



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

October 09, 2015

Ms. Wendy Spielberger
Principal Project Manager, Regulatory Affairs
Edwards Lifesciences LLC
One Edwards Way
Irvine, CA 92614

Re: P130009/S034
Edwards SAPIEN XT™ Transcatheter Heart Valve, model 9300TFX, 23, 26, and 29 mm, and accessories (NovaFlex+ delivery system, models 9355FS23, 9355FS26, and 9355FS29, with crimp stopper and Qualcrimp crimping accessory (laminated model or cloth model 9300QC); Edwards expandable introducer sheath set, models 916ES23, 918ES26, and 920ES29; Ascendra+ delivery system with crimp stopper, models 9355AS23, 9355AS26, and 9355AS29; Ascendra+ introducer sheath set, models 9350IS23, 9350IS26, and 9350IS29; and Edwards crimper, model 9350CR)
Filed: April 15, 2015
Amended: June 5, 2015
Procode: NPT

Dear Ms. Spielberger:

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, model 9300TFX, and accessories. This device is indicated for use in patients with symptomatic heart disease due to either severe native calcific aortic stenosis or failure (stenosed, insufficient, or combined) of a surgical bioprosthetic aortic valve who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (i.e., Society of Thoracic Surgeons operative risk score $\geq 8\%$ or at a $\geq 15\%$ risk of mortality at 30 days). We are pleased to inform you that the PMA supplement is approved. You may begin commercial distribution of the device as modified 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.

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" (please use this title even if the specified interval is more frequent than one year) 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 the "ODE Lead PMA PAS" listed below. Two (2) copies of each report, identified as an "ODE Lead PMA PAS 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 cohort:*
The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. This study should be conducted in accordance with the protocol submitted on October 2, 2015 via email (The PARTNER II Nested Registry 3 Post Approval Study, Version 1.0, dated October 1, 2015). The study will consist of all living subjects who were enrolled in Nested Registry 3 under the IDE, including those enrolled under the continued access protocol.

The objective of this study is to characterize the cumulative clinical outcomes of all subjects at discharge or 7 days, whichever comes first, 30 days, 1 year, and annually thereafter through 5 years post procedure. The safety and effectiveness endpoints include all-cause mortality, all stroke, moderate or severe obstruction (defined as Doppler Velocity Index [DVI] < 0.25), or moderate or severe paravalvular leak (through 1 year

only); all-cause mortality; all stroke or transient ischemic attack (TIA); all-cause mortality or major stroke; all stroke, major vascular complication, or aortic valve reintervention; New York Heart Association (NYHA) classification (additional data point at 6 months); change in 6-minute walk distance (6MWD) from baseline (through 1 year only); echocardiographic assessment of valve performance; clinical improvement per quality of life (QoL) instrument Kansas City Cardiomyopathy Questionnaire (KCCQ); and index hospitalization length of stay.

You are required to follow the reporting timeline listed in the protocol and submit one PAS progress report annually. This report should be separate from the PAS progress reports for the Inoperable Patients Cohort (PARTNER IIB), which are “OSB Lead PMA Post-Approval Study” reports.

2. *OSB Lead Surveillance - SAPIEN XT Transcatheter Heart Valve Comprehensive Linked Registry-Based Surveillance*: The Office of Surveillance and Biometrics (OSB) will have the lead for surveillance after device approval. You are required to actively participate in as a stakeholder and support the operations of the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry (TVTR) to ensure that FDA surveillance occurs for the SAPIEN XT Transcatheter Heart Valves implanted inside a failed bioprosthetic surgical aortic valve (“TAV-in-SAV”) over the next 5 years. This surveillance will monitor the following: (1) device success (intra-procedure); (2) all-cause mortality, all stroke, life-threatening (or disabling) bleeding, acute kidney injury-stage 3 (including renal replacement therapy), peri-procedural myocardial infarction, and repeat procedure for valve-related dysfunction (surgical or interventional therapy) at 30 days and 12 months; (3) neurological, vascular and quality of life outcomes at 30 days and 12 months; and (4) all-cause mortality, neurological and vascular outcomes annually through 5 year post implantation.

You are not required to submit any progress report for the surveillance. FDA will conduct our own analyses for the purpose of surveillance through access to the TVTR and will engage in quarterly discussions with you and registry to discuss the findings.

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" (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 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 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 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 six 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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If you have questions concerning this approval order, please contact Changfu Wu, Ph.D., at (301) 796-6086.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Bram D. Zuckerman". The signature is written in a cursive style and is positioned above the typed name.

for

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