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Dear Dr. Hamburg and Dr. Shuren:

Public Citizen, a consumer advocacy group representing more than 300,000 members and supporters nationwide, strongly urges the Food and Drug Administration (FDA) to withdraw its dangerous proposal to reclassify Automated External Cardiac Compressor (AECC) preamendment Class III devices to Class II (special controls) and instead publish a proposed rule that would maintain such devices in Class III and require submission of premarket approval applications (PMAs) for these devices. Clinical trials are required for these life-sustaining devices because there is not enough information available for the FDA to determine whether using these devices in cardiopulmonary resuscitation (CPR) will improve patient outcomes or instead reduce chances of survival and lead to greater brain damage among survivors.

AECC devices are used by emergency medical personnel to automate chest compressions during CPR, using a piston, strap, or vest to press down on the chest of a patient whose heart has stopped beating. In the absence of such devices, emergency medical personnel and other responders for decades have performed these chest compressions manually by pushing down on the patient’s chest with their hands (manual CPR). If AECC devices are as effective, or possibly even more effective, than manual CPR, AECCs could potentially make work easier for emergency medical personnel and might even save lives. But if the device is less effective than manual CPR, it can cause death or brain damage by providing inferior care to victims of cardiac arrest.
The devices are currently classified as Class III devices, a regulatory category offering the strictest level of premarket review the FDA can require, because the FDA determined in 1980 that these devices were life-sustaining devices for which well-controlled clinical trials are necessary to provide reasonable assurance of safety and effectiveness. Unfortunately, the FDA failed to issue, in a timely manner, final regulations that would require the manufacturers of these devices to submit clinical trial data and prove that AECCs were actually safe and effective for their intended purpose.

In the meantime, few clinical trials have ever been performed using AECC devices. In more than 30 years since the devices were first marketed in the U.S., only one large, well-powered randomized controlled clinical trial has ever tested their efficacy compared with manual CPR. That trial, which had to be stopped early for ethical reasons, found that patients given CPR using AECC devices were significantly more likely to experience brain damage than those given manual CPR. There was also a nonsignificant trend toward lower survival to hospital discharge in AECC-treated group. Some researchers have criticized this large trial, but the fact remains that no other data from well-controlled clinical trials exist to contradict this strong evidence of harm.

Given the relatively robust evidence that CPR using AECC devices for chest compression causes an increased risk of brain damage and possibly death, the FDA cannot be reasonably assured that AECC devices are safe and effective. The FDA should immediately issue a proposed order confirming their status as Class III devices and requiring PMAs with data from well-controlled clinical trials to establish whether these devices cause or prevent death and brain damage before exposing any more victims of cardiac arrest to treatment.

I. Description of the Device and Proposed Reclassification

A. Description of the Device

Automated external cardiac compressors (AECCs) are a subtype of device identified and classified under 21 C.F.R. § 870.5200, which includes devices that assist in the act of CPR, a series of lifesaving actions aimed at improving the chance of survival and preserving intact brain function following a cardiac arrest.  

AECC devices are one of two subtypes of devices the FDA has cleared for marketing under 21 C.F.R. § 870.5200. The first AECC subtype is designated by the product code “DRM” and consists of devices that are placed directly on a patient’s chest; are powered manually, pneumatically, or electrically; and provide automatic chest compressions at a fixed compression rate and depth. This subtype of device was

2 78 FR 1162, 1163, Jan. 8, 2013.
on the market in 1976, and to date the FDA has cleared 40 devices of this subtype under the 510(k) premarket clearance process (a process described in greater detail infra).\(^5\) The second subtype, CPR Aids, assigned the product code “LIX,” consists of devices that aid the emergency medical professional in delivering manual compressions at a compression depth and rate that are consistent with current guidelines. CPR Aid devices were first introduced in 1984, and the FDA has cleared 22 devices categorized under product code LIX through the 510(k) premarket clearance process.\(^6\)

Devices from a third subtype of devices used to supply automated cardiac compressions in CPR have never been cleared by the FDA through the 510(k) premarket clearance process. These “third-generation” AECC devices provide chest compressions while also aiming at improving traditional CPR hemodynamics by, for example, introducing active decompression or alternating abdominal compression with chest compressions.\(^7,8\) The FDA has determined that no predicate device exists for such third-generation AECC devices and therefore requires premarket approval applications (PMAs) for this device subtype.\(^9\) To the best of our knowledge, no PMA has ever been approved for a third-generation AECC device. One PMA was submitted previously, but the Circulatory System Devices Advisory Panel recommended against approval of the device in 1998.\(^10\) Reclassification into Class II would not immediately affect the PMA requirement for such third-generation AECC devices.\(^11\)

Only the AECC device subtype designated as DRM will be discussed in these comments. Public Citizen urges the FDA to maintain DRM-designated AECC devices in Class III and issue a final rule requiring submission of PMAs for this device subtype. Public Citizen takes no position on the reclassification of the LIX-designated CPR Aid device subtype. With regard to “third-generation” AECC devices, we believe that the current PMA requirement is appropriate and will be maintained if the AECC device subtype remains in Class III.

**B. Proposed Reclassification of AECC Devices**

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\(^10\) Ibid.

\(^11\) However, AECC devices were reclassified into Class II and a third-generation AECC device were then approved under a PMA, it is possible that subsequent third-generation AECC devices could be cleared through the 510(k) premarket clearance process, relying on the initial PMA-approved device as a predicate.
The FDA has proposed reclassifying all AECCs into Class II based on a finding that special controls, in addition to general controls, would provide reasonable assurance of safety and effectiveness. In coming to this proposed reclassification decision, the FDA evaluated the following risks to health associated with the use of AECC devices:

- Tissue damage, bone breakage, or inadequate blood flow
- Cardiac arrhythmias or electrical shock
- Adverse skin reactions

Summarizing the data upon which the reclassification of AECCs is based, the FDA noted “mixed results” from the medical literature “on whether mechanical compressions are as effective as manual chest compressions.” Nevertheless, the FDA stated:

> These devices, when indicated for use as an adjunct to manual CPR during patient transport or for use in situations where fatigue of or inaccessibility to emergency medical personnel may otherwise prevent adequate chest compressions, can be regulated as class II devices.

The FDA has proposed several special controls for AECCs, including performance testing under “simulated physiological conditions,” labeling the device with directions for use and “information on the patient population for which the device has been demonstrated to be effective,” and testing of electrical components, software, and portions of the device coming into contact with the patient’s skin. The FDA also has proposed restricting the sale, distribution, and use of such devices by prescription only and required that the labeling “include the clinical training for the safe use of this device.”

