SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name:	Aortic valve, prosthesis, percutaneously delivered
Device Trade Name:	Edwards SAPIEN 3 and SAPIEN 3 Ultra Transcatheter Heart Valve System
Device Procode:	NPT
Applicant Name and Address:	Edwards Lifesciences LLC One Edwards Way Irvine, CA 92614
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P140031/S112
Date of FDA Notice of Approval:	September 9, 2020

The original PMA of the Edwards SAPIEN 3 Transcatheter Heart Valve (THV) System, P140031, was approved on June 17, 2015, with an indication for patients deemed to be at high or greater risk for surgical aortic valve replacement (SAVR). The indication was later expanded in PMA Supplement P140031/S010 on August 18, 2016, to include patients deemed to be at intermediate risk for SAVR. The indication was further expanded in PMA Supplement P140031/S028 on June 5, 2017 to include patients with a failing (stenosed, insufficient, or combined) surgical bioprosthetic aortic or mitral valve who are deemed to be at high or greater risk for redo SAVR or surgical mitral valve replacement. More recently, in PMA Supplement P140031/S085, which was approved on August 16, 2019, the indication of the SAPIEN 3 and SAPIEN 3 Ultra THV System was expanded to include patients deemed to be at low risk for SAVR.

The SSEDs to support the above indications are available on the following FDA websites and are incorporated by reference herein:

https://www.accessdata.fda.gov/cdrh_docs/pdf14/P140031b.pdf
https://www.accessdata.fda.gov/cdrh_docs/pdf14/P140031S010b.pdf
https://www.accessdata.fda.gov/cdrh_docs/pdf14/P140031S028b.pdf
https://www.accessdata.fda.gov/cdrh_docs/pdf14/P140031S085B.pdf

The current Panel Track PMA Supplement expands the indication of the Edwards SAPIEN 3 and SAPIEN 3 Ultra THV System to include patients with a failing transcatheter

bioprosthetic aortic valve (i.e., THV-in-THV) who are deemed to be at high or greater risk for SAVR.

II. INDICATIONS FOR USE

The Edwards SAPIEN 3 and SAPIEN 3 Ultra THV System is indicated for patients with symptomatic heart disease due to failing (stenosed, insufficient, or combined) of a surgical or transcatheter bioprosthetic aortic valve or a surgical bioprosthetic 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 ≥ 8% at 30 days, based on the Society of Thoracic Surgeons (STS) risk score and other clinical co-morbidities unmeasured by the STS risk calculator).

III. CONTRAINDICATIONS

The Edwards SAPIEN 3 and SAPIEN 3 Ultra THV System are contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Edwards SAPIEN 3 and SAPIEN 3 Ultra THV System labeling.

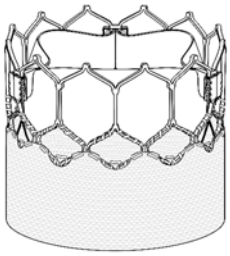
V. DEVICE DESCRIPTION

The Edwards SAPIEN 3 THV (model 9600TFX, 20, 23, 26, and 29 mm), as shown in Figure 1, is comprised of a balloon-expandable, radiopaque, cobalt-chromium (MP35N) frame, a trileaflet bovine pericardial tissue valve, a polyethylene terephthalate (PET) internal fabric skirt, and a PET external sealing skirt for reduction of paravalvular regurgitation. The leaflets are treated according to the Carpentier-Edwards ThermaFix process.

Figure 1: SAPIEN 3 Transcatheter Heart Valve

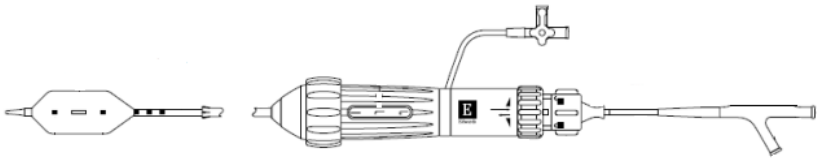
The Edwards SAPIEN 3 Ultra THV (model 9750TFX, 20, 23, and 26 mm), as shown in Figure 2, is a design iteration of the SAPIEN 3 THV, with a knitted outer skirt featuring a velour texture on one side.

