



Medtronic
PHYSIO-CONTROL

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Subject: Reclassification of Automated External Defibrillators [Docket No. 1994N-0418]

To Whom It May Concern:

Medtronic Physio-Control (MPC) is writing to provide information and comments regarding the Food and Drug Administration (FDA) notice of intent to reclassify automated external defibrillators (AEDs).

We support FDA's intent to reclassify AEDs from Class III to Class II. As mentioned in the October 28, 2003 Federal Register, AdvaMed (formally known as HIMA at that time) submitted a petition to FDA on August 14, 1996 on behalf of its members to reclassify these devices to Class II. The petition provided substantial supporting data and rationale related to a Class II designation for AEDs and specific Special Controls for providing reasonable assurance of safety and effectiveness in the regulation of these devices. The information contained in the petition is still relevant today. In addition, there have been several positive efforts and developments in recent years to further demonstrate and enhance the safe and effective use of AEDs.

Public Access Defibrillation Clinical Trial (2000-2003)

Since 1996, the most significant new information regarding the safety and effectiveness of AED use comes from the NIH-sponsored Public Access Defibrillation clinical trial, which recently concluded in the fall of 2003.

The official study website is <http://depts.washington.edu/padctc/> where most aspects of the study purpose, design, protocol and results are found. The website provides the following summary to describe the purpose of the PAD trial:

"Sudden out-of-hospital cardiac arrest (OOH-CA) remains a significant cause of death, in spite of recent declines in overall mortality from cardiovascular disease. Existing methods of emergency resuscitation are inadequate due to time delays inherent in the transport of a trained responder with defibrillation capabilities to the side of the OOH-CA victim.

This is a study of a comprehensive, integrated community approach in which volunteer non-medical responders (lay volunteers without a traditional responsibility to take charge) are trained to use automated external defibrillators (AEDs). This approach is called Public Access Defibrillation (PAD). The hypothesis to be tested is that PAD will significantly increase survival in OOH-CA by reducing the time interval from collapse to defibrillation. The specific aim of this randomized, controlled trial is to measure survival to hospital discharge following OOH-CA in community units trained and equipped to provide PAD, compared to community units trained to

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provide standard care (recognition of OOH-CA, 911 access, cardiopulmonary resuscitation [CPR]).

Participating research sites have identified 1000 distinct units (e.g., public areas, gated communities, shopping malls, airport terminals, casinos, business parks) within their service area that contain a stable population of at least 250 people aged 50 years or greater. Following preliminary data collection, each unit will be randomized to serve as either an intervention or control group. At each site, each unit will be sub-randomized to a retraining strategy/interval. Performance at retraining will be monitored, and longer intervals decreased, if indicated.

Volunteer non-medical responders (e.g., office staff, bank tellers, merchants, and neighborhood volunteers) in both the intervention and control groups will be trained to: a) recognize OOH-CA, b) access 911 or its equivalent, and c) administer CPR. Non-medical responders in the intervention group will also be taught to use an AED promptly while awaiting arrival of the first public safety emergency medical team. The criteria for number and location of trained volunteers and devices will be a maximum 3-minute "walk through" to deliver the AED to the OOH-CA victim.

OOH-CA victims in each of the two groups will be compared with respect to their: a) survival to hospital discharge (Utstein criteria); b) neurological status, c) quality of life, and d) resource use/costs. The incremental cost-effectiveness of volunteer non-medical responder defibrillation will be calculated.

This study will allow us to develop informed public policy regarding the use of AEDs by volunteer non-medical persons."

Preliminary results were reported at the American Heart Association (AHA) Scientific Sessions in November 2003 regarding both the benefits and risks experienced during the multi-center randomized trial. According to a November 11, 2003 press release by NIH:

"The number of survivors of sudden cardiac arrest markedly increased when the victims were helped by community volunteers trained to perform not only CPR but also to use an automated external defibrillator (AED), a device that shocks an ineffectively beating heart back into normal rhythm, according to the results of a large multi-center study funded by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with the American Heart Association."

Also, one of the clinical trial's primary investigators summarized the accomplishments and the absence of serious safety issues:

"This study was a major frontier to cross," said Joseph P. Ornato, M.D., chairman of the PAD steering committee, who presented the findings in Orlando. "We now have the results of the world's largest test of public access defibrillation. We trained almost 20,000 volunteers. They did an incredible job and there were no major injuries or serious safety issues," added Ornato who is Professor and Chairman of the Virginia Commonwealth University Medical Center's Department of Emergency Medicine in Richmond.