**II. Regulatory Background, Legal Standard for Reclassification, and Specific Regulatory History of the Device**

A. **General Regulatory Background**

Automated External Cardiac Compressor (AECC) Devices are a type of Class III medical device that was on the U.S. market prior to the passage of the 1976 Medical Device Amendments to the Food, Drug and Cosmetics Act (FDCA) (“the 1976 Amendments”). As “Pre-amendment” Class III device types, AECCs are subject to a unique regulatory history that has permitted them to be marketed without evidence of safety and efficacy from well-controlled clinical trials.

The 1976 Amendments established the current framework for device regulation by the FDA. This law grouped devices by type and sorted each device type into one of three regulatory classes, referred to as Classes I, II, and III. Under this regulatory framework, device types are subject to an increasingly rigorous set of regulatory requirements depending on their class.

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13 Ibid.
14 Ibid.
15 Ibid.
Devices in Class I are subject to the least rigorous regulatory requirements. These devices include such low-risk devices as tongue depressors, elastic bandages, or reading glasses.\textsuperscript{16,17,18} Class I devices need not be cleared or approved by the FDA prior to being sold in the U.S., although they are still subject to other regulatory requirements called general controls.\textsuperscript{19}

Devices in Class II are subject to slightly more rigorous regulatory requirements. These devices include more complex or higher-risk items such as electrocardiographs, powered bone drills, and mercury thermometers.\textsuperscript{20,21,22} New Class II devices generally must be cleared by the FDA prior to being sold in the U.S. To obtain premarket clearance, the manufacturer of a Class II device must submit a notification to the FDA under 510(k) of the FDCA and establish that the device is “substantially equivalent” to another Class II device already on the market in the U.S. (known as a “predicate device”).\textsuperscript{23,24} Such 510(k) clearances generally involve animal or bench testing to prove substantial equivalence, but they do not require that the company test the safety and effectiveness of the device in well-controlled clinical investigations.\textsuperscript{25} Thus, a new Class II device can be cleared based on a showing of substantial equivalence to a previously cleared predicate device that itself was not proven safe or effective in clinical trials.

The most stringent regulatory process is reserved for Class III devices, which include implantable, high-risk, or life-sustaining devices, such as silicone breast implants, implantable pacemakers, certain types of fetal monitors used in labor, and replacement heart valves.\textsuperscript{26,27,28,29} In order to introduce a new device from a Class III device type into the U.S. market, a device manufacturer generally must submit a premarket approval application (PMA) that includes evidence from well-controlled investigations (typically with clinical data from at least one well-controlled clinical trial in humans) providing reasonable assurance that the new device is safe and effective.\textsuperscript{30}

\textsuperscript{16} 21 C.F.R. § 880.6230.
\textsuperscript{17} 21 C.F.R. § 880.5075.
\textsuperscript{18} 21 C.F.R. § 886.5844.
\textsuperscript{19} 21 U.S.C. § 360(l). However, Class I devices that are “of substantial importance in preventing impairment of human health,” or that present “potential unreasonable risk of illness or injury” are also subject to 510(k) notice requirements. Ibid.
\textsuperscript{20} 21 C.F.R. § 870.2340.
\textsuperscript{21} 21 C.F.R. § 872.4120.
\textsuperscript{22} 21 C.F.R. § 880.2920.
\textsuperscript{23} 21 U.S.C. § 360(k).
\textsuperscript{24} 21 U.S.C. § 360c(f).
\textsuperscript{26} 21 C.F.R. § 870.3610.
\textsuperscript{27} 21 C.F.R. § 870.3925.
\textsuperscript{28} 21 C.F.R. § 884.2620.
\textsuperscript{29} 21 C.F.R. § 878.3540.
\textsuperscript{30} 21 U.S.C. § 360c (a)(3)(A) (requiring evidence from well-controlled investigations, including 1 or more clinical investigations where appropriate, by qualified experts).
In addition to creating the three regulatory classes, the 1976 Amendments laid out a process by which the FDA would initially classify each device. Congress included in this process a requirement that the FDA consult with an advisory panel of qualified experts prior to making the final determination in classifying each device. The composition and procedures to be used by such panels were laid out in section 513, subsection (b) of the FDCA.\(^{31}\)

The 1976 Amendments did not require that manufacturers of device types in commercial distribution before the 1976 Amendments (the “Pre-amendment Device Types”) submit PMAs immediately. Instead, makers of these Pre-amendment Device Types could continue to use the 510(k) premarket notification process until such time as the FDA published final regulations requiring PMAs for that device type.\(^{32}\)

The process for publishing final regulations requiring premarket approval for the Pre-amendment Device Types has been slow, and as a result, many device types that were initially classified into Class III have languished in a regulatory gray area, undergoing 510(k) premarket clearance rather than the stricter requirements envisioned by Congress for Class III devices. In 1990, Congress passed the Safe Medical Devices Act (SMDA), amending Section 515(i) of the FDCA and requiring the FDA to order all manufacturers of Pre-amendment Device Types to submit safety and effectiveness information to facilitate finalizing rules for these devices or reclassifying them into Class I or II. SMDA also directed the FDA to establish a schedule to finalize PMA requirements for the remaining Pre-amendment Class III devices, and established a hard deadline of December 1, 1995, for completing the process.\(^{33}\)

In April 1994, the FDA proposed a strategy for prioritizing actions on the remaining 117 Pre-amendment Class III Device Types for which final regulations had not yet been issued.\(^{34}\) Over the next decade, the FDA reclassified or issued final rules requiring PMAs for many of the remaining Pre-amendment Device Types. Nevertheless, by 2009, there remained 27 types of Class III devices that still had no final regulations requiring PMAs.\(^{35}\) On April 9, 2009, the FDA published the order required under Section 515(i) (“515(i) order”) requiring the manufacturers of 25 of the 27 remaining Class III Pre-amendment Device Types to submit the relevant safety and efficacy information needed in order to either reclassify the devices or issue a final regulation requiring PMAs.\(^{36}\)

\[B. \textit{Legal Standard for Reclassification}\]

The standard governing classification of a device into Class III is described in Section 513(a) of the Food, Drug and Cosmetics Act, codified as 21 U.S.C. § 360c(a). A device is to be classified as Class III and subject to premarket approval if:

\[\textit{Codified as 21 U.S.C. § 360c(b)}\]

\[21 \text{U.S.C. § 360c(b)}\]


\[\textit{US Government Accountability Office. Medical devices: FDA should take steps to ensure that high-risk device types are approved through the most stringent premarket review process. GAO-09-190. January 2009.}\]


\[74 \text{FR 16214, April 9, 2009.}\]


\[74 \text{FR 16214, April 9, 2009.}\]

(i) it (I) cannot be classified as a class I device because insufficient information exists to determine that the application of general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, and (II) cannot be classified as a class II device because insufficient information exists to determine that the special controls described in subparagraph (B) would provide reasonable assurance of its safety and effectiveness, and

(ii) (I) is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or (II) presents a potential unreasonable risk of illness or injury.

