:2005 Edition 3 and IEC 60601-2-4:2010 Edition 3)	Pass
Electromagnetic Compatibility Testing (IEC 60601-1-2:2007 Edition 3) with additional Home Use environment requirements	Pass
RTCA.DO-160F/G EMC Testing (Airborne Equipment)	Pass
Integrated System Testing (Combined Hardware and Software Testing)	Pass
Device Software Testing	Pass
Shock and Vibration Testing (MIL-STD 810F)	Pass
Battery Testing	Pass
Maximum Temperature Testing	Pass
VCA Dangerous Goods Certification Testing	Pass
Temperature Moderated Battery Management Testing	Pass
Membrane Testing	Pass
Pad-Pak Electrical Interface Validation Testing	Pass
TSO Pad-Pak Testing	Pass
USB Cable Validation Testing	Pass
Printed Circuit Board Assembly Testing	Pass

Table 1: Bench Testing

The ECG arrhythmia analysis algorithm performance has been evaluated by using several databases of real-life ECG recordings, including the AHA, Massachusetts Institute of Technology MIT – NST, and Creighton University databases. The devices meet the recommendations of the AHA for performance goals of arrhythmias analysis algorithms. The performance of the arrhythmia analysis algorithm is summarized below in **Table 2**. Note that the same ECG arrhythmia analysis algorithm is used in the SAM 350P, SAM 360P, and SAM 450P defibrillators.

Rhythms	Test Sample Size	Performance Goal	Observed Performance	90% One-sided Lower Confidence Limit
Shockable				
Coarse VF	350	>90% sensitivity	99.7% sensitivity	98.90%
Rapid VT	53	>75% sensitivity	90.6% sensitivity	83.20%
Non-shockable				
NSR	165	>99% specificity	100% specificity	98.60%
AF, SB, SVT, heart block, idioventricular, PVCs	153	>95% specificity	98% specificity	95.70%
Asystole	117	>95% specificity	100% specificity	98.10%
Intermediate				
Fine VF	46	Report only	47.8% sensitivity	37.50%
Other VT	29	Report only	65.5% specificity	51.90%

Table 2: Performance of ECG Arrhythmia Analysis Algorithm

Biocompatibility Testing
The only patient contacting portions of the SAM 350P, SAM 360P, and SAM 450P systems are the electrodes contained in the Pad-Paks. The electrodes were tested in accordance with ISO 10993 for cytotoxicity, irritation, and sensitization testing. The electrodes passed all testing to adequately demonstrate biocompatibility.

Software Documentation and Validation
The SAM 350P, SAM 360P, SAM 450P and Saver EVO® software was documented and validated according to the FDA guidance document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" for a major level of concern device. Software documentation included level of concern, software description, device hazard analysis, software requirements specification, software architecture diagrams, software design specifications, software module design specifications, requirements traceability matrix, software development environment description, verification and validation documentation, revision level history, unresolved anomaly report, discussion of tools to detect run-time errors, and cybersecurity documentation.

Software verification and validation testing conducted on each model included: unit, integration, and system-level protocols and test reports with pre-defined pass/fail criteria, algorithm testing, source code inspections for all software modules and algorithms, integrated system testing, Saver EVO® compatibility testing, and software summary validation testing. This testing demonstrated that the SAM 350P, SAM 360P, SAM 450P and Saver EVO® software perform as intended.

Shelf Life Testing
Shelf life testing was conducted to demonstrate the claimed 4.25-year shelf life for the three (3) available Pad-Pak models (adult, pediatric, and TSO). This testing also took into consideration the impact of battery self-discharge, operation of the device status LED, and periodic self-testing on the device shelf life. In addition, testing was conducted verifying

that the Pad-Paks perform according to the requirements of AAMI EC12 and DF80 following aging in excess of the labeled shelf life.

Pediatric Waveform Testing
Testing was conducted to demonstrate the comparability of the SAM 350P, SAM 360P, and SAM 450P pediatric waveform (enabled when a Pediatric Pad-Pak is inserted) with the pediatric waveform of the Physio-Control, Inc. LifePak AED. This testing included evaluation of oscilloscope tracings of both devices and comparisons of peak voltage, peak current, tilt, and duration for each phase of the biphasic waveform of each device. These data demonstrate the comparability of the pediatric waveforms of the two (2) devices.