Figure 2: SAPIEN 3 Ultra Transcatheter Heart Valve



The Edwards Commander Delivery System (models 9600LDS20, 9600LDS23, 9600LDS26, and 9600LDS29), as shown in Figure 3, includes a handle that provides a flex wheel for articulation of the flex catheter, a tapered tip at the distal end of the delivery system, a balloon catheter for deployment of the THV, and radiopaque markers. It is used when a long access route is planned. The Commander Delivery System uses the Edwards eSheath Introducer Set (models 914ES and 916ES), which is an off-the-shelf device cleared in 510(k) K200258, to establish vascular access.

Figure 3: Edwards Commander Delivery System

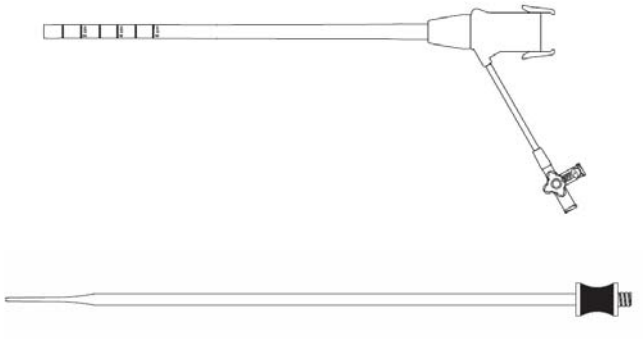


The Edwards Certitude Delivery System (models 9630TA20, 9600SDS20, 9630TA23, 9600SDS23, 9630TA26, 9600SDS26, 9630TA29, and 9600SDS29), as shown in Figure 4, includes a handle with a flex wheel for articulation of the balloon catheter and extension tubing. It is used when a short access route is planned.

Figure 4: Edwards Certitude Delivery System

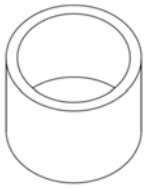
The Edwards Certitude Introducer Sheath (models 9600IS18 and 9600IS21), as shown in Figure 5, is intended to be used with the Certitude Delivery System. It has a radiopaque marker for visualization of the sheath tip and non-radiopaque depth markings on the distal end. The proximal end of the introducer sheath includes a flush tube and three hemostasis valves.

Figure 5: Edwards Certitude Introducer Sheath



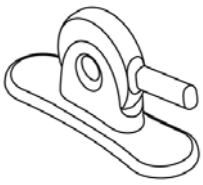
The Qualcrimp crimping accessory, as shown in Figure 6, is a non-patient contacting device that is placed around the THV to protect the leaflets during the crimping process. It is manufactured of tubular polyester polyurethane foam and laminated cylindrically on both the inner and outer surfaces with a polyether urethane material.

Figure 6: Qualcrimp Crimping Accessory



The Edwards Crimper (model 9600CR), as shown in Figure 7, is comprised of various molded plastic components which compress the valve to a controlled aperture. The aperture is created by rotating the handle until it abuts the crimp stopper. The Edwards Crimper is used with a Crimp Stopper to correctly crimp the THV.

Figure 7: Edwards Crimper



VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are other alternatives for patients with a failing transcatheter bioprosthetic aortic valve, including percutaneous balloon valvuloplasty (BAV) for temporary relief of stenosis, surgical replacement of the degenerated device, and palliative medical therapy without an obstruction-relieving procedure. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Edwards SAPIEN 3 THV is currently approved in the following foreign countries for the aortic THV-in-THV indication:

- Austria
- Algeria
- Argentina
- Bahrain
- Belgium
- Bosnia and Herzegovina
- Brazil
- Bulgaria
- Canada
- Chile
- Colombia
- Costa Rica
- Croatia
- Cyprus
- Czechia
- Denmark
- Ecuador
- Estonia
- Finland
- France
- Germany
- Greece
- Hong Kong
- Hungary
- Iran
- Ireland
- Israel
- Italy
- Kuwait
- Latvia
- Lebanon
- Lithuania
- Luxembourg
- Malta
- Netherlands
- Oman
- Pakistan
- Paraguay
- Peru
- Poland
- Portugal
- Qatar
- Romania
- South Africa
- Slovakia
- Slovenia
- South Korea
- Spain
- Sweden
- Taiwan
- Thailand
- Tunisia
- United Arab Emirates
- Uruguay
- Vietnam

It has not been withdrawn from marketing for any reason related to its safety or effectiveness.

The SAPIEN 3 Ultra THV has not been marketed in the United States or any foreign country for the aortic THV-in-THV indication.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of potential adverse effects (e.g., complications) associated with the use of the device.