“General controls” are a set of regulatory standards promulgated under the FDA’s general authority to regulate adulterated drugs and devices, impose labeling and advertising requirements, register and inspect manufacturing facilities, impose good manufacturing practice requirements, and take other regulatory actions. “Special controls” are more specific requirements that can include performance standards, post-market surveillance, patient registries, or specific FDA guidelines.

Where a device has already been classified into Class III, it may be reclassified under Section 513(e) of the FDCA, codified as 21 U.S.C. §§ 360c(e). This section was recently amended under the Food and Drug Administration Safety and Innovation Act (“FDASIA”), enacted on July 9, 2012. The FDASIA authorized the FDA to reclassify a device through an administrative order, waiving the usual administrative rulemaking process and imposing a new set of administrative requirements:

Based on new information respecting a device, the Secretary may, upon the initiative of the Secretary or upon petition of an interested person, change the classification of such device, . . . by administrative order published in the Federal Register following publication of a proposed reclassification order in the Federal Register, a meeting of a device classification panel described in subsection (b), and consideration of comments to a public docket . . .

“New information” can include additional information not available at the time of the initial classification, as well as evidence previously submitted to the agency when considered in light of additional data or knowledge drawn from clinical experience. The new information must be “valid scientific evidence” as defined in section 513(a) of the FDCA and 21 CFR § 860.7(c)(2).

The party seeking to reclassify the device bears the burden of proving that the device meets the requirements for reclassification. The standard for reclassification is provided in Section 513(e), which states that the Secretary or CDRH director and FDA commissioner may reclassify the device:

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38 21 U.S.C. §§ 360c(a)(1), 351, 352, 360, 360f, 360h, 360i, and 360j.
41 The decision to reclassify may be delegated to the Director of the Center for Devices and Radiological Health (CDRH), acting in consultation with the FDA Commissioner, but may not be delegated to a lower official. Pub. L. 112-144. Codified as 21 U.S.C. §§ 360c(e)(1)(B).
43 Upjohn v. Finch, 422 F.2d 944 (6th Cir. 1970).
to class II if the Secretary [or CDRH Director] determines that special controls would provide reasonable assurance of the safety and effectiveness of the device and that general controls would not provide reasonable assurance of the safety and effectiveness of the device, or … to class I if the Secretary determines that general controls would provide reasonable assurance of the safety and effectiveness of the device.  

C. Specific Regulatory History of the Device

Following the passage of the 1976 Amendments, the FDA convened two subsection b advisory panels assigned to make recommendations for the AECC device type. These panels, the Cardiovascular Device Classification Panel and Anesthesiology Device Classification Panel, recommended that the device type be placed in Class III because it is life supporting and potentially hazardous to life or health even when properly used, and there was not sufficient information to develop a performance standard to provide reasonable assurance of safety and effectiveness. The FDA published a notice on March 9, 1979, proposing that the External Cardiac Compressors (ECCs) be classified into Class III.

No comments were received on the proposed rule, and on February 5, 1980, the FDA published a final rule classifying external cardiac compressors into Class III. However, the FDA did not set an effective date for requiring PMAs for ECCs, and published a clarifying notice on May 11, 1987, that no such PMAs would be required until the agency had established such an effective date in a final rule. No final rule was ever issued, and as a result, ECCs continued to be approved through the 510(k) process over the following decades, despite their status as a life-supporting and potentially hazardous Class III device.

ECCs were one of 25 pre-amendment devices included in the FDA’s 515(i) order of April 9, 2009, ordering manufacturers to submit relevant safety and efficacy information needed in order to either reclassify the device or issue a final regulation requiring PMAs. Four manufacturers of ECCs submitted information. The FDA has published these submissions online at regulations.gov.

III. Efficacy and Safety Data for Proposed Reclassification of Automated External Cardiac Compressor (AECC) Devices into Class II

45 21 U.S.C. § 360c(e).
48 Ibid. (citing 45 FR 7966, Feb. 5, 1980).
49 Ibid. (citing 52 FR 17732, 17737, May 11, 1987).
A. Efficacy Data from Randomized, Controlled Clinical Trials

In situations of cardiac arrest, manual chest compressions are the well-established standard of care. In assessing whether AECC devices are effective at assisting in cardiopulmonary resuscitation (CPR) delivery, the key question is whether the devices are superior, equivalent, or inferior to manual compressions in improving short- and long-term clinical outcomes such as return of spontaneous circulation, survival to hospital admission, survival to hospital discharge, longer-term survival, and preservation of neurological (brain) function.

i. Randomized, Controlled Trials Assessing Important Clinical Outcomes

The most reliable evidence on efficacy and safety comes from randomized, controlled clinical trials comparing important short- and long-term clinical outcomes from CPR with AECC devices compared with CPR with manual chest compressions (manual CPR). Unfortunately, few such trials have been conducted, and only one trial, the AutoPulse Assisted Prehospital International Resuscitation (ASPIRE) trial, enrolled enough patients to detect a significant difference in outcomes between groups.

The ASPIRE Trial (2006)

The ASPIRE study was a multicenter, prospective, randomized trial comparing CPR delivered by a load-distributing band AECC (band AECC-CPR) with CPR delivered manually (manual CPR). The trial was conducted at five sites in the U.S. and Canada, and the primary population included subjects with cardiac arrest presumed to be of cardiac origin and occurring prior to arrival of emergency medical service (EMS) personnel. The primary endpoint was survival with spontaneous circulation to four hours after the 911 call, and secondary endpoints were survival to hospital discharge and neurological status among survivors at discharge.

The ASPIRE study was halted by an independent data and safety monitoring board after the first planned interim assessment of 1,071 subjects (with 767 subjects in the primary population meeting enrollment criteria after exclusions). No significant difference had been shown in the primary endpoint of survival to four hours, but among the primary population, survival to hospital discharge was 9.9% in the manual CPR group and 5.8% in the band AECC-CPR group, a trend that approached statistical significance (P=0.06, adjusted for covariates and clustering). Even more troubling, those in the LDB-CPR group were significantly more likely to have worse neurological outcomes at hospital discharge, with only 3.1% of subjects in the band AECC-CPR group demonstrating a cerebral performance category of 1 or 2 at hospital discharge versus 7.5% of subjects in the manual CPR group (P=0.006).