The safety and effectiveness of the Physio Control waveform was described in a 2004 publication by Berg et al entitled "Attenuated Adult Biphasic Shocks Compared with Weight-Based Monophasic Shocks in a Swine Model of Prolonged Pediatric Ventricular Fibrillation[1]." The publication demonstrated that the Physio Control biphasic waveform, which delivers escalating energies of 50, 75 and 86 Joules was comparable to weight-based monophasic shocks in terms of shock efficacy and safety and supports the concept of using an attenuated adult biphasic dosage in children. The authors published a second study in 2005 entitled "Better Outcome After Pediatric Defibrillation Dosage than Adult Dosage in a Swine Model of Pediatric Ventricular Fibrillation[2]." This study demonstrated superior outcomes of pediatric shocks compared with adult shocks and further supported the use of attenuating electrodes with adult biphasic AEDs to defibrillate children. This published data on the clinical effectiveness of the LifePak AED's pediatric waveform are therefore expected to also be representative of the clinical effectiveness of the pediatric waveform of the SAM 350P, SAM 360P, and SAM 450P defibrillators.

B.   Animal Studies
The Waveform Effectiveness Study, Pulse Width Efficacy Studies, and Bra Placement Testing detailed below apply to the SAM 350P, SAM 360P, and SAM 450P devices as they all have identical waveforms characteristics. As described below, additional animal testing was conducted on the SAM 360P and SAM 450P devices to confirm they perform as intended. A summary of the six (6) animal studies supporting device safety and effectiveness is provided below.

Waveform Effectiveness Study
HeartSine conducted this study to demonstrate the safety and effectiveness of the current energy protocol (150J-150J-200J) compared to the energy protocol used when the SCOPE® waveform was originally cleared by FDA in 2004 (100J-150J-200J).

The objective of this GLP animal study was to establish whether energy protocol A (100-150-200 Joules) was comparable to energy protocol B (150-150-200 Joules) in terms of first shock success in pigs under anesthesia. It also confirmed the safety and effectiveness of protocol B, which is used in the SAM 350P, SAM 360P, and SAM 450P. To determine whether the current energy protocol is non-inferior to the predicate protocol, the difference between proportions of successful outcomes was measured, where a successful outcome is defined as a first shock success.

A total of 15 pigs aged approximately 8-16 weeks were designated for the study and underwent surgery. Animals were prepared for surgery and then ventricular fibrillation was induced. Defibrillation was then attempted using the HeartSine Samaritan® AED at the two (2) different energy protocols. If successful defibrillation occurred, then additional tests (up to 40 per animal) were conducted (following a rest period).

This study demonstrated that there was sufficient evidence to reject the original null hypothesis that the current protocol B (150-150-200J) was inferior to the predicate protocol A (100-150-200J) in terms of proportion of first shock success. The study had a non-inferiority margin of 0.153 with a statistical significance of 95% and a power of 94.1%. The first shock success rate was 99% using the SAM 350P energy protocol of 150-150-200 Joules and 93.7% for the predicate protocol.

Pulse Width Efficacy Studies
The SCOPE® waveform is designed to automatically optimize the waveform pulse envelope (amplitude, slope, and duration) for a wide range of patient impedances from 20 ohms to 230 ohms. It is an optimized, impedance-compensated, biphasic, truncated exponential waveform that incorporates an escalating energy protocol of 150 J, 150 J, and 200 J. The duration of each phase is automatically adjusted to compensate for varying patient impedances.

Although the SAM 350P, SAM 360P, and SAM 450P labeling provides instructions regarding electrode placement to help minimize impedance, patient impedance will vary due to differences in skin and body type, degree of hair, moisture (such as sweat), and electrode placement. The SCOPE® waveform is designed to increase the pulse duration to ensure that the nominal amount of energy (i.e., either 150 J or 200 J) is actually delivered to the patient. The SCOPE® waveform is thus designed to ensure that effective therapy is available and delivered in the event of a cardiac arrest and to compensate for higher impedance due to the factors described above.