- Death
- Stroke/transient ischemic attack, clusters or neurological deficit
- Paralysis
- Permanent disability
- Respiratory insufficiency or respiratory failure
- Hemorrhage requiring transfusion or intervention
- Cardiovascular injury including perforation or dissection of vessels, ventricle, atrium, septum, myocardium or valvular structures that may require intervention
- Pericardial effusion or cardiac tamponade

- Thoracic bleeding
- Embolization including air, calcific valve material or thrombus
- Infection including septicemia and endocarditis
- Heart failure
- Myocardial infarction
- Renal insufficiency or renal failure
- Conduction system defect which may require a permanent pacemaker
- Arrhythmia
- Retroperitoneal bleed
- Arteriovenous (AV) fistula or pseudoaneurysm
- Reoperation
- Ischemia or nerve injury or brachial plexus injury
- Restenosis
- Pulmonary edema
- Pleural effusion
- Bleeding
- Anemia
- Abnormal lab values (including electrolyte imbalance)
- Hypertension or hypotension
- Allergic reaction to anesthesia, contrast media, or device materials
- Hematoma
- Syncope
- Pain or changes at the access site
- Exercise intolerance or weakness
- Inflammation
- Angina
- Heart murmur
- Fever
- Cardiac arrest
- Cardiogenic shock
- Emergency cardiac surgery
- Cardiac failure or low cardiac output
- Coronary flow obstruction/transvalvular flow disturbance
- Device thrombosis requiring intervention
- Valve thrombosis
- Device embolization
- Device migration or malposition requiring intervention
- Left ventricular outflow tract obstruction
- Valve deployment in unintended location
- Valve stenosis
- Structural valve deterioration (wear, fracture, calcification, leaflet tear/tearing from the stent posts, leaflet retraction, suture line disruption of components of a prosthetic valve, thickening, stenosis)
- Device degeneration
- Paravalvular or transvalvular leak
- Valve regurgitation

- Hemolysis
- Device explants
- Nonstructural dysfunction
- Mechanical failure of delivery system, and/or accessories
- Non-emergent reoperation

For the specific adverse events that occurred in the real-world clinical practice, please see Section X.

IX. SUMMARY OF PRECLINICAL STUDIES

A summary of previously reported preclinical studies can be found in the SSEDs for the original PMA P140031 and PMA Supplement P140031/S028.

X. SUMMARY OF PRIMARY CLINICAL DATA

The applicant performed an analysis of the real-world off-label use data captured in the Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) Registry to establish a reasonable assurance of the safety and effectiveness of the Edwards SAPIEN 3 THV System in patients receiving THV-in-THV treatment. The data from the TVT Registry were the basis of the PMA approval decision. A summary of the clinical data is presented below.

Note that the clinical data set did not include the SAPIEN 3 Ultra THV System. However, the results obtained on the Edwards SAPIEN 3 THV System are considered applicable to the Edwards SAPIEN 3 Ultra THV System based on prior demonstration of device comparability in PMA Supplement P140031/S074.

A. Study Design

A database extract was performed on August 9, 2019. Patients were excluded if their previous transcatheter aortic valve replacement (TAVR) procedure was performed prior to April 23, 2007 (first implant in the US under the PARTNER trial). The database extract yielded 404 patients that had undergone a THV-in-THV procedure with an Edwards SAPIEN 3 (N=402) or Edwards SAPIEN 3 Ultra (N=2). These patients were treated between August 4, 2015 and July 11, 2019 at 188 participating hospitals.

To obtain more complete 1-year follow-up data, a treatment cutoff date of June 9, 2018 was then applied to the data set obtained above, which yielded 263 patients (SAPIEN 3 THV only) treated at 138 participating hospitals. The cutoff date was 14 months before the database extract date, which included a +60-day window for the 1-year visit. These 263 patients constituted the clinical data set used to support this application.

1. Clinical Inclusion and Exclusion Criteria

   The initial database extract included all patients who received a commercially available

Edwards SAPIEN 3 or Edwards SAPIEN 3 Ultra THV in an aortic THV-in-THV procedure. The final data set was a subset of the initial database extract as described above.

2. Follow-up Schedule

   All patients were followed post-implantation according to their local standards of care. The TVT Registry collects follow-up data at 30 days and 1 year.

3. Clinical Endpoints

   Data entered into the TVT Registry were collected through standardized data collection forms. The endpoints analyzed in this application included: death, stroke/transient ischemic attack (TIA), valve reinterventions, key site reported adverse events, valve performance based on echocardiographic data, New York Heart Association (NYHA) classification, and the Kansas City Cardiomyopathy Questionnaire (KCCQ) score. The analyses in the application focused on 30-day and 1-year time points.