Commentators have identified various methodological issues with the ASPIRE trial, but none provide sufficient basis for rejecting the evidence showing the trend toward reduced survival and significantly

worse neurological outcomes in the AECC-treated group.\textsuperscript{56,57} For example, some have pointed out that one study site, Site C, modified the protocol midway through the study to include initial treatment with manual CPR across all groups, after a quality improvement team identified an unacceptably prolonged time without compressions while deploying the load-distributing band AECC.\textsuperscript{58} Yet the observed association between AECC treatment and decreased survival did not differ at Site C compared to other sites.\textsuperscript{59} The results of the trial are also not explained by inadequate experience with the AECC device. Had experience been a factor, the results should have improved as the study progressed. Yet during the last two months of the ASPIRE study, survival to hospital discharge for primary cases was 8.1\% for manual CPR and 5.0\% for band AECC-CPR, findings similar to those from the initial months.\textsuperscript{60} Most demographic features and cardiac arrest circumstances were also generally similar between groups, although body weight differed somewhat, with more “thin” and “morbidly obese” subjects in the band AECC-CPR group.\textsuperscript{61}

Other than the ASPIRE trial, the remaining randomized, controlled clinical studies were not designed with sufficient power to detect statistically significant differences between groups. In other words, the trials did not include enough surviving patients to ascertain whether there was a statistically significant difference in survival rates between treatment groups. Unsurprisingly, none of these studies showed any such differences in survival between groups. Also, many of the studies were plagued by imbalances in the underlying demographic and clinical features of the patient population, often with sicker or older patients enrolled in the manual CPR group. This makes the results of such studies difficult to interpret.

Smekal et al. (2011)\textsuperscript{62}

In a small prospective pilot study, 149 cardiac arrest patients meeting inclusion criteria were randomized to receive CPR performed with a piston AECC device (piston AECC-CPR) or manual CPR. The study found no difference in return of spontaneous circulation with palpable pulse (30 of 75 piston AECC-CPR (40\%), 23 of 73 manual CPR (31\%), p=0.30), survival to hospital admission (18 of 75 piston AECC-CPR (24\%), 15 of 73 manual CPR (21\%), p=0.69), or survival to hospital discharge (6 of 75 piston AECC-CPR (8\%), 7 of 73 manual CPR (10\%), p=0.78). However, the study was not powered to detect any difference between groups. Rather, the intention of the study was to use the results for power calculation in a larger randomized, multi-center trial that has yet to be completed.

Dickinson et al. (1998)\textsuperscript{63}

\textsuperscript{56} Lewis RJ, Niemann JT. Manual vs device-assisted cpr. JAMA 2006;295(22):2661-2664.
\textsuperscript{59} Ibid.
\textsuperscript{60} Ibid.
\textsuperscript{61} Ibid.
Twenty subjects with “sudden death” unrelated to trauma were randomized to receive mechanical CPR delivered with a piston AECC device or manual CPR. The piston AECC device also provided mechanical ventilation, and subjects in both groups received mechanical ventilation from the device. Reported endpoints included survival and measurement of a surrogate marker, end-tidal CO$_2$. Only one subject in the piston AECC-CPR group survived to hospital admission, but that subject died within the next 48 hours. No subjects in the manual CPR group survived to hospital admission.

Halperin et al. (1993)

Thirty four subjects with cardiac arrest who had not been successfully resuscitated by up to 20 minutes of standard CPR were randomized to receive either continued manual CPR or CPR delivered by a vest AECC device (vest AECC-CPR). Endpoints included return of spontaneous circulation and survival at 24 hours. Spontaneous circulation returned in 3 of 17 subjects (18%) who received manual CPR, and 8 of 17 subjects (47%) who received vest CPR, but the results (as expected given the limited power of the study) were not statistically significant (P=0.14). At 24 hours the difference in survival was even smaller: only one of the manual CPR subjects (6%) and three of the vest AECC-CPR subjects (18%) survived to the 24-hour point (p=0.03 for difference in 24-hour survival between groups). None of the patients survived to be discharged from the hospital. In addition, the vest AECC-CPR group was younger, on average, than the group that received manual CPR, which could have contributed to better outcomes in the vest AECC group (manual CPR: mean age 69 years ± SD 18, vest CPR: mean age 61 years ± SD 16).

Taylor et al. (1978)

Fifty subjects with cardiac arrest were randomized to receive manual CPR or CPR delivered by a piston AECC device (piston AECC-CPR). Endpoints included survival to one hour following resuscitation and survival to hospital discharge. Ten of 26 subjects from the manual group (39%) and 10 of 24 subjects from the piston AECC-CPR group (42%) survived to one hour following resuscitation. Two of 26 subjects from the manual CPR group (8%) and three of 24 subjects from the piston AECC-CPR group (13%) survived to discharge. The results were not analyzed for statistical significance, and no power analysis was reported. The two groups differed in some aspects of medical history, with 19 subjects in the manual CPR group reported to have “severe systemic illness” compared to 12 in the piston AECC-CPR group.

ii. Meta-analysis

The results of these small randomized, controlled clinical trials proved to be no better when aggregated together in a recent meta-analysis. In 2011, the Cochrane collaboration conducted a systematic review of

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64 Ibid.
AECC versus manual chest compressions for cardiac arrest. This was the first systematic review of randomized, controlled trials on this topic. The Cochrane review included randomized trials comparing any type of powered, mechanical chest compression device to standard manual chest compressions in patients suffering cardiac arrest that reported on survival or other outcomes. These outcomes included survival to hospital discharge with good neurologic function, survival to hospital admission, return of spontaneous circulation, short-term survival (less than or equal to 30 days), long-term survival (more than 30 days), or survival to hospital discharge.

