



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

June 16, 2014

Mr. Thomas Humphrey
Director, Regulatory Affairs
Edwards Lifesciences, LLC
One Edwards Way
Irvine, CA 92614

Re: P130009
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; Edwards balloon catheter, models 9350BC20, 9350BC23, and 9350BC25; Ascendra+ delivery system with crimp stopper, models 9355AS23, 9355AS26, and 9355AS29; Ascendra+ introducer sheath set, models 9350IS23, 9350IS26, and 9350IS29; Ascendra balloon aortic valvuloplasty catheter, model 9100BAVC; and Edwards crimper, model 9350CR)
Filed: May 2, 2013
Amended: May 7, May 13, July 8, July 9, August 29, September 11, and October 11, 2013; January 29 and February 18, 2014
Prococode: NPT

Dear Mr. Humphrey:

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) for the SAPIEN XT™ Transcatheter Heart Valve (THV), Model 9300TFX, and accessories. This device is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis (aortic valve area $\leq 1.0 \text{ cm}^2$ or aortic valve area index $\leq 0.6 \text{ cm}^2/\text{m}^2$, a mean aortic valve gradient of $\geq 40 \text{ mmHg}$, or a peak aortic-jet velocity of $\geq 4.0 \text{ m/s}$), and with native anatomy appropriate for the 23, 26, or 29 mm valve system, 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 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 1 year for the size 29 mm valve and 2 years for the remaining sizes and accessories. 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" (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.

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 conditions outlined above, you must conduct a post-approval study (PAS) and participate in two active surveillance plans as described below:

1. **PAS:** *Continued follow-up of the IDE inoperable patients cohort (Cohort B):* You have agreed to a study outline on June 5, 2014 (email) in addition to Revision 6.0 of the IDE protocol (G090216). The study objective is to characterize the safety and effectiveness of the SAPIEN XT THV annually from 2 years through 5 years post-procedure. The study will consist of all pivotal and continued access patients who are currently enrolled, alive and received the device in Cohort B, including nested registries NR1, NR4, NR5, and NR6.

The primary safety and effectiveness endpoint is a non-hierarchical composite of death (all cause), disabling stroke, and re-hospitalization for symptoms of aortic stenosis. The secondary safety and effectiveness endpoint is a non-hierarchical composite of all stroke, major vascular complications and re-intervention.

Additional safety endpoints to be evaluated include freedom from: major vascular complications, all neurological events (all stroke and transient ischemic attack),

myocardial infarction, acute kidney injury, conduction disturbance requiring new permanent pacemaker implantation, atrial fibrillation at each visit, and transfusion. Procedure related complications will be assessed as well.

Additional effectiveness endpoints include total days alive and out-of-hospital (from date of index procedure), clinical improvement per New York Heart Association (NYHA) Class, clinical improvement in quality of life, clinical improvement per 6 Minute Walk Test, and mean Intensive Care Unit (ICU) and total index procedure hospital length of stay.

All available subjects in the pivotal study and CAP investigation that were used to support the current PMA application will be followed annually to 5 years post implant.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete PAS protocol. Your PMA supplement should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing.

Please be advised that the results from this 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.

FDA would like to remind you that you are asked to submit PAS Progress Reports annually. The reports should clearly be identified as Post-Approval Study Report. Two copies for each study, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2).

Be advised that the failure to conduct the PAS 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.

2. **Surveillance:** You are required to actively participate 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 device for 5 years. This surveillance should 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, 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.

Note that you are not required to submit any progress report for this surveillance plan. FDA will conduct our own analyses for the purpose of surveillance through access to the TVTR.

3. ***Enhanced surveillance and monitoring:*** In addition to the conditions outlined above, you are required to implement an enhanced surveillance and monitoring plan for the device for the duration of the variance granted by FDA on June 10, 2014 in accordance with 21 CFR 820.1(e)(2). The plan shall include the following: (1) You will provide to FDA quarterly reports of clinical data extracts from the TVTR regarding the procedural assessments, with specific attention to adverse events related to delivery systems and accessories of the SAPIEN XT THV; and (2) You will notify all implanting sites in the U.S. of the enhanced surveillance and monitoring plan, set up a hotline and list it in the labeling for sites to report device quality related issues to you, and provide to FDA quarterly summary reports of such customer complaint data (e.g., in the form of customer experience reports) for all SAPIEN XT THVs, delivery systems and accessories, with a separate chart for each type of device manufactured at the facility covered in the variance.

Two copies of each quarterly report, identified as "Variance Report" and bearing the applicable PMA reference number, should be submitted to the address below.

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 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
PMA Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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

Sincerely yours,

Bram D. Zuckerman -S

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



Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Medical Device Tracking Order

6/24/14

Thomas Humphrey
EDWARDS LIFESCIENCES, LLC.
ONE EDWARDS WAY
IRVINE, CA 92614
UNITED STATES

Re: P130009

AORTIC VALVE, PROSTHESIS, PERCUTANEOUSLY DELIVERED (NPT)

Dear Thomas Humphrey:

You are notified by this letter of your obligation to adopt a method of tracking for the device referenced above, as authorized by section 519(g) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 360i(g). The implementation of section 519(g) of the Act requires the Food and Drug Administration (FDA) to issue an order to manufacturers when FDA determines that a person who manufactures and distributes a device meets the relevant statutory requirements and that tracking is required to protect the public health. This order is effective immediately.

Section 519(g) of the Act states that FDA, “may by order require a manufacturer to adopt a method of tracking a class II or class III device—

- (A) the failure of which would be reasonably likely to have serious adverse health consequences; or
- (B) which is—
 - (i) intended to be implanted in the human body for more than one year, or
 - (ii) a life sustaining or life supporting device used outside a device user facility.”

The corresponding medical device tracking regulations, found in Title 21 Code of Federal Regulations (CFR) Part 821, are intended to ensure that tracked devices can be traced from the device manufacturing facility to the person for whom the device is intended when patient notification actions under section 518(a) of the Act, 21 U.S.C. § 360h(a), or device recall actions under section 518(e) of the Act, 21 U.S.C. § 360h(e), are ordered by the FDA. The device tracking requirements for exemptions and variances; system and content requirements of tracking; the obligations of persons other than device manufacturers; records and inspection requirements; and confidentiality requirements, which were published in the Federal Register on August 16, 1993, remain in effect. (21 CFR sections 821.2, 821.25, 821.30, 821.50, 821.55 and 821.60)

This order to adopt a tracking method does not change your firm's obligations concerning other FDA regulations affecting its device. FDA published in the Federal Register on February 28, 2002, an amendment to the final rule to revise the scope of the regulation and add certain patient confidentiality requirements and non-substantive changes to remove outdated references and simplify terminology. (67 FR 6943) If you need specific guidance, please contact the Office of Compliance, FDA Center for Devices and Radiological Health, at TrackedDevicesMailbox@fda.hhs.gov. Other general information about your firm's responsibilities under the Act, or more specific information, such as non-binding guidance on medical device tracking (link provided), may be obtained from the Division of Small Manufacturers, International, and Consumer Assistance at its toll-free number, (800) 638-2041, or at the internet address www.fda.gov/cdrh.

Sincerely,

A handwritten signature in blue ink, appearing to read "Steven Silverman", is positioned above the typed name and title.

Steven Silverman
Director
Office of Compliance
Center for Devices and
Radiological Health

Enclosures/Links

[Medical Device Tracking; Guidance for Industry and FDA Staff](#)