CIRCULATORY SYSTEM
DEVICES PANEL

January 25, 2011

515(i) Regulatory Classification of Automated External Defibrillators

FDA Lead Reviewer
Oscar H. Tovar, MD
Introduction

- Background on the Reclassification Process
- Review Summary
- Discussion of Preliminary Recommendation
- Panel Questions
FDA Review Team

- Oscar Tovar, M.D.  Lead/Medical Officer
- John Sapirstein, M.D.  Clinical
- Ron Kaye  Human Factors
- Linda Ricci  Software
- Charles Ho, Ph.D  Engineering
- Hamed Ghods  Engineering
- Victor Krauthamer, Ph.D.  Electrophysiology
- Luke Ralston  Surveillance
- Melissa Torres  Compliance
- Bradley Quinn  Compliance
Background on Classification Process

FDA categorized device types into one of three classes (1976), as follows:

- **Class I – (premarket notification – 510(k), usually exempt)**
  - low risk devices, e.g., elastic bandages, examination gloves, etc.
  - general controls

- **Class II (510(k), not usually exempt)**
  - moderate risk devices, e.g., powered wheelchairs, infusion pumps, surgical drapes, etc.
  - general and special controls

- **Class III (premarket approval – PMA)**
  - high risk devices, e.g., replacement heart valves, silicone gel-filled breast implants, ICDs, etc.
  - Devices that support or sustain human life, or are of substantial importance in preventing impairment of human health
Because they were in commercial distribution at the time of the enactment of the Medical Devices Amendments of 1976, FDA allowed class III preamendment devices to enter the market by submission and clearance of a 510(k) application.

FDA intended to use the 510(k) process as a temporary measure for class III preamendment devices. However, some preamendment devices, including automated external defibrillators (AEDs), remain in class III subject to 510(k).
Background on Classification Process

FDA is now taking steps to issue regulations for class III devices currently allowed to enter the market via the 510(k) process.

Section 515(i) of the act directs FDA to:

- either reconfirm the device in class III, or
- reclassify the device into Class I or Class II
The purpose of this meeting is to give the panel the opportunity to provide a recommendation for the classification of automated external defibrillators (AEDs) by:

- either reconfirming AEDs into Class III (PMA) or,
- reclassifying AEDs to Class II or Class I [510(k)].
## Pre-Market Comparison: 510(k) and PMA

<table>
<thead>
<tr>
<th>Pre-Market Requirements</th>
<th>Pre-Market Notification 510(k)</th>
<th>Pre-Market Approval PMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bench Testing</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Animal Studies</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Clinical study</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Design is dictated by questions of safety and effectiveness.</td>
<td></td>
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<tr>
<td>Premarket review of manufacturing information</td>
<td></td>
<td>√</td>
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<tr>
<td>Pre-approval inspection.</td>
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</tbody>
</table>
# Post-Market Comparison: 510(k) and PMA

<table>
<thead>
<tr>
<th>Post-Market Requirements</th>
<th>Pre-Market Notification 510(k)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Review of any changes in manufacturing facilities</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Postmarket review of significant manufacturing changes</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Postmarket Studies</td>
<td>522 Postmarket Surveillance Studies (PSS)</td>
<td>Post-Approval Studies or 522 PSS</td>
</tr>
<tr>
<td>Annual reporting</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
Devices to Consider in Classification

- AEDs sold by prescription which include:
  - Semiautomated and fully automated defibrillators
  - Monitor/defibrillators with AED mode
  - AED Accessories

- AEDs sold over-the-counter and their accessories
Device Description

An AED is a device that:
- automatically analyzes the heart rhythm
- delivers an electrical shock to the heart to restore its normal rhythm as an important component of resuscitation efforts

AEDs are used by trained users including lay users in:
- public access defibrillation programs
- first responders
- homes
A monitor/defibrillator includes:

- monitoring capabilities (ECG, SpO2, NIBP, EtCO2, etc)
- manual defibrillation and
- automated defibrillation

These devices are used by medical professionals mostly in hospitals and emergency medical systems.
Indications for Use

Automated external defibrillators are indicated for the termination of:
- ventricular fibrillation (VF) and
- pulseless ventricular tachycardia (VT).