B. Accountability of PMA Cohorts

At the time of database extract, 242 of the 263 patients were eligible for the 30-day visit and 216 (89.3%) completed the visit within the 30-day follow-up window, defined as the period between 21 days post-procedure and 75 days post-procedure. At 1 year, 200 patients were eligible for the 1-year visit and 136 (68.0%) completed the visit within the follow-up window, defined as the period between 305 days post-procedure and 425 days post-procedure. A detailed summary of the patient accountability at 30 days and 1 year is shown in Table 3.

Table 3: Patient Visit Accountability (AI Population)

	30-day Visit	1-year Visit
Total patients	263	263
Non-eligible	21	63
Death	19	47
Withdrawal	1	3
Lost to follow-up	1	13
Eligible	242	200
Follow-up visit completed	89.3% (216)	68.0% (136)
Missed visit	10.7% (26)	32.0% (64)

The “Attempted Implant” population consisted of all patients for whom the first vascular access was attempted. The “Valve Implant” population consisted of those patients for whom the valve implant procedure has started and a “No” was indicated for both ‘procedure aborted” and “conversion to open heart surgery”. The number of patients in the analysis population is shown in Table 4.

Table 4: Analysis Populations

Analysis Population	Number of Patients
Attempted Implant Population	263
Valve Implant Population	261

C. Study Population Demographics and Baseline Characteristics

The demographics and baseline characteristics of the patients, as shown in Table 5, represent an elderly, multimorbid cohort of patients, consistent with the high operative risk of the population.

Table 5: Patient Demographics and Baseline Characteristics (AI Population)

Demographics and Baseline Characteristics	Summary Statistics* (N = 263)
Age - years	78.9 ± 10.5
Male sex	55.1% (145/263)
Society of Thoracic Surgeons (STS) score	10.2 ± 8.6 (242)
New York Heart Association (NYHA) class	
I/II	12.3% (32/261)
III/IV	87.7% (229/261)
Previous myocardial infarction	26.6% (70/263)
Previous intervention	
Coronary artery bypass grafting (CABG)	28.1% (74/263)
Percutaneous coronary intervention (PCI)	34.0% (89/262)
Prior aortic valvuloplasty	13.7% (36/263)
Stroke or Cerebrovascular accident (CVA)	18.3% (48/263)
Peripheral vascular disease (PVD)	32.1% (84/262)
Atrial fibrillation/flutter	48.7% (128/263)
Permanent pacemaker	32.2% (84/261)
Porcelain aorta	8.0% (21/262)
Hostile chest	8.7% (23/263)
Echocardiographic findings (Valve Implant Population)	
Valve area ($cm^{2)}$	1.0 ± 0.5 (115)
Mean gradient (mmHg)	29.4 ± 19.0 (135)
Mean left ventricular ejection fraction (LVEF), %	49.3 ± 15.1 (257)
Moderate or severe aortic regurgitation	79.3% (207/261)
Moderate or severe mitral regurgitation	42.1% (98/233)

*Continuous measures - Mean ± SD (Total no.); Categorical measures – % (no./Total no.)

