SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Automated External Defibrillator

Device Trade Name: Powerheart® AED G3, Powerheart® AED G3 Plus, and Powerheart® AED G5

Device Product code: MKJ

Applicant's Name and Address: Cardiac Science Corporation
N7 W22025 Johnson Drive, Suite 100
Waukesha, WI 53186

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P160033

Date of FDA Notice of Approval: December 7, 2018

Cardiac Science automated external defibrillators (AEDs) have been on the market in the US since 2003. These devices are currently marketed in the US and globally by Cardiac Science under the brand name Powerheart®. The first Cardiac Science AED branded 'Powerheart' received 510(k) Clearance in 2002 (K011901). That was followed by the 510(k) Clearance for the Powerheart® G3 (K031987) and G3 Plus (K040438). The most recent AED, Powerheart® G5, was 510(k) Cleared in 2014 (K122758) which was immediately followed by 510(k) Clearance for an optional G5 cardiopulmonary resuscitation (CPR) compression feedback accessory with four (4) district corrective CPR prompts (K143714).

P160033 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. Products affected by this Final Order are the Powerheart® AED G3 (Model 9300A and 9300E) (including the Intellisense® Lithium Battery (Model 9146), Intellisense™ Defibrillation Pad – Adult (Model 9131), and Intellisense™ Defibrillation Pad – Pediatric (Model 9730)); Powerheart® AED G3 Plus (Model 9390A and 9390E) (including the Intellisense® Lithium Battery (Model 9146), Intellisense™ Defibrillation Pad – Adult (Model 9131), and Intellisense™ Defibrillation Pad – Pediatric (Model 9730)); and the Powerheart® AED G5 (Models G5A-80A, G5A-80C, G5S-80A, and G5S-80C) (including the Intellisense® Lithium Battery (Model XBTAED001A), Intellisense™ Defibrillation Pad – Adult (Model XELAED001A), Intellisense™ Defibrillation Pad – Pediatric (Model XELAED003A), and Intellisense™ Defibrillation Pad – ICPR Adult

(Model XELAED002B)). A combination of relevant literature, clinical data, animal data, and in-vitro bench testing has been reviewed to demonstrate a reasonable assurance of safety and effectiveness for the Powerheart® AED G3, Powerheart® AED G3 Plus, and Powerheart® AED G5.

II. INDICATIONS FOR USE

The Powerheart® AED G3 is indicated for emergency treatment of victims exhibiting symptoms of sudden cardiac arrest who are:

- unresponsive,
- not breathing normally, and
- without pulse.

When the patient is a child or infant up to 8 years of age, or up to 55 lbs. (25kg), the device should be used with the Intellisense™ Defibrillation Pad – Pediatric. The therapy should not be delayed to determine the patient's exact age or weight.

The Powerheart® AED G3 is intended to be used by personnel who have been trained in its operation.

The Powerheart® AED G3 Plus is indicated for emergency treatment of victims exhibiting symptoms of sudden cardiac arrest who are:

- unresponsive,
- not breathing normally, and
- without pulse.

When the patient is a child or infant up to 8 years of age, or up to 55 lbs. (25kg), the device should be used with the Intellisense™ Defibrillation Pad – Pediatric. The therapy should not be delayed to determine the patient's exact age or weight.

The Powerheart® AED G3 Plus is intended to be used by personnel who have been trained in its operation.

The Powerheart® AED G5 is indicated for emergency treatment of victims exhibiting symptoms of sudden cardiac arrest who are:

- unresponsive,
- not breathing normally, and
- without pulse.

When a patient is a child up to 8 years of age, or up to 25kg (55 lbs.), the AED should be used with the Intellisense™ Defibrillation Pad – Pediatric. The therapy should not be delayed to determine the patient's exact age or weight.

The G5 Automated External Defibrillator (AED) is intended to be used by persons who have been trained in its operation.

When used with the optional Intellisense™ Defibrillation Pad – ICPR, the device offers CPR performance feedback to aid a trained rescuer by providing compression rate and depth performance feedback through audio prompting. The Intellisense™ Defibrillation Pad – ICPR is indicated-for use on cardiac arrest patients 8 years of age or older, or who weigh more than 25 kg (55 lbs.).

III. CONTRAINDICATIONS

Cardiac Science AEDs should not be used on patients that are responsive or breathing normally.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions for the Powerheart® AED G3, Powerheart® AED G3 Plus, and Powerheart® AED G5 can be found in the labeling.

V. DEVICE DESCRIPTION

Cardiac Science's Powerheart® AED G3, G3 Plus, and G5 are public access AEDs. They are portable, battery operated, self-testing units used to diagnose and treat life-threatening ventricular arrhythmias in patients who are unresponsive and not breathing normally. There are three (3) models and related accessories.