These devices are intended to be used on suspected victims of sudden cardiac arrest. Patients in sudden cardiac arrest are:
- unresponsive and
- do not breathe normally
Risks to Health

- The survival of a patient who has experienced a sudden cardiac arrest depends upon a sequence of events that includes the successful delivery of a defibrillation shock.

- The failure to deliver a defibrillation shock to a patient in VF or pulseless VT can result in permanent injury or prevent the rescue of the patient.
Manufacturer Recommendation for Reclassification to Class II

All AED manufacturers submitted a reclassification petition or recommendation in response to the 515(i) order.

These manufacturers are:
- Cardiac Science Corporation
- CU Medical Systems, Inc
- Defibtech LLC
- Heartsine Technologies, Inc
- Philips Medical Systems
- Physio-Control Corporation
- Welch Allyn
- Zoll Medical Corporation
- Leonhard Lang

All recommended that AEDs be reclassified from Class III to Class II subject to special controls.
Manufacturer Recommendation for Reclassification

The manufacturers responded with the rationale that special controls already exist to provide a reasonable assurance of the safety and effectiveness of AEDs based on:

- Testing to industry standards
- Guidelines e.g. AHA guidelines
- Device labeling
- Guidance documents
- Postmarket surveillance
Review Summaries
Premarket Review

Clinical Studies
Human factors
Animal Studies
Engineering
Software
Clinical Studies

- New devices/features: study design determined by the clinical questions that need to be addressed
- Complement safety and effectiveness questions addressed by preclinical testing – 510(k)
- Used to address new questions of safety and effectiveness - PMA
Clinical Studies

● New defibrillation waveforms with novel shapes, durations, or shock intensities can have significant effects on defibrillation success and require clinical studies.

● In these clinical studies it is possible to use well established requirements and can be reviewed under 510(k). The endpoints include:
  • Successful defibrillation
  • Restoration of spontaneous circulation
  • Survival to hospital admission and hospital discharge

● Study size, typically ≈ 52 subjects per group (new waveform and predicate)
Clinical Studies

● An area of active research, improved survival in sudden cardiac arrest, involves optimizing the delivery of defibrillation shocks during CPR.

● Optimizing the delivery of therapy during resuscitation efforts may raise new questions of safety and effectiveness. Therefore, these studies may require review under the pre-market approval paradigm.
Human Factors

- User interface design quality typically requires users in the design and validation process

- The nature of use for AEDs lends itself well to simulated use testing/validation
Human Factors (Lay use AEDs)

We request manufacturers to provide the following as part of their submission:

- A sample device
- Final version of auditory instructions, labeling, carrying case, and accessories
- Disc-based video recordings of the simulated use studies
The level of HF review on lay use AEDs is an essential element in the determination of the safety and effectiveness of these devices and comparable to the reviews performed for programmable infusion pumps and LVADs.

Although these reviews are not insignificant, AEDs for professional use require less testing and control.
Animal Studies

- Animal data is submitted either to support clinical studies or as stand alone data to demonstrate the safety and effectiveness of a modified shock waveform, a new feature or a new device.

- New features include technology that can improve defibrillation and resuscitation like new sensors, algorithms, etc.
Animal Studies

- Provide reasonable assurance for the safety and effectiveness of adult defibrillation waveforms attenuated for pediatric use

- Currently, the application of the equivalence concept in 510(k) becomes very difficult in some cases of new features, because there is nothing to compare to
Engineering

● FDA currently requests engineering testing of major changes in hardware and software

● Bench testing includes the defibrillation waveform in the form of oscilloscope captures and waveform parameters measurements
Hardware

● Performance standards provide test protocols with pass/fail criteria, which form a common language between manufacturers and FDA for substantiating claims

● If a manufacturer chooses not to comply with an FDA recognized standard, FDA reviews the adequacy of the test methods and results
Software

- Hazard Analysis
  - Hazards and mitigations are more similar to other devices that deliver therapy such as ICDs or wearable defibrillators (PMA)

- Software-based control
  - Highly complex and unique to each device
Software

- Software-based algorithms
  - Critical to determine patient treatment
  - More similar to other treatment devices such as ICDs

- Device self-testing
  - Unique to each device
  - Important as mitigation for device availability and utility

- Design or implementation defects could result in patient harm
Engineering

Fast changes in technology make it difficult to apply the concept of substantial equivalence, i.e. device characteristics cleared 10 years ago may not be adequate now.
Medical Device Reports