Only four studies met all the criteria for inclusion in the Cochrane review. These studies were summarized previously (The ASPIRE Trial, Halperin et al., Taylor et al., and Dickinson et al.). These four trials included data from 868 participants. Only one trial, the ASPIRE Trial (which enrolled 767 patients), reported on survival to hospital discharge with good neurologic function. That trial, as previously noted, demonstrated significantly reduced survival with good neurologic function for subjects treated with the AECC device when compared to those treated with manual CPR (RR 0.41 [95% CI 0.21-0.79]). Data from 101 participants enrolled in the remaining three studies demonstrated nonsignificant trends toward increased return of spontaneous circulation (2 studies, N = 51, pooled RR 2.81, 95% CI 0.96 to 8.22) and survival to hospital admission (1 study, N=17, RR 4.13, 95% CI 0.19 to 88.71) in patients who received mechanical chest compressions versus manual chest compressions.

iii. Randomized Trials with Surrogate Endpoints

Several studies have compared CPR delivered by AECC device (AECC-CPR) to manual CPR by measuring surrogate markers thought to be predictive of survival, such as end-tidal CO₂ and arterial pressures. End-tidal CO₂ has correlated with successful outcomes in a limited number of animal and human studies, and some have proposed it may be useful in predicting survival. Two studies...
have assessed end-tidal CO₂ in AECC-CPR versus manual CPR. One of these studies was by Dickenson et al., discussed previously, and the second was a study by Ward et. al published in 1993.\(^{80,81}\) Both studies demonstrated significant improvements in end-tidal CO₂ in the AECC-CPR group. However, these studies included very small sample sizes, and of the 35 patients enrolled in the two studies, none survived to hospital discharge.

iv. Observational or Nonrandomized Studies

Some observational and other nonrandomized studies have suggested that mechanical devices may provide improved outcomes over manual chest compressions, but these studies are plagued by methodological flaws that make the results unreliable. For example, a study by Ong et al published in 2006 measured return to spontaneous circulation, survival to hospital admission and discharge, and neurological outcome at discharge among out-of-hospital cardiac arrest patients, both before and after an urban emergency medical system switched from manual CPR to CPR delivered with a load-distributing band (LDB) AECC device.\(^{82}\) Patients treated with the LDB AECC device were significantly more likely to experience return of spontaneous circulation and survive to hospital admission and discharge. However, the trial was nonrandomized, and ambulance-response time was faster during the phase in which the device was used. Also, more of the cardiac arrests were witnessed by paramedics during the LDB-AECC phase, and one receiving hospital introduced a new protocol to address hypothermia post-resuscitation after LDB AECC had been phased-in. Each of these factors could have led to superior outcomes during the AECC treatment phase.

Other studies that are not fully randomized have shown no difference in outcome. For example, a cluster, non-randomized study by Axelsson et al published in 2006 showed no difference in return of spontaneous circulation or survival to hospital admission or discharge.\(^{83}\)

B. Safety Data from Clinical Trials Not Related to Brain Function or Survival

The 2011 Cochrane Review comparing AECC to manual chest compressions found no significant differences in adverse events, including sternal or rib fractures, hemothorax or pneumothorax, or internal organ injury.\(^{84}\) However, the total number of cases of adverse events was low, and results were mixed.


with one trial (Taylor et al, 1978), reporting increased relative harm in rib and sternal fractures with AECC, while risk of this and other events was lower with AECC in the remaining trials.

C. Device Risks: Evidence of Delays and Interruptions to CPR in Clinical Practice

Current guidelines by the American Heart Association (AHA) emphasize the need to limit delays and interruptions in compressions to less than 10 seconds, because outcomes of CPR are improved if chest compressions are initiated promptly and interruptions are kept to a minimum. Various reports have discussed evidence that AECC devices can delay or interrupt delivery of chest compressions during CPR. This has the potential to negatively affect CPR outcomes.

One study published by Wang et al in 2007 described a video-recorded time-motion analysis that compared manual compressions to compressions delivered by a piston AECC device in 20 patients. The authors found that mechanical compressions caused significantly longer average interruptions in chest compressions while patients were being unloaded from the emergency response vehicle (5.7 ± 9.9 seconds, versus 18.7 ± 9.1 seconds, P=0.01). Average interruptions in chest compressions while patients were loaded onto the vehicle were also longer with mechanical compressions, although this trend barely missed reaching significance (15.1 ± 19.7 seconds, versus 49.4 ± 39.9, P=0.06). The average length of the interruptions in chest compressions during loading and unloading for the group treated with the AECC was 49.4 and 18.7 seconds respectively, far exceeding the 10 second interruption recommended by the AHA. By contrast, patients who received manual CPR experienced much shorter average interruptions of 15.1 and 5.7 seconds respectively.

Other evidence of delays comes from the ASPIRE trial. In that trial, a quality improvement team at one of the sites (the only site with such a team) identified prolonged time without compressions while deploying the band AECC, and responded by instructing EMS personnel to begin with manual compressions and switch to the randomized treatment after the first shock assessment. Patients in the LDB-CPR group experienced longer time intervals to first shock (for those with ventricular fibrillation/ventricular tachycardia) an average of 2.1 minutes later than patients in the manual CPR group (P=0.001). The authors suggested that prolonged deployment time for the AECC device was one possible explanation for worse outcomes in the AECC-treated group.

In a cluster, non-randomized trial published by Axelsson et al in 2006, the authors noted critical delays averaging 6 minutes between arrival of the EMS team and the start of mechanical chest compression. The authors noted that manual compression could be delivered in the interim, and that the delay may decrease with experience (the delay had decreased from 6 to 4 minutes by the second year of the trial).

88 Ibid.
Nevertheless, they acknowledged that in spite of these factors, “the delay between collapse and the start of mechanical chest compression is unacceptably long.”

**D. Additional Issues Arising in Clinical Practice**

In addition to delays and interruptions in CPR attributable to use of AECCs, evidence from adverse event reports reveals a number of instances in which malfunctions led to further interruptions in chest compressions during CPR. In most of these reports, it is not clear how long these delays lasted before chest compressions were resumed. For example, in one report submitted by Zoll Circulation in May 2011:

A zoll autopulse platform model 100 (redacted) malfunctioned during a field resuscitation attempt for a male (patient) aged (redacted) old. The (patient) had a reportedly unwitnessed cardiac arrest outdoors while moving his lawn. The autopulse device was applied to the (patient) and activated. The on scene supervisor confirms that the device was correctly deployed. The device appeared to work normally, delivering compressions to the (patient) for several (minutes). After several (minutes) of operation, the device stopped compressions. The battery was replaced in an attempt to restart the device. After exchanging the battery, the device issue was not resolved. The device was removed from the (patient) and manual chest compressions were initiated for the duration of the transport of the (patient) to the emergency facility. While removing the device, tears in the lifeband sheath and creases in the internal band were noted. The band was found to be jammed against the guide mechanism on both sides. The (patient) was delivered to the hospital using manual chest compressions. The (patient) was pronounced deceased in the emergency department after the physician consulted with the (patient)’s family.