A listing of published abstracts and posters presented at the 2003 AHA Scientific Sessions and Resuscitation Science Symposium related to the PAD trial is attached (Attachment 1). Reprints of two abstracts have been attached for your review (Attachments 2 and 3). The first, The Public Access Defibrillation (PAD) Trial, Ornato et al. *Circulation* 2003; 108:2723 summarizes the study's primary purpose, method, results and conclusions. Second, Adverse Events Associated with Lay Cardiac Arrest Response Programs: The PAD Trial Experience, Peberdy et al. Supplement to *Circulation* Vol. 108, No. 17 IV-1-IV-1050, October 28, 2003 summarizes adverse event experiences of the trial. With regard to AED device performance Peberdy concludes that, "AEDs have an exceptionally high safety profile in the PAD setting."

Safety Standards

Extensive work has been done in recent years to update international and U.S. safety standards for external defibrillators, including AEDs. The primary international standard for external defibrillators is the International Electrotechnical Commission (IEC) document 60601-2-4, Medical Electrical Equipment, Part 2-4, Particular requirements for the safety of cardiac defibrillators. The second edition of this standard was published in 2002. This standard amends and supplements IEC 60601-1 (second edition, 1988): Medical electrical equipment – Part 1: General requirements for safety, an FDA-recognized standard. Improvements from the first edition include new and improved safety requirements for AEDs.

Recently, the Defibrillator Standard Committee of the Association for the Advancement of Medical Instrumentation (AAMI) approved the adoption of IEC 60601-2-4 as the new American Standard for external defibrillators. The new standard, AAMI DF80, maintains the full content of IEC 60601-2-4:2002 and also includes additional requirements that the Defibrillator Committee deemed important for standardization for self-adhesive defibrillation electrodes and external pacemakers (as applicable). The new standard replaces the previous AAMI standards, ANSI/AAMI DF2:1996 for manually operated external defibrillators and ANSI/AAMI DF39:1993 for automated external defibrillators (AEDs).

These new international and American standards now provide manufacturers, health care providers and regulators with a harmonized set of requirements for standardized control of key safety and performance aspects of both manual and automated external defibrillators.

American Heart Association

Over the last several years the American Heart Association has continued its leadership in developing clinical research and guidelines for emergency cardiovascular resuscitation. AHA published Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, International Consensus on Science, *Circulation*, 2000; 102(Supplement I). Part 4 of the guidelines, "Automated External Defibrillator, Key Link in the Chain of Survival" provides extensive background, discussion and clinical literature references regarding AEDs and is the most definitive reference on the subject today.

AHA has also addressed the requirements for essential performance of AED ECG rhythm recognition detectors. This topic has been the object of considerable clinical/industry collaboration recently, and has resulted in useful, insightful, and statistically meaningful methods of specifying the performance of such systems. The new IEC and AAMI standards have adopted

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the results of these efforts. AHA published the recommendations in the following reference:

“Automatic External Defibrillators for Public Access Defibrillation: Recommendations for Specifying and Reporting Arrhythmia Analysis Algorithm Performance, Incorporating New Waveforms, and Enhancing Safety, A Statement for Health Professionals From the American Heart Association Task Force on Automatic External Defibrillation, Subcommittee on AED Safety and Efficacy”

This reference may be accessed via the internet at
<http://www.americanheart.org/presenter.jhtml?identifier=1656>

Conclusion

Medtronic Physio-Control believes the recent developments outlined above regarding AEDs provide additional information to demonstrate that readily available special controls exist for FDA to support the reclassification of AEDs to Class II. MPC is not aware of new risks associated with AEDs beyond those identified in the 1996 AdvaMed petition and therefore, the proposed controls provided in the petition are still valid today. MPC believes that such risks are consistent with those of other similar devices classified in Class II and that they do not justify a Class III designation.

Medtronic Physio-Control's position is strengthened by the fact that since 1980 (when FDA classified these devices as a Class III device), the performance of these devices has been well documented, and the techniques for measuring the safety of these devices are well established. It is particularly relevant to stress that these devices have been effectively controlled through premarket notification for the last twenty-three years, strongly suggesting that increased regulation is not needed. Medtronic Physio-Control believes the accumulated data, clinical experience, and extremely low incidence of adverse experiences with these devices clearly demonstrate the appropriateness of a Class II designation.