Roberta Sullivan
BSN, MPH
Introduction

- FDA receives adverse events as Medical Device Reports (MDRs)
- Receives for both 510(k) and PMA devices
- 21 CFR 803 – mandatory and voluntary
- MDRs housed in MAUDE database
- Most (~80%) reports for external defibrillators are for AEDs
- AEDs are classified as product code MKJ
Frequency

Total MKJ Reports by year

- 2005: 3,336
- 2006: 3,424
- 2007: 3,948
- 2008: 4,742
- 2009: 6,751
- 2010: 6,625
Methods

● Analysis performed on MDRs in the MAUDE database

● Search Criteria
  • Product codes: MKJ
  • Date received by FDA: 1-JAN-2005 to 31-MAR-2010

● Emphasis on REPORT RATE, DEVICE PROBLEMS, and DEVICE EVALUATION
Description and Analysis

Data was analyzed according to:

1. Event type by year
2. Device problem code by year
3. Manufacturer evaluation code by year
4. Confirmed component failures
Type of event by Year received

- **Malfunction**: 3,084, 3,130, 3,787, 4,593, 6,489, 6,175
- **Injury**: 11, 20, 9, 18, 15, 30
- **Death**: 126, 103, 120, 108, 184, 279
- **Other**: 115, 171, 32, 23, 63, 141
Device Problems

- MDRs describe adverse events using one or more Device Problem Codes
  - Note: one MDR can list multiple codes so the total is greater than the number of MDRs
- Redundant codes were consolidated
  - e.g. failure to shock, failure to discharge, failure to deliver energy, etc.
- The by-year analysis showed a consistent increase the number of MDRs among all device problem codes
## Device Problem by Year

<table>
<thead>
<tr>
<th>Event (Bold terms are consolidated)</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>Total*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device displays error message</td>
<td>1713</td>
<td>1696</td>
<td>1523</td>
<td>1676</td>
<td>1567</td>
<td>33</td>
<td>8208</td>
</tr>
<tr>
<td>Failure to power-up</td>
<td>432</td>
<td>583</td>
<td>750</td>
<td>907</td>
<td>1271</td>
<td>29</td>
<td>3972</td>
</tr>
<tr>
<td>Device inoperable or operates differently than expected</td>
<td>189</td>
<td>177</td>
<td>185</td>
<td>294</td>
<td>967</td>
<td>63</td>
<td>1867</td>
</tr>
<tr>
<td>Failure to discharge</td>
<td>202</td>
<td>286</td>
<td>278</td>
<td>368</td>
<td>592</td>
<td>24</td>
<td>1747</td>
</tr>
<tr>
<td>No display or display/alarm failure</td>
<td>231</td>
<td>201</td>
<td>272</td>
<td>312</td>
<td>391</td>
<td>13</td>
<td>1419</td>
</tr>
<tr>
<td>Electrical</td>
<td>65</td>
<td>52</td>
<td>94</td>
<td>184</td>
<td>318</td>
<td>9</td>
<td>722</td>
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<tr>
<td>Failure to charge</td>
<td>71</td>
<td>95</td>
<td>127</td>
<td>164</td>
<td>114</td>
<td>8</td>
<td>579</td>
</tr>
<tr>
<td>Failure to pace or properly pace</td>
<td>64</td>
<td>66</td>
<td>53</td>
<td>56</td>
<td>179</td>
<td>7</td>
<td>425</td>
</tr>
<tr>
<td>Output specifications</td>
<td>34</td>
<td>43</td>
<td>45</td>
<td>92</td>
<td>47</td>
<td>3</td>
<td>264</td>
</tr>
<tr>
<td>Inappropriate prompts</td>
<td>11</td>
<td>5</td>
<td>4</td>
<td>24</td>
<td>37</td>
<td>2</td>
<td>83</td>
</tr>
<tr>
<td>Inappropriate shock</td>
<td>20</td>
<td>11</td>
<td>14</td>
<td>14</td>
<td>22</td>
<td>1</td>
<td>82</td>
</tr>
<tr>
<td>Software</td>
<td>1</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>37</td>
<td>2</td>
<td>51</td>
</tr>
<tr>
<td>Failure to convert rhythm</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>20</td>
<td>15</td>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>Failure of device to self-test</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>16</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Physical Component</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>2314</td>
<td>2458</td>
<td>2472</td>
<td>2864</td>
<td>3221</td>
<td>81</td>
<td>19493</td>
</tr>
</tbody>
</table>
Device Problems

