significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the proposed reclassification would relieve manufacturers of premarket approval requirements of section 515 of the FD&C Act (21 U.S.C. 360e) it would not create new burdens. Thus, the Agency proposes to certify that the proposed rule, if finalized, will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that Agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $139 million, using the most current (2011) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this proposed rule, if finalized, to result in any 1-year expenditure that would meet or exceed this amount.

Our estimate of benefits annualized over 20 years is $11.85 million at a 3 percent discount rate and $7.83 million at a 7 percent discount rate. The change in pre- and post-marketing requirements between a 510(k) and a PMA lead to benefits in the form of reduced submission costs, review-related activities, and inspections. Another unquantifiable benefit from the rule is that a decrease in entry could lead to further product innovation. FDA is unable to quantify the costs that could arise if there is a change in risk which could lead to adverse events, recalls, warning letters, or unlisted letters.

The full discussion of economic impacts is available in docket FDA–2013–N–0544 at *http://www.regulations.gov*, and at *http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/default.htm* (Ref. 4).

XV. Comments

Interested persons may submit either electronic comments regarding this document or the associated Special Controls guideline to *http://www.regulations.gov* or written comments to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at *http://www.regulations.gov*.

XVI. References

The following references have been placed on display in the Dockets Management Branch (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and are available electronically at *http://www.regulations.gov*. (FDA has verified all the Web site addresses in this reference section, but we are not responsible for any subsequent changes to the Web sites after this document publishes in the **Federal Register**.)

1. Transcript of the Tuberculosis Public Workshop, June 7, 2010, (Available at: *http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/CriticalPathInitiative/UpcomingEventsonCPI/UCM289182.doc*, accessed on January 25, 2012.)

2. Transcript of FDA's Microbiology Devices Panel Meeting, June 29, 2011. (Available at: *http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/MicrobiologyDevicesPanel/UCM269469.pdf*.)

3. ''Updated Guidelines for the Use of Nucleic Acid Amplification Tests in the Diagnosis of Tuberculosis,'' *Morbidity and Mortality Weekly Report (MMWR),* vol. 58, pp. 7–10, January 16, 2009. (Available at: *http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5801a3.htm*, accessed on July 26, 2011.)

4. Full Disclosure Preliminary Regulatory Impact Analysis of the proposed rule ''Microbiology Devices; Reclassification of Nucleic Acid-Based Systems for *Mycobacterium tuberculosis* Complex in Respiratory Specimens,'' Docket No. FDA–2013–N–0544.

List of Subjects in 21 CFR Part 866

Biologics, Laboratories, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 866 is amended as follows:

PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES

■ 1. The authority citation for part 866 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

■ 2. Add § 866.3372 to subpart D to read as follows:

§ 866.3372 Nucleic acid-based in vitro diagnostic devices for the detection of Mycobacterium tuberculosis complex in respiratory specimens.

(a) *Identification.* Nucleic acid-based in vitro diagnostic devices for the detection of *Mycobacterium tuberculosis* complex in respiratory specimens are qualitative nucleic acid-based in vitro diagnostic devices intended to detect *Mycobacterium tuberculosis* complex nucleic acids extracted from human respiratory specimens. These devices are non-multiplexed and intended to be used as an aid in the diagnosis of pulmonary tuberculosis when used in conjunction with clinical and other laboratory findings. These devices do not include devices intended to detect the presence of organism mutations associated with drug resistance. Respiratory specimens may include sputum (induced or expectorated), bronchial specimens (e.g., bronchoalveolar lavage or bronchial aspirate), or tracheal aspirates.

(b) *Classification.* Class II (special controls). The special control for this device is the FDA document entitled ''Class II Special Controls Guideline: Nucleic Acid-Based In Vitro Diagnostic Devices for the Detection of *Mycobacterium tuberculosis* Complex in Respiratory Specimens.'' For availability of the guideline document, see § 866.1(e).

Dated: June 12, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013–14552 Filed 6–18–13; 8:45 am]

BILLING CODE 4160–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 870

[Docket No. FDA–2013–N–0581]

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

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed order.

SUMMARY: The Food and Drug Administration (FDA) is issuing a proposed administrative order to reclassify intra-aortic balloon and

control system devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure, a preamendments class III device, into class II (special controls) based on new information. FDA is also proposing to require the filing of a premarket approval application (PMA) or a notice of completion of a product development protocol (PDP) for intra-aortic balloon and control systems when indicated for septic shock or pulsatile flow generation. The Agency is also summarizing its proposed findings regarding the degree of risk of illness or injury designed to be eliminated or reduced by requiring the devices to meet the statute's approval requirements when indicated for septic shock or pulsatile flow generation. In addition, FDA is announcing the opportunity for interested persons to request that the Agency change the classification of any of the devices mentioned in this document based on new information. This action implements certain statutory requirements.

DATES: Submit either electronic or written comments by September 17, 2013. FDA intends that, if a final order based on this proposed order is issued, anyone who wishes to continue to market intra-aortic balloon and control system devices indicated for septic shock or pulsatile flow generation will need to file a PMA or a notice of completion of a PDP within 90 days of the effective date of the final order. See section XVII of this document for the proposed effective date of any final order based on this proposed order.

ADDRESSES: You may submit comments, identified by Docket No. FDA–2013–N–0581, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: *http://www.regulations.gov.* Follow the instructions for submitting comments.

Written Submissions

Submit written submissions in the following ways:

- Mail/Hand delivery/Courier (for paper or CD–ROM submissions): Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the Agency name and Docket No. FDA–2013–N–0581 for this rulemaking. All comments received may be posted without change to *http://www.regulations.gov,* including any personal information provided. For additional information on submitting comments, see the ''Comments'' heading of the **SUPPLEMENTARY INFORMATION** section.

Docket: For access to the docket to read background documents or comments received, go to *http://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Angela Krueger, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 1666, Silver Spring, MD 20993, 301–796–6380, *angela.krueger@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background—Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Pub. L. 94–295), the Safe Medical Devices Act of 1990 (Pub. L. 101–629), the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Pub. L. 105–115), the Medical Device User Fee and Modernization Act of 2002 (Pub. L. 107–250), the Medical Devices Technical Corrections Act (Pub. L. 108–214), the Food and Drug Administration Amendments Act of 2007 (Pub. L. 110–85), and the Food and Drug Administration Safety and Innovation Act (FDASIA) (Pub. L. 112–144), establish a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) established three categories (classes) of devices, reflecting the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513 of the FD&C Act, devices that were in commercial distribution before the enactment of the 1976 amendments, May 28, 1976 (generally referred to as preamendments devices), are classified after FDA has: (1) Received a recommendation from a device classification panel (an FDA advisory committee); (2) published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution prior to May 28, 1976 (generally referred to as postamendments devices), are automatically classified by section 513(f) of the FD&C Act into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval unless, and until, the device is reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807).