D. Safety and Effectiveness Results

1. Safety Endpoints

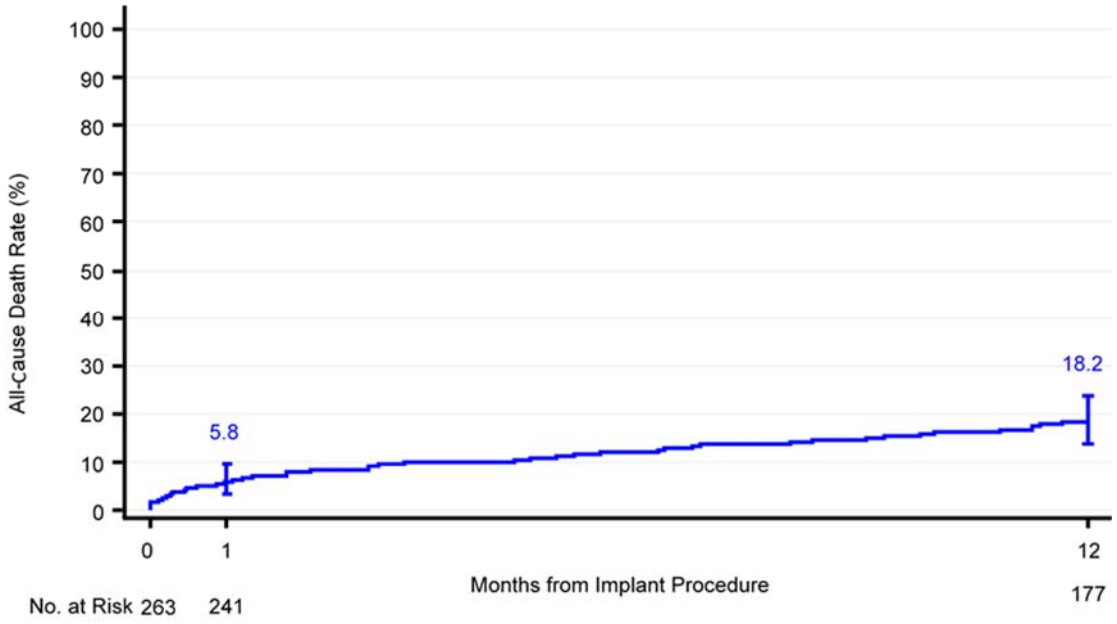
The Kaplan-Meier estimates of site-reported adverse events through 1 year are presented in Table 6. The Kaplan-Meier curve for all-cause mortality is shown in Figure 8. The all-cause mortality rate was 5.8% at 30 days and 18.2% at 1 year, including a cardiovascular death rate of 2.7% at 30 days and 5.4% at 1 year. Other relatively more frequent adverse events included conduction/native pacer disturbance requiring pacer (8.2% at 30 days and 10.6% at 1 year) and valve-related readmission (4.3% at 30 days and 8.6% at 1 year).

Table 6: Site Reported Adverse Events (AI Population)

	Kaplan-Meier Rate*	
Adverse Event	**30 Days (N=263)**	**1 Year (N=263)**
All-cause death	5.8% (15, 15)	18.2% (45, 45)
Cardiovascular death	2.7% (7, 7)	5.4% (13, 13)
All stroke	2.3% (6, 6)	2.8% (7, 7)
Ischemic stroke	1.9% (5, 5)	2.4% (6, 6)
Undetermined stroke	0.4% (1, 1)	0.4% (1, 1)
Transient ischemic attack (TIA)	0.8% (2, 2)	1.9% (4, 4)
Major vascular complication	0.4% (1, 1)	1.0% (2, 2)
Major bleeding	1.2% (3, 3)	2.5% (7, 5)
Myocardial infarction	0.8% (3, 2)	3.1% (6, 5)
New requirement for dialysis	0.4% (1, 1)	1.6% (3, 3)
Conduction/native pacer disturbance requiring pacer	8.2% (21, 21)	10.6% (25, 25)
Conduction/native pacer disturbance requiring implantable cardioverter defibrillator (ICD)	0.4% (1, 1)	2.2% (4, 4)
Aortic valve re-intervention	0.4% (1, 1)	1.2% (2, 2)
Unplanned other cardiac surgery or intervention	2.4% (6, 6)	4.5% (9, 9)
Unplanned vascular surgery or intervention	1.5% (4, 4)	2.6% (6, 6)
Device thrombosis	0.4% (1, 1)	1.0% (2, 2)
Valve-related readmission	4.3% (11, 11)	8.6% (22, 18)

*Kaplan-Meier rate - (no. of events, no. of patients with the event).

Figure 8: All-Cause Mortality through 1 Year (AI Population)