Two (2) animal studies were conducted to evaluate the safety and effectiveness of the SCOPE® waveform and to determine whether the SCOPE® waveform induces refibrillation or increases defibrillation thresholds (DFTs) at pulse durations greater than 20 ms.

The first study included six (6) porcine subjects and a total of 208 shocks were delivered. Of these, there were 153 "first" shocks delivered which successfully defibrillated the subject, of which 85 shocks had pulse durations less 20 ms and 68 shocks had pulse durations greater than or equal to 20ms. There were no incidences of refibrillation in the five (5) minutes immediately following any of the 153 successful first shocks, which includes pulse durations covering the entire range of pulse durations greater than 20 ms. The likelihood of refibrillation after a successful first shock in this study was 0% (n = 68, 95% CI: 0%; 5.3%).

In the second study, there were five (5) porcine subjects enrolled, and a total of 96 "first" shocks were recorded. Of these 96 shocks, 91 used pulse durations equal to or greater than

20ms, of which 70 were successful. As was the case in the first study, there were no incidences of refibrillation in the five (5) minutes immediately following a successful first shock. The likelihood of refibrillation after a successful first shock in the second study was 0%, (n=70, 95% CI: 0%, 5.2%).

The experimental setup of the two (2) studies, while most specifically designed to address the occurrence of refibrillation with longer pulse durations, also demonstrated that the SCOPE® waveform at longer pulse durations does not increase the defibrillation threshold (DFT). The two (2) studies collectively demonstrate that pulse durations longer than 20 ms with the SCOPE® waveform do not induce refibrillation or increase DFTs.

Bra Placement Study
An animal study was conducted to assess the impact of administering repeated shocks while the subject was wearing an underwire bra. In this study, the bra's underwire was intentionally exposed by removal of bra fabric and the electrode pad was placed so that the electrode gel on the electrode's lower surface was in direct contact with the bra's metal wire, in an attempt to maximize the potential of arcing or other adverse events.

A total of 126 shocks were administered at the maximum energy of 200 J with a recovery period of three (3), minutes between shocks. No arcing was observed and there was no redirection of current away from the subject. There was 100% first shock success with no observations of refibrillation. There were no incidences of scorching or burning to the animal or fabric or any other skin damage to the animal observed post-resuscitation, even though the metal underwire was intentionally exposed in all cases.

SAM 360P Animal Study
The purpose of the SAM 360P GLP animal study was to demonstrate the performance of the SAM 360P audio feedback. CPR motion/interference was intentionally created during the ECG rhythm analysis period to determine whether it was detected by the SAM 360P Motion Detection Algorithm. Each episode was recorded via real-time video recording and the corresponding audio and visual feedback was recorded. The rate and force of CPR were controlled for a pre-specified set of ranges for each analysis period. Visual feedback accuracy was assessed as a secondary variable.

The study used twelve (12) porcine subjects. The study demonstrated a sensitivity for the "motion detected" audio feedback of 97.9% (95% CI: 95.5%, 99.2%) according to video recording. In the Per Protocol (PP) dataset, there were only six (6) false negatives where the device did not emit a motion detection voice prompt in the actual presence of CPR compressions. The intent to treat (ITT) dataset provided similar results, with a sensitivity of 97.6% (95% CI: 95.1%, 99.0%).

Specificity was estimated to be 100% (95% CI: 92.6%, 100.0%) according to video recording in both the PP and ITT datasets, as there were no false positives. In addition, the "hands off" visual indicator was present in 100% of collected observations in the PP and ITT sets and the shock decision was appropriate in 96.4% of episodes.

SAM 450P Animal Study
The purpose of the SAM 450P GLP animal study was to demonstrate the performance of the SAM 450P CPR Rate Feedback algorithm. The study compared the CPR compression rate as measured by the ICG waveform and the actual CPR compression rate as demonstrated in video recordings. The algorithm provides audio-visual feedback on the adequacy of CPR compression rate by assessing the frequency of the ICG waveform. The corresponding audio-visual feedback was recorded over a range of CPR rates from 40 to 180 compressions per minute, each assessed for a 2-minute period.

