



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

June 5, 2017

Edwards Lifesciences LLC
Ms. Karen Reynolds
Senior Specialist, Regulatory Affairs
One Edwards Way
Irvine, California 92614

Re: P140031/S028

Trade/Device Name: Edwards SAPIEN 3 Transcatheter Heart Valve, model 9600TFX, 20, 23, 26, and 29 mm, and accessories (Edwards Commander delivery system, models 9600LDS20, 9600LDS23, 9600LDS26, and 9600LDS2; Edwards Certitude delivery system, models 9600SDS20, 9600SDS23, 9600SDS26, and 9600SDS29; with crimp stopper and Qualcrimp crimping accessory; Edwards Certitude Introducer Sheath, models 9600IS18 and 9600IS21; and Edwards crimper, model 9600CR)

Filed: December 9, 2016

Product Code: NPT, NPU

Dear Ms. Reynolds:

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 3 Transcatheter Heart Valve and accessories for expanding the indication to include patients with a failed surgical bioprosthetic aortic or mitral valve. The device is indicated for patients with symptomatic heart disease due to failure (stenosed, insufficient, or combined) of a surgical bioprosthetic aortic or mitral 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., predicted risk of surgical mortality $\geq 8\%$ at 30 days, based on the STS risk score and other clinical co-morbidities unmeasured by the STS risk calculator). We are pleased to inform you that the PMA supplement 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.

Continued approval of the 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 PMA 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. Two (2) copies of each report, identified as an "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. OSB Lead Surveillance – *Edwards SAPIEN 3 Aortic Valve-in-Valve Novel Surveillance*: The Office of Surveillance and Biometrics (OSB) will have the lead for surveillance initiated after device approval. You have agreed to work with the Transcatheter Valve Therapy (TVT) Registry to ensure that FDA surveillance occurs for the SAPIEN 3 device used for the replacement of a failing surgical bioprosthetic aortic valve over the next 2 years. You have also agreed to link the data to Centers for Medicare and Medicaid Services (CMS) database for long-term surveillance of these patients through 5 years post implantation.

This surveillance will monitor the following: (1) device success (intra-procedure); (2) all-cause mortality, all stroke, life-threatening/major bleeding, new requirement for dialysis, peri-procedural myocardial infarction, and repeat procedure for valve-related dysfunction (surgical or interventional therapy) at 30 days and 12 months; (3) neurological (non-stroke), vascular complications, and quality of life (KCCQ) outcomes at 30 days and 12

months; and (4) all-cause mortality, all stroke, and repeat procedure for valve-related dysfunction (surgical or interventional therapy) at 2-5 year post-implantation.

You are required to submit a progress report bi-annually for this surveillance for the first two years after approval, and annually thereafter.

2. OSB Lead Surveillance – *Edwards SAPIEN 3 Mitral Valve-in-Valve Novel*

Surveillance: The OSB will also have the lead for this surveillance. You have agreed to work with the TVT Registry to ensure that FDA surveillance occurs for the SAPIEN 3 device used for the replacement of a failing surgical bioprosthetic mitral valve over the next 2 years. You have also agreed to link the data to Centers for Medicare and Medicaid Services (CMS) database for long-term surveillance of these patients through 5 years post implantation.

This surveillance will monitor the following: (1) all-cause mortality, heart failure rehospitalization, and mitral valve reintervention at 30 days and 12 months; (2) 6-minute walk distance, KCCQ, and change in NYHA functional class at 30 days and 12 months; (3) device- or procedure-related adverse events, major bleeding complications, stroke and other cerebrovascular events, myocardial infarction, new requirement for dialysis, new onset atrial fibrillation, unplanned mitral valve surgery due to device/procedure failure or malfunction, requirement for valve replacement, unplanned cardiac surgery for any cause, and requirement/insertion of an implantable cardiac defibrillator at 30 days and 12 months; (4) mitral valve hemodynamics at 30 days and 12 months; (5) all-cause mortality, all stroke, and repeat procedure for valve-related dysfunction (surgical or interventional therapy) at 2-5 years post implantation.

You are required to submit a progress report bi-annually for this surveillance for the first two years after approval, and annually thereafter. You may combine the progress reports for the “Edwards SAPIEN 3 Mitral Valve-in-Valve Novel Surveillance” and the “Edwards SAPIEN 3 Aortic Valve-in-Valve Novel Surveillance.”

Be advised that protocol information, interim and final results will be published on the Post-Approval Study Webpage <http://www.fda.gov/devicepostapproval>.

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>).

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes complete protocols of your post-approval studies described above. 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. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

Before making any change affecting the safety or effectiveness of the PMA 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 final labeling. Final 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 labeling is identical to the labeling approved in draft form. If the final 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.

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

Sincerely,



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