- **The Powerheart® G3** is an AED designed for simplicity and quick response. The G3 features simple voice and text rescue prompting and Rescue Ready® technology that provides daily, weekly, and monthly assurances that the AED, electrode pads, and battery will be ready when called upon.

- **The Powerheart® G3 Plus** AED builds upon the features found in the G3 AED. This model introduced fully automatic functionality, pre-connected rescue electrode pads, use-paced rescue prompting, and CPR coaching to the public access users.

- **The Powerheart® G5** combines features of the G3 Plus with optional dual language rescue prompts / CPR functionality, large back-lit display, IP55 ingress protection, and fast shock times (post CPR) of under 10 seconds. The G5 is available with an optional CPR device that provides four (4) distinct corrective CPR prompts to aid a trained rescuer provide compression rate and depth performance feedback through audio and text prompting.

A patient's electrocardiogram (ECG) is monitored and a defibrillation shock is delivered if necessary. Voice and text prompts provide simple directions to guide the user during a rescue.

AEDs are shipped with defibrillation electrode pads already installed. The Rescue Ready® indicator assures the user that the AED is ready for use.

All models employ an impedance compensating, biphasic waveform.

All models also automatically perform daily, weekly, and monthly self-tests. Self-test results are communicated by audible alert and via the visual Rescue Ready® indicator. See Figure 1-2 below.

Figure 1: Powerheart® G5

Figure 2: Powerheart® G3 and G3 Plus

The various models of Powerheart® AEDs are summarized in **Table 1** below.

Table 1: The Powerheart® G3 and G5 AED Products

Model Number	Brand Name	Description
9300A	Powerheart® G3	Automatic
9300E	Powerheart® G3	Semi-Automatic
9390A	Powerheart® G3 Plus	Automatic
9390E	Powerheart® G3 Plus	Semi-Automatic
G5A-80A	Powerheart® G5	Automatic with adult pads
G5A-80C	Powerheart® G5	Automatic with ICPR pads
G5S-80A	Powerheart® G5	Semi-Automatic with adult pads
G5S-80C	Powerheart® G5	Semi-Automatic with ICPR pads

Batteries

The Powerheart® AED G3, G3 Plus, and G5 are powered by a user-replaceable, non-rechargeable battery with a 4-year shelf life and 1-year standby life. Powerheart® AED G3 and Powerheart® AED G3 Plus use the Intellisense® Lithium Battery (Model 9146) and the Powerheart® AED G5 uses the Intellisense® Lithium Battery (Model

XBTAED001A). The AED's automatic self-testing detects when the battery is nearing end of life and signals an alert while the unit still retains enough energy to perform a rescue. All batteries are labeled with an expiration date.

Defibrillation Electrode Pads

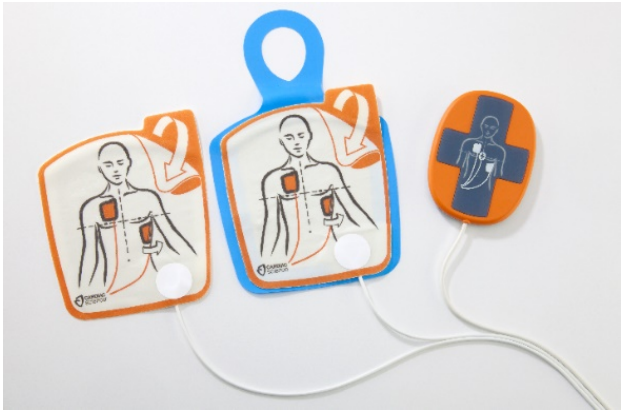

Figure 3: Adult Defibrillation Electrode Pads and ICPR sensor (optional)

Both adult and pediatric electrode pads are available for use with the Powerheart® AED G3, G3 Plus, and G5. The defibrillation electrode pads act as a conductive interface between the AED and the patient's skin. The adult defibrillation electrode pads are shown in **Figure 3** and the pediatric defibrillation electrode pads are shown in **Figure 4** below. Powerheart® AED G3 and G3 Plus use the same Intellisense™ Defibrillation Pad – Adult (Model 9131) and Intellisense™ Defibrillation Pad – Pediatric (Model 9730); Powerheart® AED G5 use Intellisense™ Defibrillation Pad – Adult (Model XELAED001A), Intellisense™ Defibrillation Pad – Pediatric (Model XELAED003A), and Intellisense™ Defibrillation Pad – ICPR Adult (Model XELAED002B). The optional Intellisense™ cardiopulmonary resuscitation (ICPR) feedback device (Intellisense™ Defibrillation Pad – ICPR Adult (Model XELAED002B)) for the Powerheart® G5 AED provides the rescuer with compression performance feedback on rate and depth performance.