The study used twelve (12) porcine subjects. The study demonstrated that the proportion of correct audio and visual feedback of the SAM 450P CPR Rate Feedback algorithm versus the actual CPR compression rate as demonstrated in video recordings was 95.2%. Since this study was leveraged from previous 510(k) data, it also included a comparison of measured accuracy against the Philips MRx Q-CPR device. The Philips MRx Q-CPR demonstrated a rate of 87.5% correct feedback when confirmed against video recording. The study adequately demonstrated the sensitivity of the SAM 450P CPR Rate Feedback algorithm over the range of 40 to 180 compressions per minute.

X. SUMMARY OF CLINICAL STUDIES

The final order, Effective Date of Requirement for Premarket Approval for Automated External Defibrillator Systems; Republication, published on January 29, 2015 and republished on February 3, 2015, states that clinical study information can be leveraged for AEDs from both published studies and clinical data previously submitted to FDA under the 510(k) process. The clinical data included in this submission derives mainly from a clinical study by Walsh et. al.[3] published in 2004 and the analysis of 805 postmarket (after 510(k) clearance) events received by HeartSine between January 2012 and December 2015.

A. Published Clinical Data
The study by Walsh et al. included the SCOPE® defibrillation waveform used in the SAM 350P, SAM 360P, and SAM 450P and was published in the American Journal of Cardiology in 2004.[3]

This study compared two (2) impedance compensated biphasic waveforms:

- HeartSine's Samaritan (100-150-200 J energy protocol at the time based on the AHA guidelines then in effect) using the same SCOPE® defibrillation waveform present in the SAM 350P, SAM 360P, and SAM 450P, and
- Philips Medical Systems Heartstream XL (150-150-150 J protocol) (HSXL)

The primary endpoint was discontinuation of ventricular arrhythmia. Success was defined as the discontinuation of ventricular arrhythmia for greater than 5 seconds. Patients were excluded from participation if they weighed less than 36 kg, had cardiac arrest due to trauma, or current "do not resuscitate" instructions.

As reported in the publication, 78 consecutive patients were studied: 40 HSXL (19 men) and 38 SAM (28 men). Mean age was 69 ± 11 years for HSXL patients and 65 ± 14 years for SAM patients (p= NS). Cardiac arrest out-of-hospital occurred in 13 of 40 HSXL patients (33%) and in 26 of 38 SAM patients (68%) (p=0.003). Mean response time from arrest to physician arrival was 1.4 ± 1.3 minutes for in-hospital patients and 9 ± 6 minutes for out-of-hospital patients.

The rhythm when first recorded was VF in 20 of 40 HSXL patients (50%) and 16 of 38 SAM patients (42%), VT in 3 of 40 HSXL patients (8%) and 1 of 38 SAM patients (3%), and electromechanical dissociation or asystole in 16 of 40 HSXL patients (40%) and 20 of 38 SAM patients (53%) (all rhythms, p= NS). One (1) patient in each group had a palpable pulse when first attended by the physician. Drugs given during cardiac arrest were similar in the two (2) groups. A total of 15 of 40 HSXL patients (38%) and 12 of 38 SAM patients (32%) received amiodarone, whereas 29 of 40 HSXL patients (73%) and 34 of 38 SAM patients (89%) received epinephrine (p= NS).

VF episodes were 107 HSXL and 117 SAM. The energy selection protocol was adhered to in 95 of 107 HSXL (89%) and 79 of 117 SAM (68%) defibrillation episodes. Protocol violations for energy selection occurred when the attending physician misinterpreted a successful shock followed by early recurrence of arrhythmia (greater than 5 seconds) as unsuccessful. This resulted in a progression to the next stage of the energy selection protocol (i.e., a higher energy was therefore selected inappropriately). Less incorrect energy selection was seen with the HSXL due to the non-escalating nature of the protocol (150-150-150 J; the physician could only select 200 J at the fourth shock or beyond).