Another report described an incident with a piston AECC device, submitted by Michigan Instruments in July 2010:

It was reported that during a use of the device to provide cardiopulmonary resuscitation, the compression depth became less and less until the compressions eventually stopped. The device was returned to the distributor in (b)(4) for repair. After the repair in (b)(4), the customer reported that it was now not performing ventilations. The unit was removed from the [patient] and manual cpr continued. The [patient] was not revived.

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In another report related to the same piston AECC device, submitted in February 2007, Michigan Instruments stated:93

As reported, the device did not deliver consistent compression depth after approximately 20 minutes of operation. Started malfunctioning during a call. The thumper did the correct depth of compressions, after approximately 20 mins, it would stop and then go only approximately 1/2 of selected depth.94

It is not clear from these reports how much time elapsed as emergency medical personnel attempted to identify and resolve issues with the devices, whether manual compressions were effectively delivered during these gaps, or whether these issues delayed or caused interruption in other elements of CPR delivery, such as defibrillation.

Moreover, studies have demonstrated that better training alone is not sufficient to address potential issues with improper device deployment. A recent manikin study of 21 Swedish ambulance crews that had previously introduced mechanical compression devices into clinical practice compared CPR delivery with manual compressions versus compressions using a piston AECC device. Staff had received a training program in the use of the device that included a four-hour hands-on training with an instructor from the manufacturer, complemented by at least one local training session. The training program focused on application of the device, correct positioning and the use of a stabilization strap. During the study, each crew was asked to perform two 10-minute full CPR scenarios according to their ordinary CPR protocol, one using mechanical compressions and one with only manual compressions. In spite of the training they had received from the manufacturer, only 12 out of 21 of the crews applied the mandatory stabilization strap on the device, resulting in a reduced rate of adequate compressions with the device (58%) compared to manual CPR (88%) (95% CI for the difference: 13–50%).95

Use of AECC devices also may encourage emergency medical personnel to modify clinical practice in ways that extend transport periods, increasing the time between the initiation of CPR and hospital admission. Zoll Circulation, an AECC manufacturer, reported to FDA in its 515(i) submission that the company had received anecdotal reports that patients in some parts of the U.S. were being treated with mechanical CPR and delivered to a regional “center for resuscitation excellence” rather being taken first to what would presumably be a closer emergency care facility to be stabilized prior to transfer for specialized care. The company stated “a clinical treatment approach like the one described above can only be reasonable (sic) accommodated with mechanical CPR.”96 It is unclear whether the risks of extending transport time are balanced by the benefits of receiving care at a regional center, as there have been no studies to date validating this practice.

E. Expert Opinion

Expert groups have concluded that AECC devices could not be recommended for routine or widespread use. The AHA recently reviewed the evidence of safety and effectiveness of two types of AECCs: those that rely on a piston device to administer compressions and those that rely on a constricting band or vest.97 Considering piston devices, the AHA noted that no clinical trial had demonstrated improvement in short- or long-term survival with the use of piston-driven AECCs compared to manual CPR. The AHA concluded, “[t]here is insufficient evidence to support or refute the routine use of mechanical piston devices in the treatment of cardiac arrest.”

Considering band or vest AECCs, the AHA noted that while case series showed promising results, the only prospective randomized, controlled trial comparing band or vest AECCs to manual CPR, the ASPIRE trial, “raised concerns about possible harm with use of this device.” The AHA concluded that while the device could be considered in specific settings, “there is insufficient evidence to support the routine use of the LDB in the treatment of cardiac arrest.”

A 2011 review by the Cochrane Collaboration came to similar conclusions. Noting the disturbing survival and neurological outcomes from the ASPIRE trial, but citing methodological concerns, the reviewers concluded:

There is insufficient evidence from human RCTs to conclude that mechanical chest compressions during cardiopulmonary resuscitation for cardiac arrest is associated with benefit or harm. **Widespread use of mechanical devices for chest compressions during cardiac is not supported by this review.** More RCTs that measure and account for CPR process in both arms are needed to clarify the potential benefit from this intervention.98

IV. Discussion

A. Prior to reclassifying the external cardiac compressor device type, the FDA must convene a subsection (b) device advisory panel to consider the question of reclassification.

Under the reclassification provision of the Food and Drug Administration Safety and Innovation Act (“FDASIA”), *codified as 21 U.S.C. § 360c(e)*, the FDA may change the classification of a device based on “new information” only after carrying out the following three actions: (1) “publication of a proposed reclassification order in the Federal Register,” (2) “a meeting of a device classification panel described in subsection (b),” and (3) “consideration of comments to a public docket. . . .”99 In construing these requirements, the courts will look to the plain meaning of the text, keeping in mind that “words of a

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99 Pub. L. 112-144. *Codified as 21 U.S.C. § 360c(e).*
It is obvious from reading the paragraph as a whole that the purpose of the device classification panel meeting is to allow the panelists an opportunity to consider the “new information” that forms the basis of the proposed reclassification decision and provide advice to the FDA that will inform the agency’s final order.

The FDA has not convened a subsection (b) device classification panel to consider the proposed reclassification of AECC devices or advise the agency on that topic. In its notice of proposed order to reclassify the external cardiac compressor device type, the FDA states that two device classification panels, the Cardiovascular Device Classification Panel and Anesthesiology Device Classification Panel, met sometime between March 9, 1979 and February 5, 1980 and recommended that the device type initially be classified into class III. These two device panel meetings obviously do not satisfy the requirement of § 360c(e), as the classification panels that met in 1979-80 did not have the opportunity to consider the device reclassification that the FDA first proposed in 2012, nor did the panels have opportunity to consider the new information upon which the proposal was based. For the FDA to consider the advice from “a meeting of the device classification panel” that is more than 30 years old and directed toward another topic besides the proposed reclassification order is akin to suggesting that the FDA could meet its statutory obligation to consider “comments to a public docket” by responding to decades-old comments from a different rulemaking process. It is clear that the FDA must convene a new meeting of an appropriate device classification panel prior to issuing a final order to reclassify the device, and that the panel should have opportunity to consider the FDA’s proposal and view the new information on which the proposal is based.

The FDA also should move immediately to update the regulations governing reclassification in 21 C.F.R. § 860.130, so that the regulations reflect the procedural changes effected by the FDASIA. This change is necessary because the current regulations incorrectly suggest that a classification panel meeting is optional with respect to proposed reclassifications, rather than mandatory. 101

B. The FDA should retain automated external cardiac compressor (AECC) devices in Class III because general and special controls are insufficient to provide reasonable assurance of safety and effectiveness.