Figure 4: Pediatric Defibrillation Pads

VI. ALTERNATIVE PRACTICES AND PROCEDURES

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

VII. MARKETING HISTORY

The Cardiac Science Powerheart® AED G3, G3 Plus, and G5 have been commercially available in the US and globally since 2003. The current AED G3, G3 Plus, and G5 models have evolved over time based on a series of 510(k) submissions. The STAR® Biphasic waveform and RhythmX ECG Analysis were first combined in the Powerheart® AED Cleared under K011901 in 2002.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device and AEDs in general, listed in decreasing order of seriousness:

- Failure to identify shockable arrhythmia;
- Failure to deliver a defibrillation shock in the presence of VF or pulseless VT, which may result in death or permanent injury;
- Inappropriate energy which could cause failed defibrillation or post-shock dysfunction;
- Myocardial damage;
- Fire hazard in the presence of high oxygen concentration or flammable anesthetic agents;
- Electromagnetic interference (EMI) from the defibrillator impacting other devices especially during charge and energy transfers;
- Incorrectly shocking a pulse sustaining rhythm and inducing VF or cardiac arrest;
- Bystander shock from patient contact during defibrillation shock;
- Interaction with pacemakers;
- Skin burns around the electrode placement area;
- Allergic dermatitis due to sensitivity to materials used in electrode construction; and
- Minor skin rash.

IX. SUMMARY OF NONCLINICAL STUDIES

The Powerheart® G3, G3 Plus, and G5 AEDs and accessories underwent bench evaluation, animal testing, biocompatibility evaluation, human factors, and usability testing, as well as software verification and validation appropriate for devices having major level of concern. Testing was conducted on key device subassemblies and the complete systems.

Cardiac Science AEDs are shown to conform to various international standards associated with its AEDs, including:

- IEC 60601-1, General requirements for basic safety and essential performance;
- IEC 60601-1-2, General requirements for basic safety and essential performance – electromagnetic compatibility;
- IEC 60601-1-6, General requirements for basic safety and essential performance – usability;
- IEC 60601-2-4, General requirements for basic safety and essential performance of cardiac defibrillators; and
- IEC 62366, Application of Usability Engineering to Medical Devices.

Bench Testing

Table 2 below summarizes the major bench testing conducted to demonstrate proper performance of the AED G3, G3 Plus, and G5, including conformance with applicable consensus performance standards. Pass/fail criteria and deviations from consensus standards were deemed appropriate to the devices considering the specific technological characteristics, intended use, and risk analysis.

Table 2: Bench Testing

	Test Title	Results
1.	Medical Electrical Equipment Safety (IEC 60601-1 3rd edition)	Pass
2.	Particular Requirements for the Basic Safety and Essential Performance of Cardiac Defibrillators (IEC 60601-2-4)	Pass
3.	Particular Requirements for the basic safety and essential performance of electrocardiographic monitoring equipment (IEC 60601-2-27)	Pass
4.	RTCA DO-160G EMC Testing (Airborne Equipment)	Pass
5.	Software Verification and Validation	Pass
6.	Environmental: Ingress (IEC 60529), Temperature Extremes, Humidity and Altitude	Pass
7.	Enclosure Protection (IEC 60529:2001)	Pass
8.	Defibrillation Shock Waveform Testing	Pass
9.	Algorithm Detection Testing	Pass
10.	Integrated System Testing (Combined Hardware and Software)	Pass
11.	Mechanical Hardware Design Verification	Pass

	Test Title	Results
12.	Functional Testing	Pass
13.	Battery Verification and Validation	Pass
14.	Shock and Vibration Testing (MIL-STD 810F)	Pass
15.	Packaging Tests (UN, ISTA)	Pass
16.	Defibrillation Electrode Pads Biocompatibility (ISO 10993)	Pass

Biocompatibility Testing

The patient contacting portions of the Cardiac Science AEDs are the electrode pads used with the devices. These accessories were tested in accordance with ISO 10993 for cytotoxicity, irritation, and sensitization testing, and passed all testing to adequately demonstrate biocompatibility.

Software Documentation and Validation

Powerheart® G3, G3 Plus, and G5 AEDs software was documented and validated according to the FDA guidance document *"Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices"* for a major level of concern device. Software documentation included level of concern, software description, device hazard analysis, software requirements specification, software architecture diagrams, software design specifications, requirements traceability matrix, software development environment description, verification and validation documentation, revision level history, unresolved anomaly report, discussion of tools to detect run-time errors, and cybersecurity documentation.

The documentation provided was deemed acceptable for Powerheart® AED G3 and Powerheart® AED G3 Plus, while for model G5 the cybersecurity controls were deemed insufficient, and the device was considered conditionally acceptable (see section XIII). Software verification and validation testing conducted on the G3, G3 Plus, and G5 AED models included unit, integration, and system-level protocols and test reports with pre-defined pass/fail criteria. This testing demonstrated that the software in the Powerheart® G3, G3 Plus and G5 AEDs performed as intended.