Excluding VF episodes when energy selection was not as per protocol, success after one (1) shock was seen for 64% of HSXL and 58% of SAM episodes (p = NS). Success occurred by shock two (2) in 78% of HSXL and 82% of SAM episodes and by shock three (3) in 83% of HSXL and 92% of SAM episodes.

An analysis of the difference of proportions in success by a certain shock was performed by the authors (see **Table 3** below). The defibrillation success rate is acceptable because it is consistent with defibrillation success rates (greater than 85%) reported in the literature for randomized controlled clinical trials using other devices and waveforms[4]. These data were not powered to demonstrate differences in return of spontaneous circulation or survival.

This study was conducted on the HeartSine Samaritan AED (cleared under 510(k) K023854) with the identical SCOPE® waveform as used in the SAM 350P, SAM 360P, and SAM 450P.

	HeartSine Samaritan (100-150-200 J)		Philips HeartstreamXL (150-150-150J)				
Success by	Frequency	Proportion	Frequency	Proportion	Mean Difference	SD	Probability that Samaritan Better than Heartstream
First Shock	46	0.582	61	0.642	-0.0598	0.0742	0.210
Second Shock	65	0.823	74	0.779	0.0438	0.0605	0.766
Third Shock	73	0.924	79	0.832	0.0925	0.0486	0.971*
Total Episodes	79		95				
*p = 0.029							

Table 3: Summary of Successful Defibrillation Episodes with Both Devices

B. Postmarket Clinical Data

HeartSine complemented the published clinical study discussed above with postmarket clinical data collected by HeartSine after 510(k) clearance. Data were received and analyzed from 28 countries worldwide including USA, Singapore, Germany, Netherlands, Canada, Australia, United Kingdom, and Sweden which comprised approximately 85% of the total number of events.

Postmarket clinical reports for 805 events were received between January 2012 and December 2015. Of these, 550 (68.3%) events involved the SAM 300P device, 122 (15.2%) events involved the SAM 350P device, three (3) (0.4%) events involved the SAM 360P device, no (0%) events involved the SAM 450P device, and 130 (16.1%) events involved the SAM 500P device. The SAM 500P is not marketed in the United States but uses the identical defibrillation waveform, the identical arrhythmia detection algorithm, and identical Pad-Paks and is discussed here because of its similarity to the devices being approved. The SAM 300P is the precursor to the SAM 350P and also uses identical defibrillation waveform, arrhythmia detection algorithm, and Pad-Paks.

Success was defined as discontinuation of ventricular fibrillation or ventricular tachycardia within 5 seconds of shock delivery. A total of 334 patients in the "All Cases" dataset initially presented with a shockable rhythm, of which 327 (97.9%) patients were in ventricular fibrillation and seven (7) (2.1%) were in ventricular tachycardia. Of these 334 patients, a shock was delivered in 322 patients. Of these 322 events, 220 (68.3%) events involved the SAM 300P device, 37 (11.5%) events involved the SAM 350P device, 2 (0.6%) events involved the SAM 360P device, no (0%) events involved the SAM 450P device, and 63 (19.6%) events involved the SAM 500P device. Of the 322 first shocks delivered, 293 (91.0%) were successful, with 95% CI estimated to be (87.3%, 93.9%). This is consistent with defibrillation success rates (greater than 85%) reported in the literature for randomized controlled clinical trials using other devices and waveforms[4].

Of the "Shock Delivered" dataset, a total of 187 (58.1%) patients were reported to have survived to hospital admission, 61 (18.9%) patients did not survive to hospital admission,

and survival information was unavailable for 74 (23.0%) patients. **Table 4** below summarizes the relationship between event location and user training, response time, and percentage survival to hospital admission.