A preamendments device that has been classified into class III and devices found substantially equivalent by means of premarket notification (510(k)) procedures to such a preamendments device or to a device within that type may be marketed without submission of a PMA until FDA issues a final order under section 515(b) of the FD&C Act (21 U.S.C. 360e(b)) requiring premarket approval or until the device is subsequently reclassified into class I or class II.

Although, under the FD&C Act, the manufacturer of class III preamendments device may respond to the call for PMAs by filing a PMA or a notice of completion of a PDP, in practice, the option of filing a notice of completion of a PDP has not been used. For simplicity, although corresponding requirements for PDPs remain available to manufacturers in response to a final order under section 515(b) of the FD&C Act, this document will refer only to the requirement for the filing and receiving approval of a PMA.

On July 9, 2012, FDASIA was enacted. Section 608(a) of FDASIA amended section 513(e) of the FD&C Act, changing the process for reclassifying a device from rulemaking to an administrative order. Section 608(b) of FDASIA amended section 515(b) of the FD&C Act changing the process for requiring premarket approval for a preamendments class III device from rulemaking to an administrative order.

A. Reclassification

FDA is publishing this document to propose the reclassification of intra-aortic balloon and control system devices when indicated for acute coronary syndrome, cardiac and non-

cardiac surgery, or complications of heart failure from class III to class II.

Section 513(e) of the FD&C Act governs reclassification of classified preamendments devices. This section provides that FDA may, by administrative order, reclassify a device based upon ''new information.'' FDA can initiate a reclassification under section 513(e) or an interested person may petition FDA to reclassify a preamendments device. The term ''new information,'' as used in section 513(e) of the FD&C Act, includes information developed as a result of a reevaluation of the data before the Agency when the device was originally classified, as well as information not presented, not available, or not developed at that time. (See, e.g., *Holland-Rantos Co.* v. *United States Department of Health, Education, and Welfare,* 587 F.2d 1173, 1174 n.1 (D.C. Cir. 1978); *Upjohn* v. *Finch,* 422 F.2d 944 (6th Cir. 1970); *Bell* v. *Goddard,* 366 F.2d 177 (7th Cir. 1966).)

Reevaluation of the data previously before the Agency is an appropriate basis for subsequent action where the reevaluation is made in light of newly available authority (see *Bell,* 366 F.2d at 181; *Ethicon, Inc.* v. *FDA,* 762 F.Supp. 382, 388–391 (D.D.C. 1991)), or in light of changes in ''medical science'' (*Upjohn,* 422 F.2d at 951). Whether data before the Agency are old or new data, the ''new information'' to support reclassification under section 513(e) must be ''valid scientific evidence,'' as defined in section 513(a)(3) of the FD&C Act and § 860.7(c)(2) (21 CFR 860.7(c)(2)). (See, e.g., *General Medical Co.* v. *FDA,* 770 F.2d 214 (D.C. Cir. 1985); *Contact Lens Association* v. *FDA,* 766 F.2d 592 (D.C. Cir.), cert. denied, 474 U.S. 1062 (1985).)

FDA relies upon ''valid scientific evidence'' in the classification process to determine the level of regulation for devices. To be considered in the reclassification process, the valid scientific evidence upon which the Agency relies must be publicly available. Publicly available information excludes trade secret and/or confidential commercial information, e.g., the contents of a pending PMA. (See section 520(c) of the FD&C Act (21 U.S.C. 360j(c)).) Section 520(h)(4) of the FD&C Act, added by FDAMA, provides that FDA may use, for reclassification of a device, certain information in a PMA 6 years after the application has been approved. This can include information from clinical and preclinical tests or studies that demonstrate the safety or effectiveness of the device but does not include descriptions of methods of manufacture or product composition and other trade secrets.

Section 513(e)(1) of the FD&C Act sets forth the process for issuing a final order. Specifically, prior to the issuance of a final order reclassifying a device, the following must occur: (1) Publication of a proposed order in the **Federal Register**; (2) a meeting of a device classification panel described in section 513(b) of the FD&C Act; and (3) consideration of comments to a public docket. FDA has held a meeting of a device classification panel described in section 513(b) of the FD&C Act with respect to intra-aortic balloon and control system devices, and therefore, has met this requirement under section 515(b)(1) of the FD&C Act.

FDAMA added section 510(m) to the FD&C Act, which provides that a class II device may be exempted from the premarket notification requirements under section 510(k) of the FD&C Act, if the Agency determines that premarket notification is not necessary to assure the safety and effectiveness of the device.

B. Requirement for Premarket Approval Application

FDA is proposing to require PMAs for intra-aortic balloon and control system devices when indicated for septic shock or pulsatile flow generation.

Section 515(b)(1) of the FD&C Act sets forth the process for issuing a final order. Specifically, prior to the issuance of a final order requiring premarket approval for a preamendments class III device, the following must occur: (1) Publication of a proposed order in the **Federal Register**; (2) a meeting of a device classification panel described in section 513(b) of the FD&C Act; and (3) consideration of comments from all affected stakeholders, including patients, payers, and providers. FDA has held a meeting of a device classification panel described in section 513(b) of the FD&C Act with respect to intra-aortic balloon and control system devices, and therefore, has met this requirement under section 515(b)(1) of the FD&C Act.

Section 515(b)(2) of the FD&C Act provides that a proposed order to require premarket approval shall contain: (1) The proposed order, (2) the proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the device to have an approved PMA or a declared completed PDP and the benefit to the public from the use of the device, (3) an opportunity for the submission of comments on the proposed order and the proposed findings, and (4) an opportunity to request a change in the classification of the device based on new information relevant to the classification of the device.

Section 515(b)(3) of the FD&C Act provides that FDA shall, after the close of the comment period on the proposed order, consideration of any comments received, and a meeting of a device classification panel described in section 513(b) of the FD&C Act, issue a final order to require premarket approval or publish a document terminating the proceeding together with the reasons for such termination. If FDA terminates the proceeding, FDA is required to initiate reclassification of the device under section 513(e) of the FD&C Act, unless the reason for termination is that the device is a banned device under section 516 of the FD&C Act (21 U.S.C. 360f).