#1- Device displays error message

- Most common failure mode
- Over 40% of MDRs use this code
- Nearly 20% of death reports use this code
- Vague narrative statements e.g. “during functional testing the device displayed a ‘unit failed’ message”
- Difficult or impossible to determine root cause or causal inferences
Device Problems

#2- Failure to power-up

• Fastest growing problem code
• These reports have nearly tripled since January 2006
• Example “the customer reported that the device failed to power up”
• Almost always the result of component or subassembly failure – not battery failure
<table>
<thead>
<tr>
<th>Count (N=25,632)</th>
<th>Top 10 Manufacturer Evaluation Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>17,330</td>
<td>DATA ELEMENT IS BLANK</td>
</tr>
<tr>
<td>3,414</td>
<td>Component/subassembly failure</td>
</tr>
<tr>
<td>2,749</td>
<td>Other (code unspecified, describe in H.10)</td>
</tr>
<tr>
<td>751</td>
<td>Device performed according to specifications</td>
</tr>
<tr>
<td>169</td>
<td>Mechanical problem (i.e. pump, motor, wiring, cable, battery, etc.)</td>
</tr>
<tr>
<td>158</td>
<td>Electrical problem – operating outside specifications</td>
</tr>
<tr>
<td>143</td>
<td>Negative results of device testing</td>
</tr>
<tr>
<td>112</td>
<td>Electrical problem (unspecified)</td>
</tr>
<tr>
<td>111</td>
<td>Manufacturing – process</td>
</tr>
<tr>
<td>149</td>
<td>Electrical problem – open circuit or short circuit</td>
</tr>
</tbody>
</table>
Device Evaluation

- 66.5% of reports did not have any manufacturer evaluation

- Possible confounding factors:
  1. Device not returned to manufacturer
  2. The use of initial reports and follow-up reports

- Most common evaluation result was component or subassembly failure
## Top 10 Component Codes

<table>
<thead>
<tr>
<th>Count*</th>
<th>Device Component Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,237</td>
<td>PC (printed circuit) board</td>
</tr>
<tr>
<td>650</td>
<td>Circuit board</td>
</tr>
<tr>
<td>514</td>
<td>Cable</td>
</tr>
<tr>
<td>363</td>
<td>Defibrillation subassembly</td>
</tr>
<tr>
<td>314</td>
<td>Battery</td>
</tr>
<tr>
<td>314</td>
<td>Transistor</td>
</tr>
<tr>
<td>309</td>
<td>Connector</td>
</tr>
<tr>
<td>305</td>
<td>Switches</td>
</tr>
<tr>
<td>213</td>
<td>Capacitor</td>
</tr>
<tr>
<td>176</td>
<td>Display</td>
</tr>
</tbody>
</table>

*Each report can list multiple Evaluation Results Codes

*CDRH / FDA/ DHHS*
Conclusions

● Total reporting increased – more than doubled from 2005 up to 2010

● The increase is consistent among event types and problem codes

● Reasons for the increased number of reports cannot be determined conclusively
Conclusions

- 66.5% of failed devices never report a root cause and are never evaluated by the manufacturer

- Despite the high volume of reporting and serious nature of adverse events, MDRs do not include a trend analysis or comparative data for even the most common failure modes
Conclusions

- Annual reporting would improve overall surveillance by:
  - Enabling FDA to possess trend data and distribution data such as units sold, units returned for cause, and units still in use
  - Requiring reporting of manufacturing changes to gain a better understanding of the types of changes that are occurring and the reasons for those changes
Compliance Analysis Overview

- Postmarket Data Review and Analysis
  - Recalls
  - Inspections
  - Regulatory Actions

- Current Tools

- Discussion
Recall Analysis

68 Voluntary recalls conducted by Automated External Defibrillator (AED) manufacturers from January 2005 – August 2010.

- 17 were classified as Class I
- 48 were classified as Class II
- 1 was classified as Class III
- 2 were Safety Alerts
Number of Recalls per Year
1/2005 – 8/2010