Location of Events	N	Percentage of total number of shock delivered events	Percentage of trained users	Mean (SD) Response Time (minutes)	Percentage Survival to Hospital Admission
Home	44	13.7	88.6	4.87 (2.56)	34.1
Medical Facility	28	8.7	89.3	4.07 (4.85)	67.9
Office	19	5.9	68.4	3.86 (2.97)	68.4
Public	110	34.2	81.8	3.82 (3.95)	69.1
School/University	4	1.2	100.0	4.00	75.0
Sports Facility	62	18.9	79.0	4.30 (5.41)	80.6
Unknown	57	17.7	30.3	5.59 (2.00)	11.8
Total	322	100.0	73.0	4.21 (4.11)	58.1

Table 4: Location of Events, Trained Users, Response Time and Survival

First shock success was found to be significantly associated with survival to hospital admission, with an Odds Ratio (OR) = 3.13, 95% CI = (1.30, 7.51), and $p = 0.0107$. The analysis was repeated when adjusting for age and gender, with consistent results (OR = 3.29, $p = 0.0095$). Age was found to be significantly associated with survival to admission in this analysis (OR = 0.98 for a 1-year increase in age, $p = 0.0324$).

Shock success and survival were similar among the HeartSine public access defibrillators studied in this analysis, which was anticipated since all the devices use the same defibrillation waveform, the same arrhythmia detection algorithm, and the same Pad-Pak electrode-battery packs. **Table 5** below summarizes shock success and survival by defibrillator model.

Device Type	Number of Patients with a Shockable Rhythm	Percentage First Shock Success (%)	Percentage Second Shock Success (%)	Percentage Third Shock Success (%)	Percentage Survival to Hospital Admission ("All Cases" dataset) (%)	Percentage Survival to Hospital Admission of those who received a shock (%)
SAM 300P	225	91.3	89.2	79.4	26.2	55.0
SAM 350P	41	89.2	76.5	90.9	22.1	62.2
SAM 360P	2	100.0	100.0	100.0	33.3	50.0
SAM 450P	0	N/A	N/A	N/A	N/A	N/A
SAM 500P	66	92.1	82.8	76.9	37.7	66.7
Total	334	91.3	86.4	81.4	27.5	58.1

Table 5: Shock Success and Survival to Hospital Admission

The primary adverse event was failure to deliver a shock when presented with a shockable rhythm. A total of 12 of the 334 patients initially presented with a shockable rhythm but no shock was delivered. Based on a review of the ECG records, only 1 of the 12 cases determined that algorithm performance was inappropriate. In addition, 12 events were associated with audio prompts indicating the user repeatedly removed the electrodes throughout the event.

In summary, the postmarket data collected after 510(k) clearance provides information on the real-world performance of the arrhythmia detection algorithm, waveform effectiveness, and the overall usability of HeartSine's public access defibrillators. First shock success and survival to admission were comparable in this study to rates reported in published literature[4]. Finally, algorithm performance for combined VF/VT had a sensitivity of 98.8% in this analysis.

C. **Human Factors and Usability Studies**
Summative usability studies were conducted on all three (3) defibrillator models. A summary of each of these studies is provided below.

SAM 350P Usability Study
A usability study of the SAM 350P was leveraged from the previously cleared 510(k) for this device. The study was conducted with 95 participants (48 males and 47 females) to assess critical task completion during a simulated rescue attempt with gender-dressed manikins. There were at least 15 participants in each user age band (15-21, 22-64 and 65+).

The median time to simulated first shock was 77 seconds for the per protocol (PP) population and 76 seconds for the all-participant population. There was no significant statistical difference between the all-participant and PP populations. Both groups were statistically significantly less than the reference time to first shock of 122 seconds (non-inferiority margin of 10 seconds). The comparison time of 122 seconds was based on data published by Andre et. al. which compared the time to shock among four (4) commercially available models of AEDs when used by lay users.[5]

Safety was assessed as the proportion of times contact was made with the patient during the shock delivery. There were no observed occurrences of contact being made during the shock delivery and the observed likelihood was 0% for both the all-participant and PP populations.

SAM 360P Usability Study
The SAM 360P usability study included 109 participants (52 males and 57 females). Age groups of the study participants were 15% aged 15-21, 64% aged 22-64, and 21% aged 65 years or older. Participants had education levels ranging from some high school through post-graduate education.