A preamendments class III device may be commercially distributed without a PMA until 90 days after FDA issues a final order (a final rule issued under section 515(b) of the FD&C Act prior to the enactment of FDASIA is considered to be a final order for purposes of section 501(f) of the FD&C Act (21 U.S.C. 351(f))) requiring premarket approval for the device, or 30 months after final classification of the device under section 513 of the FD&C Act, whichever is later. For intra-aortic balloon and control system devices, the preamendments class III devices that are the subject of this proposal, the later of these two time periods is the 90-day period. Since these devices were classified in 1980, the 30-month period has expired (45 FR 7939; February 5, 1980). Therefore, if the proposal to require premarket approval for intra-aortic balloon and control system devices indicated for septic shock or pulsatile flow generation is finalized, section 501(f)(2)(B) of the FD&C Act requires that a PMA for such device be filed within 90 days of the date of issuance of the final order. If a PMA is not filed for such device within 90 days after the issuance of a final order, the device would be deemed adulterated under section 501(f) of the FD&C Act.

Also, a preamendments device subject to the order process under section 515(b) of the FD&C Act is not required to have an approved investigational device exemption (IDE) (see part 812 (21 CFR part 812)) contemporaneous with its interstate distribution until the date identified by FDA in the final order requiring the filing of a PMA for the device. At that time, an IDE is required only if a PMA has not been filed. If the manufacturer, importer, or other sponsor of the device submits an IDE application and FDA approves it, the device may be distributed for investigational use. If a PMA is not filed by the later of the two dates, and the

device is not distributed for investigational use under an IDE, the device is deemed to be adulterated within the meaning of section 501(f)(1)(A) of the FD&C Act, and subject to seizure and condemnation under section 304 of the FD&C Act (21 U.S.C. 334) if its distribution continues. Other enforcement actions include, but are not limited to, the following: Shipment of devices in interstate commerce will be subject to injunction under section 302 of the FD&C Act (21 U.S.C. 332), and the individuals responsible for such shipment will be subject to prosecution under section 303 of the FD&C Act (21 U.S.C. 333). In the past, FDA has requested that manufacturers take action to prevent the further use of devices for which no PMA has been filed and may determine that such a request is appropriate for the class III devices that are the subject of this proposed order, if finalized.

In accordance with section 515(b) of the FD&C Act, interested persons are being offered the opportunity to request reclassification of intra-aortic balloon and control system devices indicated for septic shock or pulsatile flow generation.

II. Regulatory History of the Device

In the preamble to the proposed rule (44 FR 13369; March 9, 1979), the Cardiovascular Device Classification Panel (the 1979 Panel) recommended that intra-aortic balloon and control system devices be classified into class III because the device is life-supporting, and there was insufficient medical and scientific information to establish a standard to assure the safety and effectiveness of the device. The 1979 Panel noted that controversy exists as to whether the device is beneficial in many situations in which it is used and that it is difficult to use the device safely and effectively. The 1979 Panel further noted that accurate and precise labeling and directions for use are especially critical and voiced concern that the various components of the device would not function properly if its modular components were poorly matched. The 1979 Panel indicated that the balloon of the device is used within the main artery of the body and because this portion of the device is in contact with internal tissues and blood, the materials used with it require special controls, and because the device is electrically powered and portions of the device may be in direct contact with the heart, the electrical characteristics of the device, e.g., electrical leakage current, need to meet certain requirements. Additionally, if the design of the device is inadequate for accurate and precise blood pumping, a resulting failure could lead to death. Consequently, the 1979 Panel believed that premarket approval was necessary to assure the safety and effectiveness of the device. In 1980, FDA classified intra-aortic balloon and control system devices into class III after receiving no comments on the proposed rule (45 FR 7939; February 5, 1980).

In 1987, FDA published a clarification by inserting language in the codified language stating that no effective date had been established for the requirement for premarket approval for intra-aortic balloon and control system devices (52 FR 17736; May 11, 1987).

In 2009, FDA published an order for the submission of information on intra-aortic balloon and control system devices by August 7, 2009 (74 FR 16214; April 9, 2009). FDA received four responses to that order from device manufacturers. One manufacturer stated in their response that they were ''not aware of adequate and valid scientific information that would support reclassification of the device to Class I or II.'' The other three manufacturers recommended that intra-aortic balloon and control system devices be reclassified to class II. The manufacturers stated that safety and effectiveness of these devices may be assured based on data available in the clinical literature; preclinical and clinical testing; 40 or more years of knowledge and information regarding the clinical use of the devices; and the overall number of marketed devices.

As explained further in sections VII and XI of this document, a meeting of the Circulatory System Devices Panel (the 2012 Panel) took place December 5, 2012, to discuss whether intra-aortic balloon and control system devices should be reclassified or remain in class III. The 2012 Panel recommended that intra-aortic balloon and control system devices be reclassified to class II with special controls when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure based on available evidence that supports the safety and effectiveness of the devices for these uses and the ability of special controls to mitigate identified risks to health. The 2012 Panel also recommended that intra-aortic balloon and control system devices indicated for septic shock or pulsatile flow generation remain in class III because the devices are life-supporting and there was insufficient information to establish special controls for these uses. FDA is not aware of new information that would provide a basis for a different recommendation or findings.

III. Device Description

An intra-aortic balloon and control system, also known as an intra-aortic balloon pump (IABP), consists of a balloon, which inflates and deflates in synchronization with the cardiac cycle, and console, which provides the pneumatic flow of helium to the balloon so that it can inflate and deflate. The balloon is usually manufactured from polyurethane. It is inserted through the femoral artery and resides in the descending aorta. Conventional timing sets inflation of the balloon to occur at the onset of diastole or the aortic valve closure timepoint. During diastole, the balloon will inflate, increasing blood flow to the coronary arteries, therefore increasing myocardial oxygen supply. The balloon remains inflated throughout the diastolic phase, maintaining the increased pressure in the aorta. The deflation of the balloon takes place at the onset of systole during the isovolumetric contraction or very early in the systolic ejection phase. This deflation will cause a decrease in pressure in the aorta and this decrease in pressure assists the left ventricle by reducing the pressure that needs to be generated to achieve ejection through the aortic valve. As the balloon deflates during systole, it increases blood flow to the systemic circulation by reducing afterload and also decreases the oxygen demand of the myocardium.

The console includes software that controls the inflation and deflation of the balloon based upon the patient's electrocardiogram or arterial pressure waveform. The console also controls the amount of helium that is transferred from the internal helium cylinder to the balloon. Most balloons come in sizes of 30cc, 40cc, and 50cc with a catheter diameter of 7.5Fr or 8Fr.

IV. Proposed Reclassification

FDA is proposing that intra-aortic balloon and control system devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure be reclassified from class III to class II. In this proposed order, the Agency has identified special controls under section 513(a)(1)(B) of the FD&C Act that, together with general controls applicable to the devices, would provide reasonable assurance of their safety and effectiveness. Absent the special controls identified in this proposed order, general controls applicable to the device are insufficient to provide reasonable assurance of the safety and effectiveness of the device.