Shelf Life Testing

A sterility review is not necessary because the AEDs, the electrode pads, and the battery are provided non-sterile. Shelf life testing was conducted to demonstrate the labeled shelf life for the defibrillation electrode pads and batteries used with the Powerheart® G3, G3 Plus, and G5 AEDs. Battery life is 4-year shelf life and 1-year standby life (all models); **Table 3** below lists defibrillation electrode pad shelf life information.

Table 3: Defibrillation Electrode Pads Shelf Life

Defibrillation Electrode Pads	Labeled Shelf Life
G3, G3 Plus Adult	27 months
G3, G3 Plus Pediatric Adult	30 months
G5 Adult	27 months
G5 ICPR adult	30 months
G5 Pediatric	30 months

Animal Testing

Animal testing was conducted to validate the effectiveness of the Cardiac Science pediatric waveform using Powerheart® pediatric electrodes. The defibrillation waveform of the Powerheart AED, AED G3, and AED G3 Plus is identical as it is produced by the same circuitry, therefore in this section "G3" is used to indicate AED G3 and AED G3 Plus indifferently. The following animal data was collected with the Powerheart AED, which used the same defibrillation waveform of the AED G3 and AED G3 Plus.

Powerheart® Defibrillation Success for Short and Long Duration Ventricular Fibrillation

Study objective: Animal study to assess the defibrillation effectiveness of the Powerheart AED Pediatric Electrode System.

Method: Animal testing was performed on a total of seven (7) pigs (domestic crossbreeds) weighing 14 to 24kg. Ventricular fibrillation was induced in the pig and after 15 - 30 seconds VF, a 200J shock was delivered through the attenuator to the electrode. Two (2) additional shocks of 270J were delivered if required for defibrillation. After a minimum of 30 minutes a second episode of ventricular fibrillation was induced in the pig and sustained for four minutes.

Results: For short duration VF, the Powerheart® AED could resuscitate five (5) out seven (7) pigs on the first shock, and the remaining two (2) pigs with a second shock. The test results for the fibrillation episode of 4 minutes with simulated CPR were that the Powerheart AED successfully defibrillated all seven (7) pigs with an average of 2.1 shocks ± 1 shock. The average delivered energy was 46.6J ± 3.4J and 59.3J ± 1.2J.

Conclusion: The Powerheart® AED successfully defibrillated all seven (7) pigs for both short and long duration ventricular fibrillation episodes.

Powerheart® G3-G5 Pediatric Return of Spontaneous Circulation (ROSC)

The pediatric defibrillation waveform delivered by the G3 AED and G3 AED Plus is the same. However, the pediatric waveform at different energy levels and impedances is different between the G3s models and the Powerheart® G5.

Study objective: The purpose of the animal study was to demonstrate that the defibrillation success defined as ROSC of the Powerheart® G5 AED is not inferior to the G3 and G3 Plus AEDs.

Methods: The animals were induced into VF, then remained unsupported for the 30 second-VF duration. The AED under test was activated such that at 30 seconds, shock energy was delivered. The defibrillation protocol and energy selection was fixed for each induction: 50J, 67J, and 67J in a 3-shock stack. Each successive shock was delivered at 15 second intervals, under the control of the AED analysis protocol. Up to eight (8) VF inductions were performed in each animal at 15-minute intervals between VF inductions.

Results: There were 64 first shocks delivered in the G3 group (of which 44 or 69% had ROSC) and 69 in the G5 group (of which 45 or 65%) had ROSC. There is >99% power with this sample size to detect a noninferiority margin difference between the group proportions of -0.10, where the actual difference detected was 0.0353.

There were 64 stacked shock sets in the G3 group (of which 57 or 89% with ROSC) and 69 in the G5 group (of which 61 or 88% with ROSC). There is >99% power with this sample size to detect a noninferiority margin difference between the groups of -0.10, where the actual difference detected was 0.0065.

Conclusion: The defibrillation rates that resulted in ROSC in the two (2) devices are consistent with the non-inferiority of the G5 relative to the G3, in a porcine animal model of defibrillation. In no case was there any observed damage related to defibrillation.

X. SUMMARY OF CLINICAL STUDIES

The final order, Effective Date of Requirement for Premarket Approval for Automated External Defibrillator Systems, 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) Premarket Notification process. Cardiac Science submitted the following clinical studies in support of reasonable safety and effectiveness of the Cardiac Science AEDs.

A. RhythmX® ECG Analysis and STAR® Biphasic defibrillation waveform

The RhythmX® ECG Analysis and STAR® Biphasic defibrillation waveform were tested during two (2) separate clinical studies, IDE G920078 and IDE G970230.

1. RhythmX® ECG Analysis IDE G920078

Study objective: To prove the effectiveness of the RhythmX ECG analysis using the Powerheart® Automated External Defibrillator device (K011901), which uses the exact same RhythmX technology as Cardiac Science's current AEDs (G3, G3 Plus, and G5) in this PMA.