Thank you for the opportunity to comment in this matter. We trust that the information provided will be useful and supportive of FDA's intent to reclassify automated external defibrillators to Class II. If you have any questions or need additional information, please do not hesitate to call me at 425-867-4329.

Sincerely,

MEDTRONIC PHYSIO-CONTROL CORP.



Michael D. Willingham
Vice President, Regulatory Affairs

**PAD Trial Abstracts Presented at the 2003 AHA Scientific Sessions and
Resuscitation Science Symposium**

1. The effect of time between first retraining and subsequent retraining on AED and CPR skill evaluation in the Public Access Defibrillation (PAD) Trial. Christenson et al. Supplement to Circulation Vol. 108, No. 17 IV-1-IV-1050, October 28, 2003.
2. Characteristics Associated with CPR and AED Skill Retention: Results of the Public Access Defibrillation (PAD) Trial. Reigel et al. Supplement to Circulation Vol. 108, No. 17 IV-1-IV-1050, October 28, 2003.
3. The PAD Study: Input and Output but Not Outcome.e et al. Supplement to Circulation Vol. 108, No. 17 IV-1-IV-1050, October 28, 2003.
4. Computing CPR and AED Skills Assessment Scores. Birnbaum et al. Supplement to Circulation Vol. 108, No. 17 IV-1-IV-1050, October 28, 2003.
5. The Presence of an Automated External Defibrillator (AED) and the Frequency of CPR Performance in the Public Access Defibrillation (PAD) Trial. Sehra et al. Supplement to Circulation Vol. 108, No. 17 IV-1-IV-1050, October 28, 2003.
6. Characteristics of Volunteers Who Respond to Cardiac Arrests: Results from the North American Public. Groh et al. Supplement to Circulation Vol. 108, No. 17 IV-1-IV-1050, October 28, 2003.
7. The effect of time between first retraining and subsequent retraining on AED and CPR skill evaluation in the Public Access Defibrillation (PAD) Trial. Vijayaragahavan et al. Supplement to Circulation Vol. 108, No. 17 IV-1-IV-1050, October 28, 2003.
8. Adverse Events Associated with Lay Cardiac Arrest Response Programs: The PAD Trial Experience. Peberdy et al. Supplement to Circulation Vol. 108, No. 17 IV-1-IV-1050, October 28, 2003.
9. The Public Access Defibrillation (PAD) Trial. Ornato et al. Circulation 2003; 108:2723

The Public Access Defibrillation (PAD) Trial

Presenter: Joseph P. Ornato, MD

Introduction: Over 460 000 Americans die each year from out-of-hospital cardiac arrest (OOH-CA). The purpose of the Public Access Defibrillation (PAD) Trial was to determine whether laypersons trained and equipped to call 9–1–1, perform cardiopulmonary resuscitation (CPR), and use automated external defibrillators (AEDs) in public and residential locations, compared with laypersons trained only to call 9–1–1 and perform CPR, could increase survival for patients experiencing OOH-CA.

Methods: This prospective, community-based, multicenter clinical trial randomized 993 community units at 21 US and 3 Canadian sites to receive volunteer training in CPR (CPR only) or CPR with defibrillation capability (CPR+AED). All volunteer rescuers were laypersons. A 2- to 4-hour course, mostly American Heart Association HeartSaver ABC and Heart-Saver AED training, was provided for CPR-only and CPR+AED arms, respectively. Eligible study units had to have an estimated 50% risk of experiencing one OOH-CA per year. The primary patient population was defined as individuals (age ≥ 8 years) with confirmed, treatable OOH-CA of cardiac etiology. The primary end point was the number of these patients surviving through hospital discharge. A subgroup comparison of residential versus public facilities was prespecified. The primary comparison, per the protocol, utilized a stratified 2-sample *t* test, with site and public/residential as strata. However, since exposure time varied substantially (std. dev.= 5 mo), a secondary analysis and analyses of other outcomes used a Poisson generalized linear model treating facility exposure-months as an offset.