Therefore, in accordance with sections 513(e) and 515(i) of the FD&C

Act and § 860.130, based on new information with respect to the devices and taking into account the public health benefit of the use of the device and the nature and known incidence of the risk of the device, FDA, on its own initiative, is proposing to reclassify this preamendments class III device into class II when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure. FDA believes that this new information is sufficient to demonstrate that the proposed special controls can effectively mitigate the risks to health identified in the next section, and that these special controls, together with general controls, will provide a reasonable assurance of safety and effectiveness for intra-aortic balloon and control system devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure.

Section 510(m) of the FD&C Act authorizes the Agency to exempt class II devices from premarket notification (510(k)) submission. FDA has considered intra-aortic balloon and control system devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure in accordance with the reserved criteria set forth in section 513(a) of the FD&C Act and decided that the device requires premarket notification. Therefore, the Agency does not intend to exempt this proposed class II device from premarket notification (510(k)) submission.

V. Risks to Health

After considering available information, including the recommendations of the advisory committees (panels) for the classification of these devices, FDA has evaluated the risks to health associated with the use of intra-aortic balloon and control system devices and determined that the following risks to health are associated with its use:

- *Cardiac arrhythmias or electrical shock:* Excessive electrical leakage current can disturb the normal electrophysiology of the heart, leading to the onset of cardiac arrhythmias.
- *Ineffective cardiac assist (poor augmentation):* Failure to sense or synchronize on heartbeat, failure to inflate and deflate at the proper intervals, and/or failure of the balloon to fully unwrap can lead to improper or ineffective pumping of blood.
- *Thromboembolism:* Inadequate blood compatibility of the materials used in this device and/or inadequate surface finish and cleanliness can lead to potentially debilitating or fatal thromboemboli.
- *Aortic rupture or dissection:* Improper sizing or over inflation of the balloon can cause a rupture in the main artery.
- *Limb ischemia:* Improper operation of the device which restricts blood flow to the peripheral vascular tree results in tissue ischemia in the limbs.
- *Gas embolism:* Balloon rupture or a leak in the balloon can cause potentially debilitating or fatal gas emboli to escape into the bloodstream.
- *Hemolysis:* Poor material-blood compatibility or excessive disruption of the normal hemodynamic flow patterns can cause hemolysis.
- *Infection:* Defects in the design or construction of the device preventing adequate sterilization can allow pathogenic organisms to be introduced and may cause an infection in a patient.
- *Insertion site bleeding:* Improper sizing of the cannula can cause trauma to the artery during insertion of the catheter.
- *Thrombus/large blood clots:* Leaks of the membrane (balloon surface) or catheter can result in gaseous embolic injury of organs or cause a large blood clot to form within the balloon membrane requiring surgical removal of the catheter.
- *Balloon entrapment:* A balloon perforation can cause blood to enter the balloon forming a large hardened mass of blood within the balloon. This can cause the balloon to become ''entrapped ''in the femoral/iliac system upon removal. Balloon entrapment is characterized by undue resistance to balloon removal.
- *Insertion difficulty/inability to insert the catheter:* Device sizing, insertion technique and/or patient anatomy, specifically tortuous and/or narrowed femoral arteries, can cause insertion difficulties. As a result, therapy can be delayed and there could be an increased risk of vascular damage and/or bleeding due to forceful insertion.
- *Vessel occlusion resulting in ischemia, infarction to an organ (including paraplegia) and/or compartment syndrome:* Malposition of the balloon can compromise circulation due to large vessel occlusion from catheter migration, resulting in ischemia, infarction to an organ or increased compartment pressures, leading to muscle and nerve damage. Vessel occlusion can also be caused by dislodged atherosclerotic plaque and/or clots.
- *Thrombocytopenia:* Improper inflation of the balloon can cause a drop in platelets.
- *Stroke:* Mechanical disruption of atheroma or thrombus liberation causing embolism; disruption of the cranial circulation by the balloon, including obstruction, dissection or perforation; or complications resulting from the use of anticoagulation, can lead to stroke.
- *Death:* Mechanical failure of the device, vascular complications or bleeding can lead to death.

VI. Summary of Reasons for Reclassification

If properly manufactured and used as intended, intra-aortic balloon and control system devices can provide a treatment option for patients when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure, by increasing myocardial oxygen supply, decreasing myocardial oxygen demand, and improving cardiac output. FDA believes that intra-aortic balloon and control system devices indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure, should be reclassified from class III to class II because, in light of new information about the effectiveness of these devices, FDA believes that special controls, in addition to general controls, can be established to provide reasonable assurance of the safety and effectiveness of the device, and because general controls themselves are insufficient to provide reasonable assurance of its safety and effectiveness.

VII. Summary of Data Upon Which the Reclassification Is Based

Since the time of the original 1979 Panel recommendation, sufficient evidence has been developed to support a reclassification of intra-aortic balloon and control system devices to class II with special controls when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure. FDA has been reviewing these devices for many years and their risks are well known. FDA conducted a comprehensive review of available literature for IABP devices for acute coronary syndrome, cardiac and non-cardiac surgery, and complications of heart failure. FDA's review found 18 cohort studies (9 retrospective and 9 prospective), 6 randomized controlled trials, 3 case-control studies, 2 case series, 4 systematic reviews, and a meta-analysis, which provided consistent evidence of the safety and effectiveness of intra-aortic balloon and control system devices for acute coronary syndrome, cardiac and non-cardiac surgery, and complications of heart failure.

Collectively these studies support that the overall complication rates for intra-aortic balloon and control systems is low. For example, in the Benchmark Registry (Ref. 1), there were low IABP complication rates, including IABP-related mortality (0.05 percent and 0.07 percent in the United States and European Union, respectively), major limb ischemia (0.09 percent, 0.8 percent) and severe bleeding (0.9 percent, 0.8 percent). This is consistent with other studies of IABP use with large sample sizes. Additionally, in the most recently published trial of IABP use, the IABP SHOCK II trial (Ref. 2), published in October 2012, 600 patients were randomized to IABP (301 patients) or no IABP (299 patients). The IABP group and the control group did not differ significantly with respect to the rates of adverse events, including major bleeding (3.3 percent and 4.4 percent, respectively; P = 0.51), peripheral ischemic complications (4.3 percent and 3.4 percent, P = 0.53), sepsis (15.7 percent and 20.5 percent, P = 0.15), and stroke (0.7 percent and 1.7 percent, P = 0.28). These rates represent recent IABP usage outcomes in a randomized trial of patients with high associated morbidity using modern aggressive interventional approaches to acute myocardial infarction (MI) and cardiogenic shock, which include the use of percutaneous coronary intervention and aggressive anticoagulation. The trial demonstrates low rates of adverse events that can be attributed directly to the IABP itself.