Method: The study was divided into two (2) phases: Phase I and Phase II. Phase I was further divided into two (2) sub-phases. In Phase I, the Powerheart® AED operated as an arrhythmia detector only and did not deliver shock therapy. Phase I was not randomized. In Phase II, the Powerheart® AED operated as an arrhythmia detector and optionally delivered shock therapy. Phase II was a blind, randomized trial.

Results: A total of 156 patients were enrolled in the trials. Data from the first 15 patients was excluded because the arrhythmia detection algorithm changed after they were studied. The remaining 141 patients experienced 92 shockable episodes, with 117 patients attached to the Powerheart® AED, and the remaining 24 randomized to the standard of care only. The sensitivity of the Powerheart® AED was 100.0%, the positive predictivity was 93.3%, and the specificity was 99.4%. **Table 4** shows the clinical data of all patients with 95% lower confidence limit scores when attached to the Powerheart® AED.

Table 4: Clinical Data – All Patients Attached to Powerheart® AED

# of Patients	Hours Attached	True Positives	False Positives	True Negatives	False Negatives	Sensitivity	Positive Predictivity	Specificity
117	1138.8	92	6	1065	0	100% (96.8%)	93.9% (88.3%)	99.4% (98.9%)

Conclusion: These data support the conclusion that Powerheart® AEDs accurately detect ventricular tachyarrhythmias and provide appropriate therapy according to physician selected parameters. The data collected demonstrated sensitivity of 100.0%, positive predictivity as 93.9%, and specificity as 99.4%. The initial sample size calculations assumed an expected sensitivity of 90%. The actual sensitivity of 100% calculated in this trial allowed a smaller number of patients to be entered in the study while still providing the necessary high confidence limits. The Powerheart® AED's arrhythmia detection and therapeutic capabilities, as well as its safety and effectiveness have been demonstrated with a high confidence level.

Post Market Performance of the RhythmX Analysis Algorithm

Study objective: Post-market, retrospective study evaluating the field performance of the RhythmX Algorithm during field uses.

Method: The rescue data from Cardiac Science AEDs was collected between December 1999 and December 2016 from AEDs deployed in various locations globally. All the rescue files represent actual field use of Cardiac Science AEDs (i.e., AED G3, AED G3 Plus, AED G5, and other models with identical RhythmX Analysis Algorithm) during rescue attempts. All reviews and classifications of the ECG rhythm were consistent with the rhythm classifications outlined in Kerber *et al.*[1].

Results: The Performance Goals and Lower Confidence Limit Goals are from the Kerber recommendation. A total 5,522 AED analysis periods were available for evaluation. Exclusions consisted of 592 rhythm segments from AEDs no longer available or supported and not relevant to the performance of RhythmX. Eight (8) rescues, consisting of 52 separate analysis periods, were rejected due missing or corrupted ECG data. The results of the analysis of the remaining AED records are summarized in **Table 5**.

Table 5: RhythmX Results

Rhythms	Goal: Sample Size	Actual: Sample Size	Goal: Performance	Observed: Performance	Goal: 90% One-sided Lower Confidence Limit	Observed: Performance with 90% CI
Shockable						
Coarse VF	200	1035	>90%	>93%	>87%	>93%
Rapid VT	50	58	>75%	>97%	>67%	>91%
Non-Shockable						
NSR	100	428	>99%	100%	>97%	>99%
AF, SB, SVT, heart block, idioventricular, PVCs, other	30	965	>95%	>96%	>88%	>95%
Asystole	100	1969	>95%	>99%	>92%	>99%
Intermediate						
Fine VF	25	229	Report only	56%	N/A	66%
Other VT	25	9	Report only	100%	N/A	75%
Artifact						
Artifact	N/A	185	Report only	94%	N/A	91%

2. **<u>Adult Defibrillation Waveform: STAR® Biphasic Waveform IDE G970230</u>**

Study objective: To evaluate the first shock effectiveness of monophasic and STAR® Biphasic Waveforms for external defibrillation.

Methods: A prospective, randomized, blinded, multi-center study of 118 patients undergoing electrophysiologic testing or receiving an implantable defibrillator was conducted. Ventricular fibrillation was induced, and defibrillation was attempted in each patient with a biphasic and a monophasic waveform. Patients were randomly placed into two (2) groups: Group 1 received shocks of escalating energy, and Group 2 received only high energy shocks.

Results: The STAR® Biphasic Waveform achieved a first-shock success rate of 100% in Group 1 (95% confidence interval [CI] 95.1% to 100%) and Group 2 (95%

CI 94.6% to 100%), with average delivered energies of 201±17J and 295±28 J, respectively. The monophasic waveform demonstrated a 96.7% (95% CI 89.1% to 100%) first-shock success rate and average delivered energy of 215±12J for Group 1, and a 98.2% (95% CI 91.7% to 100%) first-shock success rate and average delivered energy of 352±13J for Group 2. **Figure 5** shows the defibrillation results.