Results: A total of 19 762 volunteer rescuers (17.5/CPR-only unit vs 23.0/CPR+AED unit, $P=0.001$) consented to participate in the trial prior to January 1, 2003. Study units consisted of the following types of locations: shopping (24%); recreation (24%); residential (15%); entertainment complexes (9%); community centers (7%); office complexes (7%); and hotels, factories, transit centers and other facilities (14%). There was a difference between CPR-only and CPR+AED groups with respect to number of OOH-CA (103, .118/unit/yr vs 129, .138/unit/yr), and the difference occurred in the public (69 vs 96) rather than residential (34 vs 33) units (this difference is likely due to differential ascertainment and was an expected result that prompted our a priori decision to use the number of successful resuscitations rather than rates). Characteristics of the events were not different: patient age (72+15 vs 69+15 yrs); % male (65% vs 70%); indoor location (82% vs 76%); nonsedentary activity at time of arrest (66% vs 66%); witnessed (68% vs 76%); initial rhythm ventricular fibrillation (47% vs 39%). Adverse events did not differ between treatment arms (0.2% vs 0.3%). No inappropriate shocks were delivered by lay rescuers. Successful resuscitation in residential units with either CPR-only or CPR+AED was rare (1 vs 1). There were fewer survivors in the CPR-only vs CPR+AED group (15 vs 29, $P=0.042$ adjusted for sequential monitoring; $P=0.039$ adjusted for exposure-months and sequential monitoring).

Conclusion: The number of survivors from OOH-CA in public locations approximately doubles when laypersons trained in CPR are also trained in and provided access to early defibrillation using an AED. The survival rate in residential units was very low (less than 3%) whether or not an AED was available. Finally, the PAD Trial supports the notion that a large number of trained laypersons can use AEDs to provide early defibrillation safely.

Limitation: As of the time of this writing, 1 potential survivor in the CPR+AED arm was still in hospital, in good health, while undergoing a catheterization and possible percutaneous procedures.

Adverse Events Associated with Lay Cardiac Arrest Response Programs

Mary Ann Peberdy, Virginia Commonwealth University Health System, Richmond, VA; Lois Van Ottingham, University of Washington, Seattle, WA; William J Groh, Indiana University School of Medicine, Indianapolis, IN; Jerris Hedges, Oregon Health Sciences University, Portland, OR; Thomas E Terndrup, University of Alabama, Birmingham, AL; Ronald G Pirralo, Medical College of Wisconsin, Milwaukee, WI; Clay N Mann, University of Utah School of Medicine, Salt Lake City, UT; Jonathan Van Zile, University of Cincinnati Medical Center, Cincinnati, OH; Ruchir Sehra, Loma Linda University Medical Center, Loma Linda, CA; for the PAD Investigators

Background: The adverse event profile of widespread implementation of lay volunteer CPR and Public Access Defibrillation (PAD) programs is unknown. The purpose of this study was to investigate the frequency, severity, and type of adverse events (AE) occurring in widespread PAD implementation.

Methods: The PAD trial randomized 993 public and residential units (1,260 individual facilities) at 24 sites in the US and Canada to have on-site, volunteer, lay personnel trained in CPR only vs. CPR+automated external defibrillators (AED). Data on adverse events are reported from 7/21/00 to 3/18/03. An AE is defined as an event of significance that caused or had the potential to cause harm to a patient or volunteer, or a criminal act.

Results: A total of 19,700 lay volunteers were trained in either CPR or CPR+AED and 1,500 AEDs were placed in units randomized to the AED arm. This dataset contained 22,050 unit exposure months. Only 31 adverse events (AE) were reported. There were 2 patient AE: both experienced fractured ribs after volunteer and EMS CPR. There were 7 volunteer related AE: 1 case of muscle pull, 4 experienced emotional stress severe enough to require follow-up and 2 reported pressure to participate by their employer. There did not appear to be any prolonged or irreversible AE to volunteers in either group. There were 22 AED AE: 13 involved devices that were stolen or lost, 3 involved AEDs that were placed in locations inaccessible to the volunteer, 3 AEDs had mechanical problems that did not interfere with patient care or safety, and 3 devices were improperly maintained. No inappropriate shocks and no failures to shock when indicated occurred. There was one patient AE per 1,468 emergency response episodes and 1 volunteer AE per 2,814 volunteers trained. The overall AE profile was 1 event per 711 unit exposure months.

Conclusions: Widespread training of lay persons in CPR and AED is generally safe for the volunteer and the patient. Lay volunteers may report severe, usually transient, emotional stress following response to a potential cardiac arrest. Volunteer emotional well being should be followed after events. AEDs have an exceptionally high safety profile in the PAD setting.