



ANNIEAPPLESEEDPROJECT



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Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, Maryland 20852

Comments of Members of the Patient, Consumer, and Public Health Coalition

on Proposed Order

“Cardiovascular Devices; Reclassification of Intra-Aortic Balloon and Control Systems (IABP) for Acute Coronary Syndrome, Cardiac and Non-Cardiac Surgery, or Complications of Heart Failure; Effective Date of Requirement for Premarket Approval for IABP for Other Specific Intended Uses”

[Docket No. FDA-2013-N-0581]

As members of the Patient, Consumer, and Public Health Coalition, we strongly support the FDA’s proposed order for Intra-Aortic Balloon and Control Systems (IABP) devices used to treat septic shock or pulsatile flow generation (Other Specific Intended Uses) to remain in Class III with Premarket Approval applications (PMA) required. The evidence of safety and effectiveness for these indications has not been established. As the FDA noted in its assessment of the device, there is no “theoretical or demonstrated benefit to using the intra-aortic balloon and control systems for this clinical syndrome.”¹

However, we strongly oppose the FDA’s proposed order to down-classify IABPs for Acute Coronary Syndrome, Cardiac and Non-Cardiac Surgery, or Complications of Heart Failure from Class 3 to Class 2. As the FDA’s Circulatory System Devices Panel noted last year, IABPs are “life-supporting devices.” FDA specifies that life-supporting devices should be considered Class III (high-risk devices), and require the more rigorous PMA review, unless special controls are adequate to ensure that the products are safe and effective, making clinical trials, inspections, and other provisions of the PMA process unnecessary. That would be a rare circumstance and is certainly not the case for this device.

We understand that these are life saving devices used in urgent situations where many patients will die regardless of treatment. It is not possible to do randomized clinical trials under those circumstances and that is not what we are suggesting. It would, however, be possible to compare the outcome of patients who were treated with these devices compared to those treated with other devices or other treatments. That's what a PMA could require and we think should require in addition to post-market studies.

FDA's own evaluation of the risks to health associated with the use of IABPs includes more than a dozen serious risks, including cardiac arrhythmias, aortic rupture, large blood clots, balloon entrapment, and death. The Agency stated, "Mechanical failure of the device, vascular complications or bleeding can lead to death." That is exactly why clinical trials, inspections, and other safeguards of the PMA process are essential to protect the health of patients.

According to the FDA's Manufacturer and User Facility Device Experience (MAUDE) database, there have been 21 reports of deaths associated with IABP devices (Product Code DSP) for this year alone (through August 31, 2013). For the last five years (August 31, 2009 through August 31, 2013) there were 119 deaths reported to MAUDE. FDA has downplayed the deaths by stating "that the intended population is a group of patients with high morbidity." However, it is the expected mortality of these patients that is likely to result in even greater under-reporting in the MAUDE system than is usually the case. Physician reporting is voluntary for the MAUDE database, and there is substantial evidence of under-reporting.

A review of FDA's Total Product Life Cycle (TPLC) database shows 7,244 problems with the device including more than 800 balloon ruptures and more than 500 balloon leaks.² The TPLC database also shows eight recalls for IABP devices (six Class II recalls and two Class I recalls) over the last six years. More than 130,000 devices were recalled in the two Class I recalls, which are high-risk recalls that could cause serious health problems or death. The reasons for the Class I recalls were that the "IAB catheter becomes stuck in the sheath...causing a delay in therapy, bleeding or arterial injury,"³ and "a fault in the connector of the pump tubing assembly may result in the volume setting on the pump defaulting to 2.5 cc or 5 ccs...rather than the appropriate 30, 40, or 50 cc volume."⁴

As part of the down-classification of IABPs to Class 2 devices, FDA is proposing special controls but these controls rely on non-clinical testing and non-clinical performance evaluation. These special controls are inadequate to provide reasonable assurance of safety and effectiveness for these complex, life-supporting devices. Also, adding special controls to a 510k review will not provide four essential safeguards that Class III devices receive when they are reviewed under the Pre-market approval process:

1. Proof of safety and efficacy based on short-term clinical trials.
2. FDA's authority to require post-market, long-term clinical trial safety data as a condition of approval.
3. FDA's authority to inspect the manufacturing facility prior to approval.
4. FDA authority to rescind approval if the device is later found to be unsafe.

A major problem with this proposed order is that it splits the device into two classifications (Class III and Class II). A down classification from Class III to Class II (and 510(k) clearance) would not require a sponsor to prove that their product is safe or effective. Even if the device were cleared by the 510(k) process for one particular indication, it could easily be used off-label for treatments that require a PMA. In other words, down-classification for any indication would create an enormous and dangerous loophole that would allow manufacturers to avoid the more rigorous PMA review process.

In addition, the FDA proposal suggests that the safety of IABPs that are currently on the market is the only concern, and suggests that safety has been established. The down-classification of these devices means that companies manufacturing new models with unique characteristics in the future would not be required to prove that their products are safe or effective. The companies would only need to prove that their products are substantially equivalent to other IABPs on the market, and would not require clinical trials to ensure equivalent safety or efficacy. The 510(k) pathway is also inadequate for this device because it does not include inspections to ensure quality control, and there have been significant problems with balloon rupture and leaks in the past. As the Institute of Medicine report on the 510(k) process for Class II devices pointed out, the criteria that the FDA uses to determine equivalence is not sufficient to ensure that the products are safe or effective.

In conclusion, clinical trials are needed to ensure the safety and efficacy of such high-risk, life-sustaining devices. FDA should not approve the IABP for septic shock or any indication unless there is clear evidence of its safety or efficacy. The FDA's TPLC database shows serious problems related to this device and the MAUDE database has recorded deaths associated with this device, which one has to assume is the tip of the iceberg in a voluntary reporting system. For these reasons IABPs should remain class III devices for all indications and all new IABPs should require PMAs.

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¹ Federal Register (June 19, 2013). Cardiovascular Devices; Reclassification of Intra-Aortic Balloon and Control Systems (IABP) for Acute Coronary Syndrome, Cardiac and Non-Cardiac Surgery, or Complications of Heart Failure; Effective Date of Requirement for Premarket Approval for IABP for Other Specific Intended Uses. Docket No. FDA-2013-N-0581.

² Food and Drug Administration's Total Product Life Cycle database (January 1, 1996 – August 31, 2013). Intra-Aortic Balloon and Control system (Product Code DSP).

³ Food and Drug Administration's Medical & Radiation Emitting Device Recalls (December 23, 2010). Recall numbers Z-0969-2011, and Z-0790-2011 through Z-0793-2011

⁴ Food and Drug Administration's Medical & Radiation Emitting Device Recalls (April 16, 2009). Recall numbers Z-1210-2009 through Z-1222-2009.