	Group 1		Group 2		Combined	
Variable	**MTE**	**BTE**	**MTE**	**BTE**	**MTE**	**BTE**
Impedance (Ω)	64 ± 19	65 ± 18	65 ± 23	64 ± 22	64 ± 21	65 ± 20
E_D (J)*	215 ± 12	201 ± 17	352 ± 13	295 ± 28	NA	NA
Total no. of first shocks	60	60	55	55	115	115
No. of successful first shocks	58	60	54	55	112	115
First shock success rate (%)	96.7	100	98.2	100	97.4	100
95% CI	89.1-100	95.1-100	91.7-100	94.6-100	92.6-100	97.4-100
E_D - Delivered energy. *Data are shown as average ± SD						

Figure 5: Defibrillation Results

Conclusion: The STAR® Biphasic Waveform was validated in a multicenter clinical trial led by researchers at the Cleveland Clinic and Cedars-Sinai Medical Center. The analysis showed that the overall first-shock defibrillation success rate with the STAR® Biphasic Waveform is statistically higher than the monophasic damped sine or the 150J non-escalating biphasic waveform.

Post Market Performance of the STAR® Biphasic Waveform

Study Objective: Post-market, retrospective study evaluating the performance of the Powerheart® STAR® Biphasic Waveform during field uses.

Method: The Cardiac Science data from the FirstSave (subsequently discontinued), G3, G3 Plus, and G3 Pro AEDs used for this study were collected from 584 patients between December 1999 and December 2016. All devices used in this study use the same defibrillation waveform, the STAR Biphasic Waveform. The AEDs were deployed in various locations throughout the world. The data were captured from electronic files created by Cardiac Science AEDs during rescue attempts. All rescue files included in these data represent actual field use of Cardiac Science AEDs.

The Cardiac Science retrospective data were collected using a method which limits bias by having minimal exclusion criteria. Cardiac Science allowed any data received from a customer to be included into its database, regardless of the variability in the AED deployment model or resuscitation protocols.

Results: Data were divided into two (2) major groupings. The primary group contains the Cardiac Science data sources broadly identified as Retrospective data. A total of 748 shocks met the inclusion criteria and were available for evaluation. These data were split into four (4) identifiable subgroups. The Complaint data set

included 394 shocks and showed shock success of 90% (95% lower CI of 88%). The Fort Worth data set included 164 shocks and showed shock success of 90% (95% lower CI of 86%). The Pittsburgh data set included 97 shocks and showed shock success of 94% (95% lower CI of 88%). The San Diego data set included 93 shocks and showed shock success of 94% with (95% lower CI of 88%).

The other group included two (2) additional data sets: (1) the Netherlands study, and (2) the Health Club data, that were analyzed with the same inclusion criteria. The Netherlands data set included 249 shocks and showed shock success of 93% (95% lower CI of 89%). The Heath Club data set included 65 shocks and showed shock success of 97% (95% lower CI of 91%).

The data were also pooled for a total of 1,062 shocks that met inclusion criteria and were available for evaluation. Overall results showed shock success of the pooled data as 92% (95% lower CI of 90%). The first shock results showed shock success of the pooled data of 584 shocks as 93% (95% lower CI of 91%). Overall restoration of spontaneous circulation (ROSC)/restoration of an organized rhythm (ROR) was determined for all 584 patient rescue attempts. Overall ROSC/ROR was 75%.

B. Pediatric Defibrillation

1. Powerheart® Defibrillation Success for Short and Long Duration Ventricular Fibrillation

Study objective: Animal testing was conducted to validate the effectiveness of the Cardiac Science pediatric waveform using the Powerheart® AED with pediatric electrodes. The Powerheart AED used the same defibrillation waveform, the STAR Biphasic Waveform as the AED G3 and AED G3 Plus.

Method: Animal testing was performed on a total of seven (7) pigs (domestic crossbreeds) weighing 14 to 24kg. Ventricular fibrillation was induced in the pig and after 15 - 30 seconds of VF, a 200J shock was delivered through the attenuator to the electrode. Two (2) additional shocks of 270J were delivered if required for defibrillation. After a minimum of 30 minutes, a second episode of VF was induced in the pig and sustained for 4 minutes.

Results: For short duration VF, the Powerheart AED could resuscitate five (5) out of seven (7) pigs on the first shock, and the remaining two (2) pigs with a second shock. The test results for the fibrillation episode of 4 minutes with simulated CPR were that the Powerheart AED successfully defibrillated all seven (7) pigs with an average of 2.1 shocks ± 1 shock. The average delivered energy was 46.6J ± 3.4J and 59.3J ± 1.2J.

Conclusion: The Powerheart® AED successfully defibrillated all seven (7) pigs for both short and long duration ventricular fibrillation episodes.