The usability study observed a median time to first shock of 70.0 seconds (95% CI = 69.0, 74.0) in the ITT set, demonstrating both non-inferiority and superiority compared to the reference time of 122 seconds. The results are comparable to the results for the SAM 350P device. There were no instances of any participant causing significant interference during the analysis period, eliciting the motion detection prompt to be delivered. In the ITT and PP sets, the median time to pad placement was 50 seconds and the median time to switch-on was three (3) seconds. One (1) participant made contact with the manikin during simulated shock delivery.

The post-test questionnaire did not reveal any device-use issues or negative responses requiring additional summative testing. All participants stated that they felt they could use the device in an emergency.

SAM 450P Usability Studies
Two (2) usability studies were conducted for the SAM 450P. The first study included 156 participants (72 males and 84 females). Age groups of the study participants were 18% aged 15-21, 65% aged 22-64, and 17% aged 65 years or older. Participants had education levels ranging from some high school through post-graduate education.

The usability study observed a median time to first shock of 67 seconds, with the upper limit of the 95% CI being 68 seconds. These results demonstrated superiority in time to first shock when compared to the reference time of 122 seconds. Safety was assessed as the proportion of times contact was made with the patient during the shock delivery. There were no observed occurrences of contact being made during the shock delivery and the observed likelihood was 0% (95%CI: 0%, 2.3%).

It was observed in this study that 87.2% achieved the secondary endpoint of appropriate CPR compression speed within 45 seconds of beginning CPR. Audio and visual CPR compression rate feedback showed a comparative rate of 92.5% when verified by video recording compression rate values. Video recording also verified that 87% of the compression rate values were in the 100 – 120 CPM range, reflecting the adherence to the optimal rate of CPR compressions as prescribed in current AHA guidelines.

The observations and statistical analysis performed from the findings of this study demonstrate that the SAM 450P can be used appropriately by a representative sample of the intended user population. The addition of CPR Rate feedback capability in the SAM 450P optimizes CPR rate in untrained users while maintaining a very high CPR fraction, thereby helping to maintain CPR effectiveness.

A second (supplemental) usability study was conducted to determine whether CPR compression depth or other CPR quality parameters such as chest recoil, hand position, or duty cycle (CPR fraction) were compromised by the SAM 450P's CPR rate feedback feature. The study included a SAM 450P and a control device in which the CPR audio and visual rate feedback had been disabled. Subjects were randomized to use either the test or control device. There were 140 participants in the ITT population, including 31 participants aged 15-21 years, 84 participants aged 22-64 years, and 25 participants aged 65

years or older. Sixty-seven (67) participants were male and 73 participants were female. The demographics of the 133-participant PP set were similar.

The supplemental study demonstrated that CPR rate feedback in the SAM 450P does not detrimentally affect the depth of CPR compressions when compared to a non-CPR feedback device. In addition, there was no significant difference in chest recoil or hand placement observed between the test and control device populations. The study also confirmed the results of the first SAM 450P usability study in terms of the benefit of the SAM 450P's CPR rate feedback capability in achieving good CPR compression speed and CPR fraction. The measured CPR fractions in both studies were above the 80% recommended by the AHA Guidelines Consensus Statement.

Pediatric Extrapolation
In this premarket application, existing clinical data was leveraged to support the reasonable assurance of safety and effectiveness of the proposed device in pediatric patients.

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

As of December 31, 2015, a total of 48 complaints have been received on the SAM 350P since its launch in October 2012. One (1) complaint has been received for the SAM 360P since its launch in August 2014 and no complaints have been reported for the SAM 450P since its launch in June 2015. Reportable complaints have been submitted to FDA as required by the Medical Device Reporting regulation; however, no adverse events have been reported for any of the three (3) devices.