* 2010 data only includes recalls classified between Jan.- Aug. 2010

* 2010 data only includes recalls classified between Jan.- Aug. 2010

CDRH / FDA/ DHHS
Recall Analysis: QS Failures

- Purchasing Controls and Receiving Acceptance Activities
- Design Controls
- Production and Process Controls and Process Validation
- In-process and Final Acceptance Activities

- Limitations of analysis
In 2006, AEDs were included in a Risk Based Work Program (RBWP)

- Four out of nine inspections resulted in a classification of Official Action Indicated (OAI) and the issuance of at least two Warning Letters.
Inspections

- AED firms are inspected more frequently than most other 510(k) devices.
  - Increased frequency based in part on Directed Inspection requests and RBWP assignments.
  - Often resulting from increased number of recalls or Medical Device Reports.
- QS deficiencies often identified during the inspections.
Regulatory Actions

- Nine Warning Letters have been issued to AED manufacturers since 2005 citing issues in:
  - Quality System (QS)
  - Medical Device Reporting (MDR)
  - Corrections and Removal
  - Medical Device Tracking
- One Consent Decree (Injunction)
Regulatory Actions

- Top 5 Common Quality System Problems identified in Warning Letters:
  - Corrective and Preventive Action
  - Complaint Handling
  - Design Controls
  - Nonconforming Product
  - Purchasing Controls and Servicing
Current Surveillance Methods

- Awareness of problems through internal pathways or external complaints.
  - Adverse Events
  - Design Issues
  - Whistleblower Complaint
  - Trade Complaint

- Issue inspectional assignments or guidance to address issues.
  - Routine Inspections
  - Directed Inspections
Current Surveillance Methods

● **Awareness of problems through inspections.**
  - Find serious deficiencies in the firm’s quality system.
  - Safety issues that should be recalled by the manufacturer.
  - Voluntary recall may not occur after discussion with firms that may take months or years after knowing devices are defective.
  - Can often be seen in the spike of recalls following an inspection.
Compliance Conclusions

- Current general controls in place are not sufficient to ensure devices remain safe and effective.
- Issues identified with recalls, inspections, and regulatory actions occur after the AEDs have been manufactured and distributed using flawed procedures and processes.
Compliance Discussion

To ensure safety and effectiveness:

- Premarket review of manufacturing information including procedures and processes.
- Preapproval inspections.
- Review of any changes in manufacturing facilities.
OC can ensure that a manufacturer has adequate systems in place for tracking, trending, and taking appropriate corrective actions on potential safety issues once they have been identified.
Compliance Discussion

● Additional postmarket assurances through:
  • Postmarket review of significant manufacturing changes to ensure that the changes are adequately evaluated and tested prior to implementation.
  • Annual reporting of manufacturing changes to gain a better understanding of the types of changes and reasons for implementation.
Preliminary Recommendation
Preliminary Recommendation

Based on the data reviewed and the current regulatory structure of 510(k) and PMAs; our preliminary recommendation is that AEDs be classified as Class III medical devices and be subject to the regulations in accordance with premarket approval (PMA) applications.
Downclassification of AEDs

Perspective from a clinician-reviewer

John S. Sapirstein, M.D.
Consideration of Alternative Opinion

Not a dissenting recommendation

FDA Commissioner: Innovation and regulation

“...scientific discovery is moving much faster than is the ability to translate those advances into real-world products. We are failing, as a scientific community and as a nation, to adequately deliver the promise of science to diagnose, treat, prevent, or cure disease. We can bridge this gap, but success will require that we work together on a new set of flexible standards of product review for the 21st century through the emerging field of regulatory science... We must invest in regulatory science to develop new methods, assays, standards, and models that will help speed the development, review, and approval of medical products that patients need and can rely on.”

Consideration of Alternative Opinion

Concerns with PMA approach

• Rapid pace of AED development
  Will it overwhelm the PMA review process?

• Real and perceived burdens of PMA paradigm
  Will they discourage innovation and refinement?

• Limiting to regulatory flexibility
  Successful precedent for a “non-PMA” approach
  Humanitarian Use Devices

Can Class II better benefit the public health?
Consideration of Alternative Opinion

Can Class II provide adequate safeguards?