2. **Powerheart® G3-G5 Pediatric ROSC**

The pediatric defibrillation waveform delivered by the G3 AED and G3 AED Plus is the same. However, the pediatric waveform at different energy levels and impedances is different between the G3 s models and the Powerheart G5.

Study objective: The purpose of the animal study was to demonstrate that the defibrillation success defined as ROSC of the Powerheart® G5 AED is not inferior to the G3 AED or G3 AED Plus.

Method: The animals were induced into VF, then remained unsupported for the 30 second-VF duration. The AED under test (G3 AED or G5 AED) was activated such that at 30 seconds a shock energy was delivered. The defibrillation protocol and energy selection was fixed for each induction: 50J, 67J, and 67J in a 3-shock stack. Each successive shock was delivered at 15 second intervals, under the control of the AED analysis protocol. Up to eight (8) VF inductions were performed in each animal at 15-minute intervals between VF inductions.

Results: There were 64 first shocks delivered in the G3 group (of which 44 or 69% had ROSC) and 69 in the G5 group (of which 45 or 65%) had ROSC. There is >99% power with this sample size to detect a noninferiority margin difference between the group proportions of -0.10, where the actual difference detected was 0.0353.

There were 64 stacked shock sets in the G3 group (of which 57 or 89% with ROSC) and 69 in the G5 group (of which 61 or 88% with ROSC). There is >99% power with this sample size to detect a noninferiority margin difference between the groups of -0.10, where the actual difference detected was 0.0065.

Conclusion: The defibrillation rates that resulted in ROSC in the two (2) devices are consistent with the non-inferiority of the G5 relative to the G3, in a porcine animal model of defibrillation. In no case was there any observed damage related to defibrillation.

C. Pediatric Extrapolation

In this premarket approval application, two (2) animal studies were submitted to support the reasonable assurance of safety and effectiveness of the STAR® Biphasic defibrillation waveform in pediatric patients. The pre-clinical studies of the STAR® Biphasic defibrillation demonstrated that this waveform successfully defibrillated all animals for both short and long duration ventricular fibrillation episodes in the pediatric model.

D. Human Factors and Usability Studies

Human factors data were collected and analyzed in the Cardiac Science's various usability studies which support the conclusions that the user interfaces for the various

AED models, when used by lay users, are safe and effective. The studies and total number of participants are listed below:

- Human Factors study Powerheart® G3 - 15 participants,
- Human Factors study Powerheart® G3 Plus – 45 participants,
- Human Factor study Powerheart® G5 – 62 participants,
- Supplemental Human Factors study Powerheart® G3 and G5 AEDs – 30 participants.

The Cardiac Science human factors usability study represents one part of the overall Powerheart® AED validation study plan, which includes the following AED devices:

- **Powerheart® G3:** AED that available in automatic and semi-automatic models.
- **Powerheart® G3 Plus**: G3 AED with more detailed voice prompting to support untrained users, available in automatic and semi-automatic models.
- **Powerheart® G5:** AED that available in automatic and semi-automatic models. Includes an optional CPR assistance device (iCPR device) that provides additional feedback for proper CPR technique.

Each device was validated in independent usability studies and included both the automatic and semi-automatic models where applicable. Participants were not allowed to participate in multiple studies to ensure that there was no negative transfer between the models. Unique AED features, such as the manual shock mode and iCPR device attachment, were also tested whenever applicable.

Table 6 shows the distribution of user groups across each study. Note that each applicable user group was represented by a minimum of 15 participants. This sample size was chosen to capture the majority of known use errors with the AED devices and is not intended to produce statistically significant results.

Table 6: User Group Distribution

	G3	G3 Plus	G5
Professional Rescuers	See G3 Plus	✓	✓
Targeted Responders	See G3 Plus	✓	✓
Lay People	✓	✓	✓

The Powerheart® AEDs have been found to be safe and effective for the intended users, uses, and use environments. Additionally, while not included as Cardiac Science's intended users, untrained lay users were able to deliver a shock despite lack of the training (training is recommended in Cardiac Science's AED Indications for Use). These findings were based of the following results shown in **Table 7**.

Table 7: Usability Study Results

AED Model		# of Participants	Shock Delivery Success %	Median time to Shock (seconds)
G3		15	100%	100.3
G3 Plus		45	100%	75.1
G5		62	98%	63.4

E. Complaint Analysis

To further demonstrate the safety and effectiveness of the Powerheart® AEDs in clinical use, relevant adverse event data were analyzed between January 1,2014 and August 10, 2016.

The results identified nineteen (19) deaths and nineteen (19) malfunctions associated with Powerheart® AED model numbers 9300A, 9300E, 9390A, 9390E, and G5A.