It is important to note that the patients in whom IABP is used have severe comorbidities and underlying illnesses. As a result, overall mortality in these patients is high. Patients recruited for studies on the IABP are of a population segment that is at an inherently greater risk of mortality because of the high-risk procedures they require, and the illnesses that necessitated the procedures. Additionally, there are trends to less balloon-related mortality over time, as balloon catheter sizes have decreased and procedural techniques have improved.

The literature data also supports the effectiveness of IABP for acute coronary syndrome, cardiac and non-cardiac surgery, and complications of heart failure. With respect to acute coronary syndrome, the Benchmark Registry (Ref. 1) demonstrated that the mortality of patients with cardiogenic shock was 30.7 percent, which was low compared to other cardiogenic shock trials, and has been cited as evidence of a benefit from IABP use. Further evaluation of this registry has shown that in U.S. patients, compared to patients outside the United States (OUS), an IABP was placed at earlier stages of the disease. After appropriate adjustment of risk factors, U.S. patients showed decreased mortality (10.8 percent (U.S.) vs. 18 percent (OUS), P < 0.001). The results of the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO–1 trial) (Ref. 3) also demonstrated a 12-month survival advantage in cardiogenic shock with early IABP implantation. This was a retrospective study of IABP use in patients presenting with acute MI and cardiogenic shock who received systemic fibrinolysis. Sixty-eight of 310 cardiogenic shock patients received an IABP. The significantly higher frequency of IABP use in the United States in relation to Europe in these two trials was associated with more bleeding complications, but also with a lower mortality rate, both nonsignificantly at 30 days (47 percent vs. 60 percent) and significantly at 1 year (57 percent vs. 67 percent). This mortality benefit is also supported by two publications regarding the National Registry of Myocardial Infarction (Refs. 4 and 5).

The literature regarding the effectiveness of IABPs in cardiac and non-cardiac surgery has demonstrated utility in some studies and in others has been equivocal in demonstrating effectiveness. However, FDA and the 2012 Panel (as described in further detail in this document) find that there are certain subgroups of patients that may benefit from IABP use for cardiac and non-cardiac surgery indications. This is demonstrated in Christenson et al. (Ref. 6), which randomized 30 high-risk off-pump coronary artery bypass graft (CABG) surgery recipients to receive an IABP preoperatively or no IABP. The use of an IABP improved preoperative and postoperative cardiac performance significantly (P < 0.0001). The postoperative course was also improved, including decreased pneumonia and acute renal failure, shorter duration of ventilator support, and fewer patients requiring postoperative inotropic medications for greater than 48 hours. The lengths of stay in the intensive care unit and in the hospital were shorter in the IABP group. Additionally, Miceli et al. (Ref. 7) studied 141 consecutive patients from 2004–2007 undergoing CABG, in which 38 patients (27 percent) received a prophylactic IABP. After risk-adjusting for propensity score, prophylactic IABP patients had a lower incidence of postcardiotomy low cardiac output syndrome (adjusted OR 0.07, P < 0.006) and postoperative myocardial infarction (adjusted OR 0.04, P < 0.04), as well as a shorter length of hospital stay (10.4±0.8 vs. 12.2±0.6 days, P < 0.0001) compared to those who did not receive an IABP.

Much of the evidence that supports the effectiveness of an IABP for complications of heart failure is outlined previously in this document with respect to acute coronary syndrome (e.g., cardiogenic shock from acute MI). However, there are additional smaller studies that support use in heart failure specifically, including bridge to transplant and acute decompensated dilated cardiomyopathy. For example, Norkiene et al. (Ref. 8) studied 11 patients with decompensated dilated cardiomyopathy (CMP) listed for heart transplant who were recorded in the Benchmark Registry from September 2004 to December 2005, with New York Heart Association Class IV functional status. Frequency of complications and clinical outcomes were assessed prior to and after IABP insertion as well as hemodynamics and end-organ function (renal and hepatic). After 48 hours of IABP support, there was a significant increase of mean systemic arterial pressure from 74.5±9.6 to 82.3±4.7 mmHg (P = 0.02), and ejection fraction from 14.7±6.4 to 21.0±8.6 (P = 0.014). Improvement of the cardiac index, pulmonary wedge pressure, and end-organ perfusion markers did not reach statistical significance. The authors concluded that IABP support may be successfully and safely used in acute decompensated dilated cardiomyopathy patients as an urgent measure of cardiac support to stabilize the patient and maintain organ perfusion until transplant is available, ventricular assist device is placed, or the patient is weaned from the IABP.

Rosenbaum et al. (Ref. 9) studied 43 patients with end-stage congestive heart failure in whom an IABP was used as a bridge to transplant. Twenty-seven patients had non-ischemic CMP (NICM), and 16 had ischemic CMP (ISCM). Hemodynamics improved in both groups, immediately (15 to 30 minutes) following IABP insertion, with greater improvement (p < 0.05) in cardiac index and a trend toward greater reduction in filling pressures in the NICM group. Systemic vascular resistance fell to a similar degree in both groups. During continued IABP support (0.13 to 38 days in NICM, 1 to 54 days in ISCM), all hemodynamic changes persisted in both groups, with a larger decrease (p < 0.05) in systemic vascular resistance and greater increase (p < 0.05) in cardiac index in the patients with NICM. The reduction in filling pressures, however, tended to be greater in patients with

ISCM. Complications from the IABP were low. The authors concluded that IABP use was both safe and effective in this group as a bridge to transplant.

The literature data outlined previously in this document supports a conclusion of reasonable evidence for the safety and effectiveness of intra-aortic balloon and control system devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, and complications of heart failure. In addition, bench studies designed to demonstrate the devices' ability to function as intended have been well characterized.

FDA's presentation to the 2012 Panel included a summary of the available safety and effectiveness information for intra-aortic balloon and control system devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure, including adverse event reports from FDA's Manufacturer and User Facility Device Experience (MAUDE) database and available literature. Based on the available scientific literature, which supports that use of intra-aortic balloon and control system devices may be beneficial for patients when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure, FDA recommended to the 2012 Panel that intra-aortic balloon and control system devices indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure be reclassified to class II (special controls). The 2012 Panel discussed and made recommendations regarding the regulatory classification of intra-aortic balloon and control system devices to either reconfirm to class III (subject to premarket approval application) or reclassify to class II (subject to special controls) as directed by section 515(i) of the FD&C Act. The 2012 Panel agreed with FDA's conclusion that the available scientific evidence is adequate to support the safety and effectiveness of intra-aortic balloon and control system devices when indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure. Several members of the 2012 Panel noted that not all available data supports the effectiveness of the device conclusively; however, there was consensus that IABPs improve hemodynamics and provide an important tool for clinicians in treating a patient population with high morbidity and mortality. The 2012 Panel also acknowledged that intra-aortic balloon and control systems are life-supporting devices and provided the following rationale per § 860.93 for recommending that IABPs for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure be reclassified to class II: (1) There is a wealth of clinical experience that attests to the benefit of the device; (2) there is an important advantage to use of intra-aortic balloon counter-pulsation to provide hemodynamic stability or protection from ischemia in precarious or unstable patients; and (3) the recommended special controls will mitigate the health risks associated with the device.