E. Financial Disclosure
The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The investigator-initiated, peer-reviewed clinical study was published in the American Journal of Cardiology in 2004.[3] Multiple physician and EMS staff participated in the study and treated patients both in-hospital and out-of-hospital. The study device was available to all hospital wards, the cardiac arrest team, and the out-of-hospital physician-led cardiac ambulance service. This information was supplemented by postmarket clinical experience data from all 805 recorded events between January 2012 and December 2015 (refer to Section X.B above). The postmarket events represent 725 unique users in 28 countries. It is for these reasons that we believe that none of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

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

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

XII. CONCLUSIONS DRAWN FROM THE PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions
The effectiveness analysis was based on bench testing of the arrhythmia analysis algorithm, animal testing of the shock waveform, and postmarket clinical data collected after 510(k) clearance. The bench testing demonstrates that the arrhythmia analysis algorithm meets AHA recommendations for sensitivity and specificity for detecting shockable and non-shockable arrhythmias. The animal testing collectively provides experience with over 770 shocks and demonstrates first shock success of over 90%. The published clinical data[3] demonstrates greater than 90% success rate of the SCOPE® waveform and escalating three (3) shock protocol in terminating life-threatening arrhythmias. Postmarket clinical data from 805 events collected from 2012 to 2015 also demonstrates first shock success rate of greater than 90%. The effectiveness of the HeartSine SCOPE® waveform and escalating shock sequence meets and exceeds the performance described more generally for external defibrillation[4].

B. Safety Conclusions
The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in published literature[1,2]. The results from the preclinical laboratory testing performed on the HeartSine SAM 350P, SAM 360P, and SAM 450P devices demonstrated appropriate electrical safety, electromagnetic compatibility, biocompatibility, mechanical integrity, and overall performance. The animal studies demonstrated the safety of the devices' energy protocol, that pulse durations greater than 20 ms do not induce refibrillation or increase defibrillation thresholds. The animal studies also demonstrated that placement of the electrodes in proximity with a bra does not pose a safety risk, and that the SAM 360P motion/interference detection algorithm and SAM 450P CPR Rate Feedback feature do not delay or prolong the time needed to analyze the ECG rhythm and deliver a defibrillation shock. The clinical data, including a published clinical study on the SCOPE® waveform[3] and usability studies, further demonstrate the safety of the device.

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

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

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

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

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

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

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

XIII. **CDRH DECISION**

CDRH issued an approval order on January 12, 2017. FDA has developed unique conditions of approval to pursue real world information and in response to panel comments from the 515i Panel discussed in Section XI above. The final conditions of approval cited in the approval order are described below.

1. The number of devices returned to the applicant for cause from domestic sources, with a breakdown into:
   a. Those returned for normal end-of-life.
   b. Those returned with any alleged failures or malfunctions, including a summary of root causes and the frequency of occurrence for each identified root cause.
2. The number of replacement defibrillation pads and replacement batteries issued to customers domestically for all causes.
3. A summary of information available to you related to individual domestic uses of your device that may include, but is not limited to:
   a. Defibrillation success and the number of shocks required for success.

      b. Identification of any error codes or malfunctions during use and their related MDR number.
4. A listing of any safety alerts, technical service bulletins, user communications, or recalls for devices under this PMA.

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

XIV. <u>APPROVAL SPECIFICATIONS</u>

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

XV. <u>REFERENCES</u>

1. Berg, Robert A. et. al., Attenuated Adult Biphasic Shocks Compared with Weight-Based Monophasic Shocks in a Swine Model of Prolonged Pediatric Ventricular Fibrillation, Resuscitation 61 (2004), p. 189-197.

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3. Simon J. Walsh, Anthony J.J. McClelland, Colum G. Owens, James Allen, John McC.Anderson, Colin Turner, A.A. Jennifer Adgey, Efficacy of Distinct Energy Delivery Protocols Comparing Two Biphasic Defibrillators for Cardiac Arrest, Am J Cardiol 2004;94:378–380.

4. ILCoR, International Liaison Committee on Resuscitation. "Part 3: Defibrillation." *Resuscitation* (2005): 67, 203-211.

5. Andre, A.D., Jorgenson, D.B., Froman, J.A., Snyder, D.E. and Poole, J.E., 2004. Automated external defibrillator use by untrained bystanders: Can the public-use model work? Prehospital Emergency Care, 8(3), pp.284-291.