DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

February 29, 2016

Edwards Lifesciences, LLC.
Ms. Sherrie Rinne
Project Manager, Regulatory Affairs
One Edwards Way
Irvine, California 92614

Re: P130009/S037
Trade/Device Name: SAPIEN XT Transcatheter Heart Valve and Accessories
Filed: July 1, 2015
Amended: September 8, 2015, November 25, 2015
Product Code: NPV

Dear Ms. Rinne:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) supplement for the SAPIEN XT Transcatheter Heart Valve and Accessories. This device is indicated for use in pediatric and adult patients with a dysfunctional, non-compliant Right Ventricular Outflow Tract (RVOT) conduit with a clinical indication for intervention and:

- pulmonary regurgitation ≥ moderate and/or
- mean RVOT gradient ≥ 35 mmHg.

We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at two years. This is to advise you that the protocol you used to establish this expiration dating is considered an

approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84. This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final UDI rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. For more information on these requirements, please see the UDI website, http://www.fda.gov/udi.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below. Separate PAS Progress Reports must be submitted for each study every six (6) months during the first two (2) years of the study and annually thereafter, unless otherwise specified by FDA. Two (2) copies of each report, identified as an "ODE Lead PMA Post-Approval Study Report" or "OSB Lead PMA Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

1. ***ODE Lead PMA Post-Approval Study*** - Continued Follow-Up of the Premarket COMPASSION Cohort: The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval.

   The objective of this study is to evaluate longer-term safety and effectiveness of the device in the pulmonic position for all living subjects who were enrolled under the IDE. This study will be conducted as per the protocol (protocol J) dated November 3, 2010 (Supplement G060242/S063). Subject follow-up will continue based on the timelines outlined in the IDE protocol.

   The study is a prospective, non-randomized, multi-center clinical trial designed to follow subjects from the IDE trial up to 5 years. Data will be collected per the protocol including

freedom from device- or procedure-related death or reintervention, freedom from MACCE, functional improvement (decrease in pulmonary regurgitation, improvement in NYHA functional class, freedom from recurrent pulmonary stenosis), procedural- and device-related adverse events, stent fracture, reintervention on the THV or conduit, and death.

2. ***OSB Lead PMA Post-Approval Study*** - New enrollment SAPIEN XT Pulmonic PAS: The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. On February 18, 2016 (email), you agreed to conduct a study as follows:

   The objective of this study is to evaluate long-term safety and effectiveness of the SAPIEN XT THV in the pulmonic position for the intended patient population (especially pediatric) when used as indicated with all valve sizes. It is a single-arm, prospective, multicenter post-approval study using a performance goal based on the original COMPASSION trial.

   The study patients are pediatric and adult patients with a dysfunctional, non-compliant right ventricular outflow tract (RVOT) conduit with a clinical indication for intervention and pulmonary regurgitation ≥ moderate and/or mean RVOT gradient ≥ 35 mmHg. The eligibility criteria will be consistent with the final FDA-approved IFU and labeling. A sample size of 162 subjects is required for the hypothesis test on the primary effectiveness endpoint with at least 80% of the power. A total of 191 patients will be enrolled at up to 10 sites in the US to account for loss to follow-up. The patients will be followed at hospital discharge, 30 days, 1 year and annually thereafter through 5 years.

   The primary effectiveness endpoint is the freedom from device- or procedure-related death or reintervention at one year. The secondary effectiveness endpoints include 1) Improved THV hemodynamics at 1 year via transthoracic echocardiogram (TTE), 2) Improvement of ≥1 NYHA functional class at 30 days and 1 year from baseline for patients with NYHA functional class ≥2 at baseline, 3) freedom from recurrent pulmonary stenosis, defined as RVOT peak gradient <36 mmHg at one year as demonstrated via TTE for patients with stenosis at baseline (RVOT peak gradient ≥ 36 mmHg at baseline), and 4) device success, which is defined as a composite of deployment of the valve to the target area, removal of the delivery catheter out of the body, and improvement in pulmonary regurgitation to mild or less per the earliest evaluable TTE. The secondary safety endpoint is the composite endpoint MACCE at 30 days and 1 year. MACCE is defined as a composite of death, myocardial infarction, reintervention, vascular injury resulting in the need for an unplanned vascular intervention, stroke and pulmonary embolism.

   The acceptance criterion for the primary effectiveness endpoint is 11.1% (or 89.6% freedom from death and reintervention). If the lower 95% confidence limit for the freedom from the primary effectiveness endpoint at 1 year is greater than 89.6%, the acceptance criterion for the primary endpoint will have been met. Other endpoints and clinically relevant baseline and follow-up variables will be provided descriptively.

   Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your OSB lead post-approval study. Your PMA supplements should be clearly labeled as an "OSB Lead PMA Post-Approval Study Protocol" as noted

above and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing.

In addition, the results from any post-approval study or surveillance should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement.

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA. In addition, the results from any post approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm).

Before making any change affecting the safety or effectiveness of the device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm.

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to:

(1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at http://www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. Final printed labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in 6 copies, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
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10903 New Hampshire Avenue
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If you have any questions concerning this approval order, please contact Jaime Raben at 301-796-1137 or Jaime.Raben@fda.hhs.gov.

Sincerely yours,

for

Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and Radiological Health