The 2012 Panel also agreed with the identified risks to health presented at the meeting; however, the 2012 Panel recommended that compartment syndrome, death, and stroke be added to the list of risks to health and that ischemia be added to ''vessel occlusion resulting in infarction to an organ (including paraplegia)''. FDA agrees with the 2012 Panel's recommendations and modified the risks to health accordingly as outlined in section V. The 2012 Panel also agreed with FDA's proposed special controls outlined in section VIII; however, the 2012 Panel further recommended that information about IABP clinical trials should be added to the device labeling as a special control. FDA does not agree with this recommendation from the 2012 Panel. FDA determined that it was not appropriate to require that clinical trial information be included in the device labeling as a special control because available clinical trial information would most accurately represent the device type, not individual devices, so including such information in the labeling for a specific device may be misleading. On this basis, the special controls outlined in section VIII were not modified based on this recommendation from the 2012 Panel.

The 2012 Panel transcript and other meeting materials are available on FDA's Web site (Ref. 10).

VIII. Proposed Special Controls

FDA believes that the following special controls, together with general controls, are sufficient to mitigate the risks to health described in section V: (1) Appropriate analysis and non-clinical testing must be conducted to validate electromagnetic compatibility and electrical safety of the device; (2) appropriate software verification, validation, and hazard analysis must be performed; (3) the device must be demonstrated to be biocompatible; (4) sterility and shelf life testing must demonstrate the sterility of patient-contacting components and the shelf life of these components; (5) non-clinical performance evaluation of the device must provide a reasonable assurance of safety and effectiveness for mechanical integrity, durability, and reliability; and (6) labeling must bear all information required for the safe and effective use of the device, including a detailed summary of the device- and procedure-related complications pertinent to use of the device.

Intra-aortic balloon and control system devices are prescription devices restricted to patient use only upon the authorization of a practitioner licensed by law to administer or use the device. (Proposed 21 CFR 870.3535(a); see section 520(e) of the FD&C Act and 21 CFR 801.109 (Prescription devices)). Prescription-use requirements are a type of general controls authorized under section 520(e) of the FD&C Act and defined as a general control in section 513(a)(1)(A)(i) of the FD&C Act; and under 21 CFR 807.81, the device would continue to be subject to 510(k) notification requirements.

IX. Dates New Requirements Apply

In accordance with section 515(b) of the FD&C Act, FDA is proposing to require that a PMA be filed with the Agency for intra-aortic balloon and control systems indicated for septic shock or pulsatile flow generation within 90 days after issuance of any final order based on this proposal. An applicant whose device was legally in commercial distribution before May 28, 1976, or whose device has been found to be substantially equivalent to such a device, will be permitted to continue marketing such class III devices during FDA's review of the PMA provided that the PMA is timely filed. FDA intends to review any PMA for the device within 180 days of the date of filing. FDA cautions that under section 515(d)(1)(B)(i) of the FD&C Act, the Agency may not enter into an agreement to extend the review period for a PMA beyond 180 days unless the Agency finds that ''the continued availability of the device is necessary for the public health.''

An applicant whose device was legally in commercial distribution before May 28, 1976, or whose device has been found to be substantially equivalent to such a device, who does not intend to market such device for septic shock or pulsatile flow generation, may remove such intended uses from the device's labeling by initiating a correction within 90 days after issuance of any final order based on this proposal. Under 21 CFR 806.10(a)(2) a device manufacturer or importer initiating a correction to remedy a violation of the FD&C Act that

may present a risk to health is required to submit a written report of the correction to FDA.

FDA intends that under § 812.2(d), the preamble to any final order based on this proposal will state that, as of the date on which the filing of a PMA is required to be filed, the exemptions from the requirements of the IDE regulations for preamendments class III devices in § 812.2(c)(1) and (c)(2) will cease to apply to any device that is: (1) Not legally on the market on or before that date, or (2) legally on the market on or before that date but for which a PMA is not filed by that date, or for which PMA approval has been denied or withdrawn.

If a PMA for a class III device is not filed with FDA within 90 days after the date of issuance of any final order requiring premarket approval for the device, the device would be deemed adulterated under section 501(f) of the FD&C Act. The device may be distributed for investigational use only if the requirements of the IDE regulations are met. The requirements for significant risk devices include submitting an IDE application to FDA for review and approval. An approved IDE is required to be in effect before an investigation of the device may be initiated or continued under § 812.30. FDA, therefore, recommends that IDE applications be submitted to FDA at least 30 days before the end of the 90-day period after the issuance of the final order to avoid interrupting any ongoing investigations.

Because intra-aortic balloon and control systems indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure, can currently be marketed after receiving clearance of an application for premarket notification and FDA is proposing to reclassify these devices as class II requiring clearance of an application for premarket notification, this order, if finalized, will not require a new premarket submission for intra-aortic balloon and control systems indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure.

X. Proposed Findings With Respect to Risks and Benefits

As required by section 515(b) of the FD&C Act, FDA is publishing its proposed findings regarding: (1) The degree of risk of illness or injury designed to be eliminated or reduced by requiring that this device have an approved PMA when indicated for septic shock or pulsatile flow generation and (2) the benefits to the public from the use of intra-aortic balloon and control systems indicated for septic shock or pulsatile flow generation.

These findings are based on the reports and recommendations of the advisory committees (panels) for the classification of these devices along with information submitted in response to the 515(i) order (74 FR 16214; April 9, 2009), and any additional information that FDA has obtained. Additional information regarding the risks as well as classification associated with this device type is discussed in Section XI B., *Summary of Data,* and can also be found in 44 FR 13284–13434, March 9, 1979; 45 FR 7907–7971, February 5, 1980; and 52 FR 17736, May 11, 1987.

XI. Device Subject to the Proposal To Require a PMA—Intra-Aortic Balloon and Control System Devices When Indicated for Septic Shock or Pulsatile Flow Generation (§ 870.3535(c))

A. Identification

An intra-aortic balloon and control system is a prescription device that consists of an inflatable balloon, which is placed in the aorta to improve cardiovascular functioning during certain life-threatening emergencies, and a control system for regulating the inflation and deflation of the balloon. The control system, which monitors and is synchronized with the electrocardiogram, provides a means for setting the inflation and deflation of the balloon with the cardiac cycle.