• Class II device must first demonstrate “not” Class III
  • New questions of safety or effectiveness
  • Individual Class III devices generally cannot become Class II

• FDA has developed complex Special Controls in past
  Software
    • Bone Sonometers, 2008
    • Computerized Labor Monitoring Systems, 2007

Electrical Output
  • Transcutaneous Electrical Nerve Stimulator for Pain Relief, 2010 (draft)

“High-Risk” devices
  • Certain Percutaneous Transluminal Coronary Angioplasty Catheters, 2010
  • Coronary and Carotid Embolic Protection Devices, 2008
  • Vascular and Neurovascular Embolization Devices, 2004
Consideration of Alternative Opinion

Potential benefits of Class II AEDs

• Ensuring clinical data requirements are device-specific
  • Trials may delay timely introduction of new technology
    Clinical data not always necessary or appropriate

• Does PMA designation affect scope of clinical trials?
  “Most original PMAs and some supplements require clinical data in order to meet the statutory threshold for approval.”

  “Clinical data are not required for most 510(k)s. Consequently, the Agency should clearly document the issue that warrants a request for such data. In addition, FDA should work with industry to identify the type and extent of data that will be required for clearance.”

    (Final Guidance for FDA and Industry, 10/4/2002)

• All Special Controls provide for appropriate clinical trials
Consideration of Alternative Opinion

Potential benefits of Class II AEDs

- Consistent with FDA’s Least Burdensome Principles
  
  “… to encourage the timely development of new medical device technologies.”

- May avoid consequences of expanded regulatory oversight

- Substantial Equivalence is a focussed determination
  
  “…unless there is a substantial likelihood that the problem may present a risk to health.”

- Disincentive to design iterations
Discussion of Preliminary Recommendation

● FDA understands the importance of maximizing the availability and innovation of AEDs for the public health

● At the same time, FDA has identified serious post market deficiencies related to AEDs arising from:
  • analysis of adverse event reports
  • AED recalls, and
  • information from FDA inspections of manufacturers
FDA has identified the following requirements as necessary to address these problems:

- Premarket review of manufacturing information
- Pre-approval inspections
- Review of any changes in manufacturing facilities
- Postmarket review of significant manufacturing changes
- Annual reporting
## Regulatory Pathways for AEDs

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<td>Same</td>
</tr>
<tr>
<td><strong>Animal Studies</strong></td>
<td>Extensive review of test protocols and reports.</td>
<td>Same</td>
</tr>
<tr>
<td><strong>Clinical study</strong></td>
<td>Extensive review of test protocols and reports.</td>
<td>Same</td>
</tr>
<tr>
<td><strong>Manufacturing Review</strong></td>
<td>Have the authority</td>
<td>Substantial review of manufacturing information</td>
</tr>
<tr>
<td><strong>Pre- Approval Inspections</strong></td>
<td>Have the authority</td>
<td>Pre-approval inspections are conducted</td>
</tr>
</tbody>
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## Regulatory Pathways for AEDs

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<tr>
<td><strong>Manufacturing Process Changes</strong></td>
<td>Would require issuance of guidance</td>
<td>Premarket review of significant manufacturing changes</td>
</tr>
<tr>
<td><strong>Manufacturing Site Changes</strong></td>
<td>Would be reviewed when process changes are included</td>
<td>Premarket review conducted and eligible for inspection</td>
</tr>
<tr>
<td><strong>Postmarket Surveillance Studies</strong></td>
<td>522 Postmarket Surveillance Studies (PSS)</td>
<td>Post-Approval studies or 522 PSS</td>
</tr>
<tr>
<td><strong>Annual Reporting</strong></td>
<td>Not submitted</td>
<td>Routine review of Annual Reports</td>
</tr>
</tbody>
</table>
Discussion of Preliminary Recommendation

If FDA were to reclassify AEDs into class II subject to 510(k), FDA would need to create special controls for:

- manufacturing requirements
- scientific and clinical requirements
  - engineering
  - software
  - human factors
  - animal studies
  - clinical studies
Discussion of Preliminary Recommendation

- The additional requirements recommended for AEDs under 510(k)s are already integrated in the PMA paradigm

- There is a lack of precedent for these requirements as special controls
FDA has significant concerns that the number and types of special controls required for the 510(k) with special controls for AEDs would create a parallel regulatory paradigm. A parallel paradigm that would significantly blur the line between a 510(k) and a PMA.
Based on the data reviewed and the current regulatory structure of 510(k) and PMAs; our preliminary recommendation is that AEDs be classified as Class III medical devices and be subject to the regulations in accordance with premarket approval (PMA) applications.