The FDA may reclassify a Class III device to Class II if the agency “determines that special controls would provide reasonable assurance of the safety and effectiveness of the device and that general controls would not provide reasonable assurance of the safety and effectiveness of the device.” 102 With respect to AECC devices, neither general controls nor special controls are sufficient to provide reasonable assurance of safety and effectiveness, because evidence from randomized controlled clinical

101 21 C.F.R. § 860.130(d). Last revised by 57 F.R. 58404, Dec 10, 1992 (Westlaw, Accessed April 5, 2013). These regulations continue to direct the agency to apply standard administrative rulemaking procedures and leave the subsection (b) advisory panel meeting requirement as a discretionary option, stating: “The rulemaking procedures in § 10.40 of this chapter apply to proceedings to reclassify a device under section 513(e), except that the Commissioner may secure a recommendation with respect to a proposed reclassification from the classification panel to which the device was last referred.” Id. (emphasis added).
102 21 U.S.C. § 360c(e).
trials indicates that AECC devices probably increase the risk of death and neurological damage compared to manual compressions, the appropriate standard care comparator.

In the ASPIRE trial,\(^{103}\) the only well-powered randomized, controlled clinical trial conducted to date, nearly twice as many subjects who received manual cardiopulmonary resuscitation (CPR) survived to hospital discharge and were significantly more likely when compared to subjects treated with the load-distributing band AECC device (LDB-CPR). These results may have been even more pronounced had the study not been halted early after a planned interim assessment revealed significant harms to the device-treated group.

Given the harm demonstrated in the ASPIRE trial, the FDA cannot state with any degree of certainty, let alone “reasonable assurance,” that AECC devices are effective in preventing death and brain damage when used in CPR. This remains true even if the results of the ASPIRE trial had run counter to expectations from prior studies. These prior studies relied on surrogate markers such as end-tidal CO\(_2\),\(^{104,105}\) or enrolled only a small number of patients.\(^{106,107,108}\) None of these studies were designed to detect any differences in clinically meaningful outcomes, such as survival to hospital discharge.\(^{109}\) The studies therefore cannot possibly refute the survival and neurological outcomes seen in the ASPIRE trial.

The results of the ASPIRE trial are clear even if the exact mechanism for the negative outcomes observed in that trial remains unknown. It is plausible that the negative outcomes are due to delays and interruptions in the delivery of CPR caused by the device. Alternatively, the negative outcomes observed may be due to some indiscernible bias in the design of the trial. Yet ultimately, the FDA need not assure itself of the precise reasons why a device has been demonstrated ineffective and unsafe in order to retain the device in Class III and require premarket approval. This is because the party seeking to reclassify the device bears the burden of proving that the device meets the requirements for reclassification.\(^{110}\) If such burden is not met, the FDA must retain the device in Class III. Prior to reclassifying to Class II, the FDA must determine, based on new information in the form of valid scientific evidence, that proposed general and special controls are sufficient to provide reasonable assurance that the device is safe and effective. None of the evidence currently available can support such a determination.

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\(^{106}\) Ibid.


\(^{109}\) While one study, Halperin et al., achieved a statistically significant difference in 24-hour survival, with more patients surviving to 24 hours in the device-treated group, no patient in the study survived to hospital discharge, rendering these results of questionable clinical significance.

Moreover, the results seen in the ASPIRE trial probably underestimate potential risks of AECC devices when deployed in the field, where the risk of malfunction and inappropriate use of the device are probably higher. Adverse event reports demonstrate that AECC devices can malfunction in the field in ways that could contribute to additional delays and interruptions in chest compressions during CPR. These malfunctions include: (1) stopping suddenly and unexpectedly,\textsuperscript{111} (2) slowly decreasing compression depth until compressions eventually stop,\textsuperscript{112} and (3) delivering inconsistent depth of compressions.\textsuperscript{113} Moreover, even trained personnel can improperly use AECC devices, with over 40% of the trained ambulance crews in one study failing to properly apply a mandatory stabilization strap, resulting in suboptimal compressions.\textsuperscript{114}

Additional risks may manifest if the device prompts changes in clinical practice. At least one company has reported that use of an AECC device has prompted EMS personnel to modify clinical practice in ways that potentially extend transport periods, increasing the time between the initiation of CPR and hospital admission.\textsuperscript{115} It is unclear whether the risks of extending transport time are balanced by any hypothetical benefits of receiving care at a regional center, as there have been no studies to date validating this practice.

Given the likelihood that the device will malfunction or be used improperly at least some of the time, it is all the more imperative for the FDA to require clear evidence of efficacy when the device functions and is used properly. Without such evidence, the unconscious cardiac arrest victims are placed in a position in which they are forced to gamble their health on a risky and error-prone intervention without any hope of achieving a benefit, even if the device functions and is deployed as intended.

The FDA has supported its proposed order by asserting that the devices “can be regulated as class II devices” because: (1) “it is well-established that chest compressions are crucial to maintaining perfusion and that compressions of adequate rate and depth are necessary to increase the probability of survival in victims of sudden cardiac arrest,” and (2) “fatigue of or inaccessibility to emergency medical personnel may otherwise prevent adequate chest compressions.”\textsuperscript{116} This inference is faulty for three reasons:

- First, while adequate chest compressions are necessary in CPR, effective compressions can be delivered manually, without the assistance of an AECC device. Moreover, the best evidence to

\textsuperscript{116} 78 FR 1164. January 8, 2013.
date indicates that manual CPR is actually superior in efficacy to CPR delivered by an AECC device.

- Second, an AECC device is never appropriate for situations in which “...inaccessibility to emergency medical personnel may otherwise prevent adequate chest compressions,” because the device requires substantial training for safe use. The FDA acknowledges this in its proposed special controls, which require both labeling on clinical training for safe use and the requirement that the sale of the device be restricted to prescription use only.

- Third, while AECC devices may hypothetically improve clinical outcomes in situations in which fatigue would undermine the quality of manual CPR, the best evidence suggests the opposite effect: AECC devices significantly decrease survival with good neurological function compared with manual CPR. Thus, even if manual chest compressions are not adequate in some circumstances, AECC devices have not been demonstrated to provide an improvement in safety and efficacy.

The special controls proposed by the FDA do not provide adequate assurance of safety and effectiveness in light of the current clinical evidence indicating that AECC use is associated with death and brain damage. These special controls include performance testing under “simulated physiological conditions,” testing of various components, labeling describing clinical training for the safe use of the device, restricting the sale of the device to prescription use only, and labeling that includes “information about the patient population for which the device has been demonstrated to be effective.” These special controls are not sufficient because:

- Testing under simulated conditions or testing of various device components is no substitute for well-controlled clinical trials assessing clinical outcomes in real-life clinical settings, because bench testing cannot establish whether the device reduces or causes death, neurological damage, or other injuries at a higher rate than manual CPR when used in clinical practice.