B. Summary of Data

When indicated for septic shock or pulsatile flow generation, FDA concludes that the safety and effectiveness of these devices have not been established by adequate scientific evidence. There is limited scientific evidence regarding the effectiveness of intra-aortic balloon and control system devices for these indications. Specifically, based on FDA's review of the published scientific literature, it appears that there are no studies regarding intra-aortic balloon and controls systems indicated for septic shock in humans. The use of the IABP for pulsatile flow generation made up less than 1 percent of the indications for use evaluated in FDA's literature search. Three observational studies regarding pulsatile flow generation were found during FDA's review of the literature. All three articles state that the device is associated with low mortality and adverse event rates; however, none of the studies was stratified by indication. As a result, it cannot be concluded that these results apply to septic shock or pulsatile flow generation specifically.

FDA presented the findings of our literature search for intra-aortic balloon and control system devices for the indications of septic shock and pulsatile flow generation to the 2012 Panel on December 5, 2012. Based on FDA's findings, the Panel recommended that available scientific evidence is not adequate to support the effectiveness of intra-aortic balloon and control system devices for the indications of septic shock or pulsatile flow generation. As a result, the 2012 Panel concluded that intra-aortic balloon and control system devices for the indications of septic shock or pulsatile flow generation should remain in class III (subject to premarket approval application). The 2012 Panel transcript and other meeting materials are available on FDA's Web site (Ref. 10).

C. Risks to Health

The risks to health for intra-aortic balloon and control system devices for the indications of septic shock or pulsatile flow generation are the same as outlined in section V.

D. Benefits of Intra-Aortic Balloon and Control System Devices

As discussed previously in this document, there is limited scientific evidence regarding the effectiveness of intra-aortic balloon and control system devices for the indications of septic shock or pulsatile flow generation. For indications of septic shock, the hemodynamic effects generated by use of intra-aortic balloon and control systems do not address the fundamental hemodynamic derangements of septic shock syndrome. FDA is not aware of any theoretical or demonstrated benefit to using intra-aortic balloon and control systems for this clinical syndrome. For indications of pulsatile flow generation, it is impossible to estimate the direct effect of the devices on patient outcomes based on the lack of effectiveness data for this indication as described previously.

XII. PMA Requirements

A PMA for intra-aortic balloon and control system devices indicated for septic shock or pulsatile flow generation must include the information required by section 515(c)(1) of the FD&C Act. Such a PMA should also include a detailed discussion of the risks identified previously, as well as a discussion of the effectiveness of the device for which premarket approval is sought. In addition, a PMA must include all data and information on: (1) Any risks known, or that should be reasonably known, to the applicant that have not been identified in this

document; (2) the effectiveness of the device that is the subject of the application; and (3) full reports of all preclinical and clinical information from investigations on the safety and effectiveness of the device for which premarket approval is sought.

A PMA must include valid scientific evidence to demonstrate reasonable assurance of the safety and effectiveness of the device for its intended use (see § 860.7(c)(1)). Valid scientific evidence is ''evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use . . . Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness.'' (see § 860.7(c)(2)).

XIII. Opportunity To Request a Change in Classification

Before requiring the filing of a PMA for a device, FDA is required by section 515(b)(2)(D) of the FD&C Act to provide an opportunity for interested persons to request a change in the classification of the device based on new information relevant to the classification. Any proceeding to reclassify the device will be under the authority of section 513(e) of the FD&C Act.

A request for a change in the classification of intra-aortic balloon and control system devices indicated for septic shock or pulsatile flow generation is to be in the form of a reclassification petition containing the information required by § 860.123, including new information relevant to the classification of the device.

XIV. Codification of Orders

Prior to the amendments by FDASIA, section 513(e) of the FD&C Act provided for FDA to issue regulations to reclassify devices and section 515(b) of the FD&C Act provided for FDA to issue regulations to require approval of an application for premarket approval for preamendments devices or devices found to be substantially equivalent to preamendments devices. Because sections 513(e) and 515(b) as amended require FDA to issue final orders rather than regulations, FDA will continue to codify reclassifications and requirements for approval of an application for premarket approval, resulting from changes issued in final orders, in the Code of Federal Regulations. Therefore, under section 513(e)(1)(A)(i) of the FD&C Act, as amended by FDASIA, in this proposed order, we are proposing to revoke the requirements in § 870.4360 related to the classification of non-roller type cardiopulmonary and circulatory bypass blood pump devices as class III devices and to codify the reclassification of non-roller type cardiopulmonary and circulatory bypass blood pump devices into class II.

XV. Environmental Impact

The Agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

XVI. Paperwork Reduction Act of 1995

This proposed order refers to collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520).

The collections of information in 21 CFR part 814 have been approved under OMB control number 0910–0231. The collections of information in part 807, subpart E, have been approved under OMB control number 0910–0120.

The effect of this order, if finalized, is to shift certain devices from the 510(k) premarket notification process to the PMA process. FDA estimates that there will be two fewer 510(k) submissions as a result of this order, if finalized. Based on FDA's most recent estimates, this will result in a 91-hour burden decrease to OMB control number 0910–0120, which is the control number for the 510(k) premarket notification process. However, because FDA does not expect to receive any new PMAs as a result of this order, if finalized, we estimate no burden increase to OMB control number 0910–0231 based on this order, if finalized. Therefore, on net, FDA expects a burden hour decrease of 91 due to this proposed regulatory change.

The collections of information in 21 CFR part 812 have been approved under OMB control number 0910–0078.

XVII. Proposed Effective Date

FDA is proposing that any final order based on this proposed order become effective 90 days after date of publication of the final order in the **Federal Register**.

XVIII. Comments

Interested persons may submit either electronic comments regarding this document to *http://www.regulations.gov* or written comments to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to submit one set of comments. Identify comments with the docket number found in the brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at *http://www.regulations.gov*.

XIX. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**), and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and are available electronically at *http://www.regulations.gov*. (FDA has verified the Web site address in this reference section, but FDA is not responsible for any subsequent changes to the Web site after this document publishes in the **Federal Register**.)

