Overview of the 2012 Food and Drug Administration circulatory system devices panel meeting on the reclassification of external counterpulsation, intra-aortic balloon pump, and non–roller-type cardiopulmonary bypass blood pump devices

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The Food and Drug Administration held a Circulatory System Devices Advisory Panel meeting, December 5 and 6, 2012, to review the classification or potential reclassification of the following device types: external counterpulsation, intra-aortic balloon pump (IABP), and non–roller-type cardiopulmonary bypass blood pumps. These 3 devices are preamendment (Medical Device Amendments of 1976) class III devices. The advisory panel discussed the data and provided recommendations for reclassification of these devices. The panel recommended reclassification of ECP to class II for stable angina pectoris and to retain a class III for all other indications. For IABP, the recommendation was to reclassify IABP to class II for several indications (acute coronary syndrome, cardiac and noncardiac surgery, and heart failure complications) and remain class III for all other indications. As for non–roller type, the panel recommended that for cardiopulmonary bypass and temporary circulatory bypass, these devices should be reclassified to class II while retaining a class III device status for all other indications, including ventricular support both for hemodynamically unstable patients and for prophylactic support in high-risk percutaneous interventions. (Am Heart J 2013;166:414-20.)

To release a medical device into the US market, the device must first be classified into 1 of 3 categories based on the controls needed to mitigate risks to human health (Table I). Devices are placed into the lowest class for which specified controls provide reasonable assurance of safety and effectiveness.[1] Any medical device that is implantable, life-supporting, or life-sustaining is a class III device unless both of the following criteria are met: (1) reasonable assurance of safety and effectiveness exists and (2) identification of the risks to health can be supported by data (Title 21 CFR 860.93).[2] For example, stents are considered class III devices.

The premarket approval (PMA) application is the Food and Drug Administration's (FDA's) process for scientific and regulatory review of the safety and effectiveness of class III devices (section 515 of the Food, Drug & Cosmetic Act).[3] Many devices, however, were in commercial distribution before May 28, 1976, the date the Medical Device Amendments were signed into law. The FDA labeled these devices as "pre-amendment" and cleared them via the class III 510(k) notification program as a class III device. The amendment mandated that all such devices would require a PMA once the FDA published a regulatory announcement calling for PMA submissions. Before this call, the FDA would (1) issue a 515(i) order requesting references, documentation, and data regarding each device type (issued most recently for the Circulatory System Devices on April 9, 2009)[4] and (2) invite an advisory panel to review the current status of each device type indication cleared as a preamendment class III 510(k) device. The FDA would then seek panel recommendations for the reclassification or affirmation of class III assignment/PMA requirements for each cleared device indication. Panel input, in combination with other available information, helps the FDA develop the final order on updated regulatory requirements for the remaining class III preamendment devices.

On December 5 and 6, 2012, the Circulatory System Devices Panel met to review the following device types:

1. External counterpulsation (ECP),
2. Intra-aortic balloon pump (IABP), and
3. Non–roller-type (NRP) cardiopulmonary bypass blood pump.

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Table I. Food and Drug Administration device classification

Device classification	Controls needed
Class I Devices not intended to help support or sustain life or be substantially important in preventing human health impairment and may not present an unreasonable risk of illness or injury	*General controls* • Defined as provisions that relate to adulteration, misbranding, device registration, good manufacturing practices, etc • Devices typically do not require FDA premarket review before market release
Class II Devices for which general controls alone cannot assure safety and effectiveness, and existing special controls can be established to provide such assurances	*General controls and special controls* • General controls are not sufficient to provide reasonable assurance of safety and effectiveness and special controls would provide such • Special controls are items specific to the device/indication that would allow for mitigations of risks to health • Devices typically require FDA premarket notification before market release
Class III Devices for which insufficient information exists to assure safety and effectiveness solely through the general or special controls sufficient for the above 2 classes	*Requires premarket approval application*

These device types were initially marketed before the amendments and will remain on the market as 510(k) devices until a final order is set forth by the FDA indicating possibly updated regulatory requirements, such as the need to file a PMA.

The FDA requested panel review with 2 general agenda items: (1) Should the device remain as class III and require a PMA application or would down-classification to class I or class II be appropriate based on current scientific knowledge for the device class? (2) Would a split indication for any of these device types be warranted to more appropriately regulate each device class?

The panel reviewed 3 device types during the 2-day session and discussed the classification/reclassification strategy by indication per device. Table II presents the different devices, current status, FDA proposal, and panel recommendations.

External counterpulsation devices

The concept of peripheral counterpulsation, introduced over a half century ago,[5] consists of rapid compressions of the lower extremities by inflatable cuffs during diastole followed by timely deflation during systole. The physiological effect of the pulse wave created by ECP during diastole augments the coronary blood flow and ventricular filling while rapid deflation creates lower resistance in the peripheral arteries, which leads to decreased afterload and heart workload. It is also suggested that ECP has a positive effect on myocardial collateralization through arteriogenesis leading to angina relief.[6,7]

Chronic stable angina

The FDA proposed that, for chronic stable angina, ECP should be reclassified to class II with the rationale to down-classify based on clinical experience, safety profile, and available data from a literature review. The pivotal Multicenter Study of Enhanced External Counter-Pulsation was the largest to explore ECP usage for stable angina.[7] Here, 139 patients were randomized to either ECP or sham ECP. The primary end point, a change in exercise duration, did not differ between the 2 groups (P = .31), but significant differences were noted in both time to ST depression and decreased angina frequency.[8] This and other trials have demonstrated both short- and long-term improvement in Canadian Cardiovascular Society angina class,[8–10] decreased angina frequency,[10] exercise duration,[8,11] and quality of life.[8]

External counterpulsation has a favorable safety profile as evidenced by minimal Medical Device Reports (n = 54) from 2001 to now. During this time period, ≈18,000 to 20,000 patients were treated annually within this period. This safety profile, the suggested effectiveness, and the ability to mitigate the potential health risks (eg, arrhythmia, trauma to limb) supported the panel recommendation to down-classify to class II. Of note, the panel mentioned that the clinical effectiveness data relied on "soft" clinical end points and did not reflect contemporary practice (ie, use of novel antianginal therapies, including ranolazine). The panel recommended reclassification of ECP to class II with special controls for chronic stable angina and should be reserved until current and complete medical therapies are exhausted.

Acute coronary syndrome, congestive heart failure, cardiogenic shock, and peripheral artery disease

Regarding the other currently cleared indications for ECP, only a few trials have addressed the use of ECP for congestive heart failure. The largest trial, PEECH,[12] randomized 187congestive heart failure patients to ECP and medical therapy versus medical therapy only. The primary end point, the increase in exercise duration at 6 months, was significantly longer in patients treated with ECP versus control (35% vs 25%, P = .016), whereas peak VO_2 and New York Heart Association class did not differ.

Only a few observational trials have assessed the use of ECP in peripheral artery disease, acute coronary syndrome (ACS), or cardiogenic shock. The lack of data demonstrating effectiveness, along with uncertainty regarding safety (possible increase in pulmonary congestion in congestive heart failure patients due to increased