- Restricting the device to prescription use does not mitigate risks, because there is no reasonable assurance of safety and effectiveness even when the device is used by professional personnel in the relatively controlled setting of a clinical trial.

- Describing recommended clinical training in the labeling is grossly inadequate to alleviate the risk that EMS personnel will use an AECC device improperly. Evidence from clinical practice suggests that professional first-responders continue to apply the device improperly at an alarming rate, even after receiving extensive hands-on training from an AECC device manufacturer.

- Finally, requiring labeling to include information on “the patient population for which the device has been demonstrated to be effective” cannot possibly protect the public when the device has not been demonstrated to be effective in any population.

The FDA should not disregard the best available evidence of clinical effectiveness in favor of hypothetical benefits. Instead, the FDA should fulfill its mission as a public health agency and require

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adequate testing of safety and efficacy prior to further exposing the general public to the mass-marketing of these unproven and potentially dangerous devices.

C. The FDA improperly failed to consider death and neurological damage as “risks to health” of the device.

In evaluating the “risks to health” of the device, the FDA failed to properly consider death or neurological injury as a health risk associated with the use of AECC devices. Instead, the agency considered only tissue damage, bone breakage, inadequate blood flow, cardiac arrhythmias or electrical shock, and adverse skin reactions as possible health risks. Yet in the ASPIRE trial, treatment with an AECC device was associated with a significant decrease in the rate of survival with good neurological function at hospital discharge, and with a nonsignificant decrease in overall survival to hospital discharge.

In considering these risks, the FDA cannot find reasonable assurance that the devices are safe without assessing data from randomized, controlled clinical trials. This is because death and neurological damage are common outcomes among patients undergoing CPR. Other injuries, such as broken bones and tissue damage, are also common, both with manual CPR and automated CPR. Adverse event reports submitted to the FDA cannot be reasonably compared with historical data from studies of manual CPR to determine the relative risk of various injuries, because adverse events tend to be under-reported, leading to injury rates that would appear artificially low. Instead, this type of comparison can only be made with data from well-powered randomized controlled trials, submitted through a premarket approval application (PMA).

D. Premarket approval of new devices would remain necessary to test the effectiveness of subsequent modifications.

Even if one version of AECC device were established to be safe and effective – and none have – that evidence would not justify reclassification of the entire device type into Class II. AECC devices work through a variety of different mechanisms, delivering chest compressions using a piston, vest, or load-distributing band. The different mechanisms have the potential to present distinct challenges that could exacerbate safety concerns or result in variable efficacy. Different features may subtly affect performance, for example by extending the amount of time needed to deploy the device or by increasing the chance that the device will be used incorrectly. The only way for the FDA to accurately assess the impact such changes may have on safety and efficacy is by requiring well-controlled clinical trials through the premarket approval process each time a new version of the device is proposed for market entry.

E. Device manufacturers are capable of conducting well-controlled trials to support applications for premarket approval.

It is both feasible and appropriate for the FDA to require PMA submissions from manufacturers of AECC devices to prove the safety and efficacy of these products. The manufacturers of AECC devices

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are capable of conducting well-controlled trials to support such PMAs. For example, Zoll Circulation stated in its 515(i) submission to the FDA that it “continues to invest its efforts in R & D . . .” and would therefore “certainly understand if the FDA concludes that the Device Classification “Compressor, cardiac, external” remains at Class III and requires PMA, particularly if [the requirement] is rigorously applied to all current and future products in this Device Classification.”

Moreover, several protocols for large, well-powered, randomized, controlled trials have been published recently that will provide better evidence on the safety and efficacy of AECC devices. For example, the Circulation Improving Resuscitation Care (CIRC) trial, expected to end in November 2013, is designed as a well-powered, randomized, controlled clinical trial comparing mechanical chest compression using a load-distributing band to manual CPR. The CIRC trial purports to address some of the concerns raised after previous trials, by reducing delays between EMS arrival and initiation of mechanical compressions, verifying compliance, minimizing bias, and adequately powering the study to detect between-group differences. Another large randomized, controlled study, the Prehospital Randomised Assessment of a Mechanical Compression Device In Cardiac Arrest (PaRAMeDIC), expected to end in August 2013, will compare manual CPR to CPR delivered with a piston AECC device.

These protocols prove that the manufacturers of AECC devices are capable of testing the safety and efficacy of their devices. It remains to be seen whether the two proposed studies will confirm the results of the ASPIRE trial, or provide evidence to refute that trial’s results and establish the safety and efficacy of specific AECC devices. Yet the results of these tests cannot be intuited in advance by the FDA or support making a safety and efficacy determination before the trials are complete. Instead, the FDA must require premarket approval and withhold judgment until the safety and efficacy of these potentially dangerous devices can be determined with reasonable assurance.

V. Conclusion

Public Citizen strongly urges the FDA to withdraw its dangerous proposal to reclassify Automated External Cardiac Compressor (AECC) preamendment Class III devices to Class II (special controls) and instead publish a proposed rule that would maintain such devices in Class III and require submission of premarket approval applications (PMAs) for these devices. Clinical trials are required for these life-sustaining devices, because there is not enough information available for the FDA to determine whether

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using these devices in CPR will improve patient outcomes or instead reduce chances of survival and lead to greater brain damage among survivors.

The only large, well-powered, randomized, controlled clinical trial that has ever tested the effectiveness of AECC devices compared with manual CPR found that patients given CPR using AECC devices were significantly more likely to experience brain damage than those given manual CPR. There also was a nonsignificant trend toward lower survival to hospital discharge in the AECC-treated group. Some researchers have criticized this large trial, and it is possible that a better-designed trial may lead to different results in the future. Yet to this day, no other well-controlled clinical trials have provided data that could contradict this relatively strong evidence of harm.

Given the relatively robust evidence that AECC devices cause brain damage and possibly death, the FDA cannot be reasonably assured that AECC devices are safe and effective. Neither general controls, nor any of the special controls proposed by the FDA, are sufficient to compensate for this basic lack of data on safety and efficacy. The FDA should therefore immediately withdraw its existing proposed order and issue a new proposed order confirming the status of these devices as Class III devices and requiring PMAs with data from well-controlled clinical trials. Only through such action can the FDA avoid exposing more victims of cardiac arrest to treatment that may cause brain damage and further narrow their already slim chances of survival.

Thank you for the opportunity to comment on this important matter.

Sincerely,

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