1. Cohen, M., P. Urban, J.T. Christenson, et al., ''Intra-Aortic Balloon Counterpulsation in U.S. and non-U.S. Centres: Results of the Benchmark (Registered Trademark) Registry,'' *European Heart Journal,* vol. 24, pp. 1763–1770, 2003.
2. Thiele, H., U. Zeymer, F.J. Neumann, et al. for the IABP–SHOCK II Trial Investigators, ''Intraaortic Balloon Support for Myocardial Infarction With Cardiogenic Shock.'' *New England Journal of Medicine,* vol. 367, pp. 1287–1296, 2012.
3. Anderson, R.D., M.E. Ohman, and D.R. Holmes for the GUSTO–I Investigators, ''Use of Intraaortic Balloon Counterpulsation in Patients Presenting With Cardiogenic Shock: Observations from the GUSTO–I Study,'' *Journal of the American College of Cardiology,* vol. 30, pp. 708–715, 1997.
4. Chen, E.W., J.G. Canto, L.S. Parsons, et al., ''Relation Between Hospital Intra-Aortic Balloon Counterpulsation Volume and Mortality in Acute Myocardial Infarction Complicated by Cardiogenic Shock,'' *Circulation,* vol. 108, pp. 951–957, 2003.
5. Barron, H.V., N.R. Every, L.S. Parsons, et al., ''The Use of Intraaortic Balloon Counterpulsation in Patients With Cardiogenic Shock Complicating Acute Myocardial Infarction: Data From the National Registry of Myocardial Infarction 2,'' *American Heart Journal,* vol. 141, pp. 933–939, 2001.
6. Christenson, J.T., M. Licker, and A. Kalangos, ''The Role of Intraaortic Counterpulsion in High Risk OPCAB Surgery: A Prospective Randomised Study,'' *Journal of Cardiac Surgery,* vol. 18, pp. 286–294, 2003.

7. Miceli, A., B. Fiorani, T.H. Danesi, et al., ''Prophylactic Intra-Aortic Balloon Pump in High-Risk Patients Undergoing Coronary Artery Bypass Grafting: A Propensity Score Analysis,'' *Interactive Cardiovascular and Thoracic Surgery,* vol. 9, pp. 291–294, 2009.
8. Norkiene, I., D. Ringaitiene, K. Rucinskas, et al., ''Intra-Aortic Balloon Counterpulsation in Decompensated Cardiomyopathy Patients: Bridge to Transplantation or Assist Device.'' *Interactive Cardiovascular and Thoracic Surgery,* vol. 6, pp. 66–70, 2007.
9. Rosenbaum, A.M., S. Murali, and B.F. Uretsky, ''Intra-Aortic Balloon Counterpulsation as a 'Bridge' to Cardiac Transplantation. Effects in Nonischemic and Ischemic Cardiomyopathy,'' *Chest,* vol. 106, pp. 1683–1688, 1994.
10. The panel transcript and other meeting materials are available on FDA's Web site, available at *http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/ucm300073.htm.*

List of Subjects in 21 CFR Part 870

Medical devices, Cardiovascular devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 870 be amended as follows:

PART 870—CARDIOVASCULAR DEVICES

■ 1. The authority citation for 21 CFR part 870 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

■ 2. Revise § 870.3535 to read as follows:

§ 870.3535 Intra-aortic balloon and control system.

(a) *Identification.* An intra-aortic balloon and control system is a prescription device that consists of an inflatable balloon, which is placed in the aorta to improve cardiovascular functioning during certain life-threatening emergencies, and a control system for regulating the inflation and deflation of the balloon. The control system, which monitors and is synchronized with the electrocardiogram, provides a means for setting the inflation and deflation of the balloon with the cardiac cycle.

(b) *Classification.* (1) Class II (special controls) when the device is indicated for acute coronary syndrome, cardiac and non-cardiac surgery, or complications of heart failure. The special controls for this device are:

(i) Appropriate analysis and non-clinical testing must be conducted to validate electromagnetic compatibility and electrical safety of the device;

(ii) Appropriate software verification, validation, and hazard analysis must be performed;

(iii) The device must be demonstrated to be biocompatible;

(iv) Sterility and shelf life testing must demonstrate the sterility of patient-contacting components and the shelf life of these components;

(v) Non-clinical performance evaluation of the device must provide a reasonable assurance of safety and effectiveness for mechanical integrity, durability, and reliability; and

(vi) Labeling must bear all information required for the safe and effective use of the device, including a detailed summary of the device- and procedure-related complications pertinent to use of the device.

(2) Class III (premarket approval) when the device is indicated for septic shock and pulsatile flow generation.

(c) *Date premarket approval application (PMA) or notice of completion of product development protocol (PDP) is required.* A PMA or notice of completion of a PDP is required to be filed with FDA on or before [*A DATE WILL BE ADDED 90 DAYS AFTER DATE OF PUBLICATION OF A FUTURE FINAL ORDER IN THE* ***FEDERAL REGISTER***], for any intra-aortic balloon and control system indicated for septic shock or pulsatile flow generation that was in commercial distribution before May 28, 1976, or that has, on or before [*A DATE WILL BE ADDED 90 DAYS AFTER DATE OF PUBLICATION OF A FUTURE FINAL ORDER IN THE* ***FEDERAL REGISTER***], been found to be substantially equivalent to any intra-aortic balloon and control system indicated for septic shock or pulsatile flow generation that was in commercial distribution before May 28, 1976. Any other intra-aortic balloon and control system indicated for septic shock or pulsatile flow generation shall have an approved PMA or declared completed PDP in effect before being placed in commercial distribution.

Dated: June 12, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013–14553 Filed 6–18–13; 8:45 am]

BILLING CODE 4160–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Chapter I

[Docket Nos. FDA–2013–N–0683, FDA–2013–N–0684, and FDA–2013–N–0685]

Food and Drug Administration Safety and Innovation Act Title VII—Drug Supply Chain; Standards for Admission of Imported Drugs, Registration of Commercial Importers and Good Importer Practices; Notification of Public Meeting; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notification of public meeting; request for comments.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing a public meeting regarding FDA's implementation of Title VII of the Food and Drug Administration Safety and Innovation Act (FDASIA), which provides FDA with important new authorities to help it better protect the integrity of the drug supply chain. In addition to providing a general overview of Title VII and FDA's approach to implementing these provisions, the meeting will give interested persons an opportunity to provide input that will assist FDA in the development of regulations implementing two sections of Title VII, which relate to standards for admission of imported drugs and commercial drug importers. Specifically, FDA is seeking information on the types of information that importers should be required to provide under Title VII as a condition of admission. FDA is also seeking information regarding registration requirements for commercial drug importers and good importer practices to be established under Title VII.

DATES: The public meeting will be held on July 12, 2013, from 9 a.m. to 5 p.m. at the FDA White Oak Campus, 10903 New Hampshire Ave., Bldg. 31 Conference Center, the Great Room (rm. 1503), Silver Spring MD 20993. Please note that visitors to the White Oak Campus must enter through Building 1. The White Oak Campus location is a Federal facility with security procedures and limited seating. There is no fee to register for the meeting and registration will be on a first come, first serve basis. Early registration is recommended because seating is limited. Onsite registration will also be permitted if there is available space. See section IV of this document, ''How to Participate in