For the reported 19 deaths, there were 11 reports in which the device kept prompting users to tear open the pads package after the pads had already been placed on the patients. Cardiac Science evaluated these returned devices and confirmed the user error of improper removal of the pad from liner prior to the placement which caused an insufficient electrical contact between the patients and the pads. Five (5) other reports stated that the AED failed to deliver the shock after analyzing the correct rhythm. Cardiac Science investigated the returned devices and confirmed that the users pressed the shock button before it started flashing, which would result in no shock being delivered. The remaining three (3) of 19 MDRs reported that there were no voice prompts after opening the AED's lid to remove pads as well as no voice prompts for shock advised. Cardiac Science replaced damaged speakers due to mishandling.

For the reported 19 malfunctions, the identified root causes and quantities as determined by Cardiac Science are: device not returned (13), unexpected battery failure (4), user error (2).

F. Conclusions

The retrospective analysis of Cardiac Science AEDs in real world use demonstrates effectiveness of the STAR® Biphasic waveform consistent with the cited industry studies. STAR® Biphasic Waveform performed well across a representative range of deployment environments. In conclusion, the above data, taken together with the other clinical data and preclinical data analyzed are sufficient to demonstrate safety and effectiveness of the performance of the Powerheart® G3, G3 Plus, and G5 AEDs.

G. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The Financial Disclosure by Clinical Investigators regulation was not provided for this file, as the information leveraged was reviewed for the approval of prior IDEs (e.g., G920078, G970230). Other data included post-market data collected and analyzed by the applicant. Overall, the rationale provided in lieu of formal financial disclosure for this file was acceptable and information provided does not raise any questions about the reliability of the data.

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

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

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLNICAL STUDIES

A. Effectiveness Conclusions

Benefits outweigh the risks with which it is associated. This is verified through the longevity of the commercialization of the products, through the literature on clinical safety and effectiveness, and through the post-market data, including tracking and trending of complaints and vigilance.

B. Safety Conclusions

The preclinical and clinical testing and data collected from the published literature did not identify or result in any unacceptable safety concerns associated with use of the Powerheart® G3, G3 Plus, and G5 AEDs.

C. Risk-Benefit Determination

The benefit of early defibrillation therapy is the survival of patients in SCA. 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 is 7% - 10%.

The magnitude of this benefit is either life or death. Patients are likely to 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 (or may) survive a life-threatening cardiac arrest situation and will be able to seek further treatment.

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

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 support that for Powerheart® AED G3, Powerheart® AED G3 Plus, and Powerheart® AED G5 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 December 7, 2018. FDA has developed unique conditions of approval to pursue real world information and in response to panel comments from the 515i Panel discussed in Section XI above. The final conditions of approval cited in the approval order are described below.

The applicant will provide the following non-clinical information as part of the annual report, which may be followed by a PMA supplement, where applicable:

1. The number of devices returned to the applicant for cause from domestic sources, with a breakdown into:
   a. Those returned for normal end-of-life; 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 also agreed to provide the following non-clinical information:

FDA notes that you have implemented some cybersecurity controls in the Powerheart® AED G5 (Model G5A-80A, G5A-80C, G5S-80A, and G5S-80C). In addition, you have described additional controls you intend to implement but have not yet done so. In order to assure that this device is sufficiently secured from end-to-end (i.e., from the server to the AED itself), you must address this condition of approval. Specifically, you must develop and implement a plan, with FDA's approval, to address end-to-end security of this device. Further, you may not distribute the Powerheart® AED G5 (Model G5A-80A, G5A-80C, G5S-80A, and G5S-80C), until you have been notified by FDA that this condition has been satisfied, including but not limited to the items listed below.

1. You must provide a proposed plan to address this condition of approval no later than January 15, 2019. This plan should include at least the following information:

   a. A description of the controlled measures that have been or will be implemented to provide end-to-end security of the subject device.

   b. A timeline for all activities planned to address this condition of approval.

2. You must have a finalized plan to address this condition of approval that FDA deems acceptable no later than March 1, 2019.

3. You must provide to FDA the following no later than April 1, 2019:

   a. A comprehensive cybersecurity risk management plan.

   b. A comprehensive threat model that identifies all critical assets (e.g., firmware and backend servers), threats, and design information for the protection control measures for each identified asset.

4. You must have implemented the controlled measures to provide end-to-end security of the subject device as outlined in the finalized plan no later than September 3, 2019. Note that these controlled measures may require FDA approval prior to implementation.

Please note, future submissions should incorporate these items into the PMA submission as part of the premarket review prior to device approval.

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

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

XV. REFERENCES

1. RE Kerber, LB Becker, JD Bourland, RO Cummins, AP Hallstrom, MB Michos, G Nichol, JP Ornato, WH Thies, RD White, BD Zuckerman. "Automated External Defibrillators for Public Access Defibrillation: Recommendations for Specifying and Reporting Arrhythmia Analysis Algorithm Performance, Incorporation New Waveforms, and Enhancing Safety." Circulation (1997), Vol 95, No 6, 1677-1681.