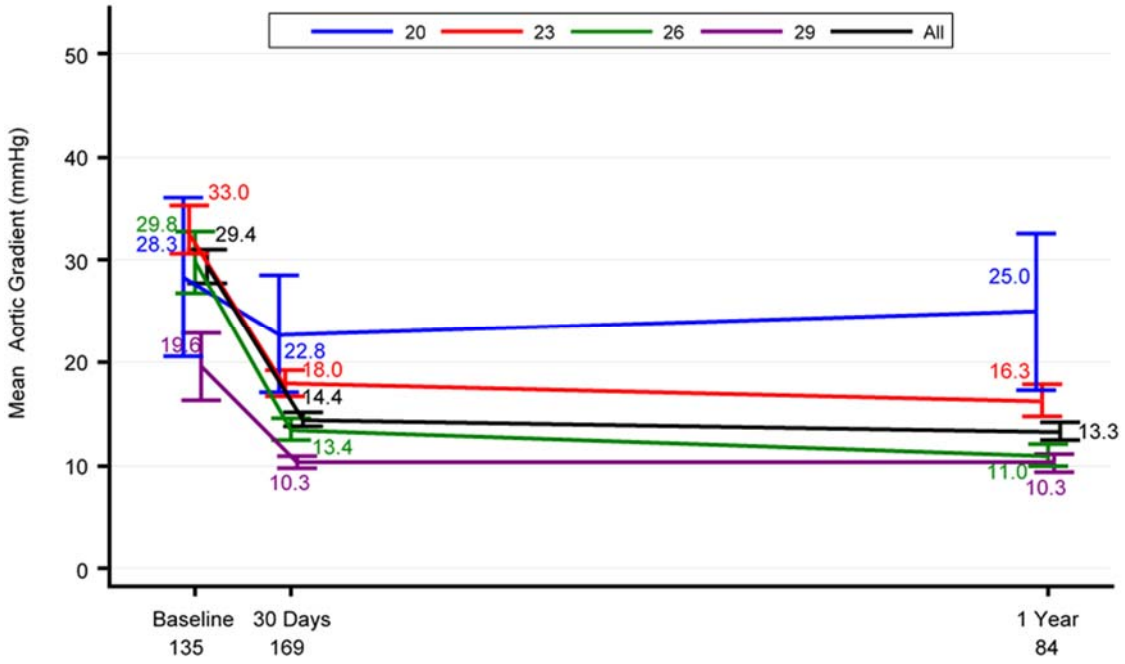
Note: The 95% confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion.

2. Effectiveness Endpoints

Valve Performance

The echocardiographic valve performance results are shown in Figures 9-11. The decrease in gradients were sustained through 1 year. The mean aortic gradient decreased from 29.4 mmHg at baseline to 14.4 mmHg at 30 days, which was maintained through 1 year (13.3 mmHg). Moderate or severe total aortic regurgitation was observed in 79.3% of the patients at baseline, which decreased to 4.6% at 30 days and 3.4% at 1 year. The proportion of patients with ≥ moderate paravalvular regurgitation was 4.5% at 30 days and 2.6% at 1 year.

Figure 9: Mean Aortic Gradient (VI Population)



Note: Line plot with mean and standard error. The total number of patients at each visit time point only counted the patients with valid values.

Figure 10: Total Aortic Regurgitation (VI Population)

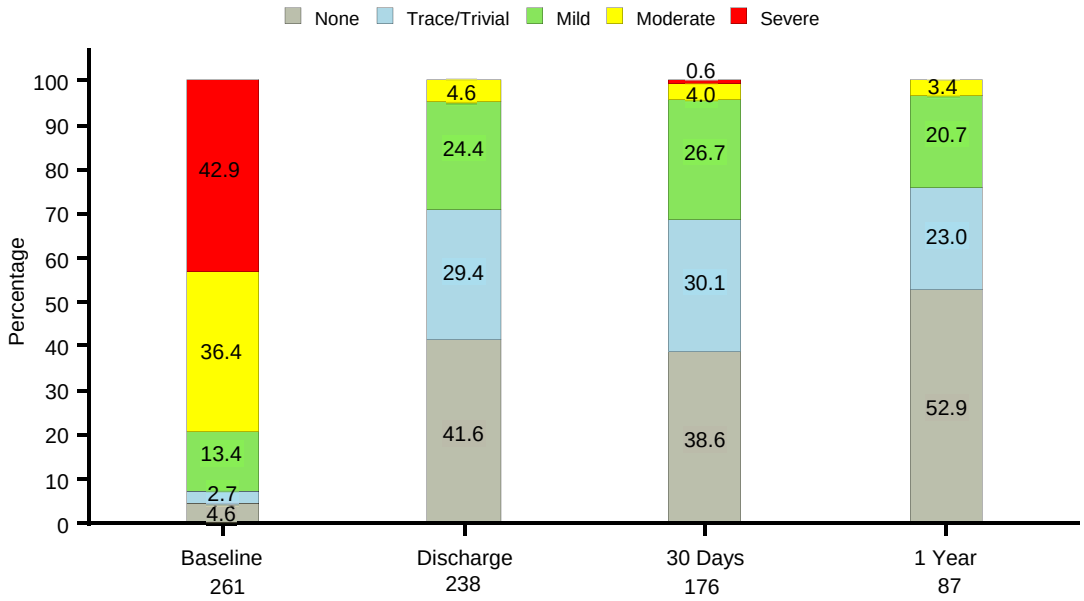
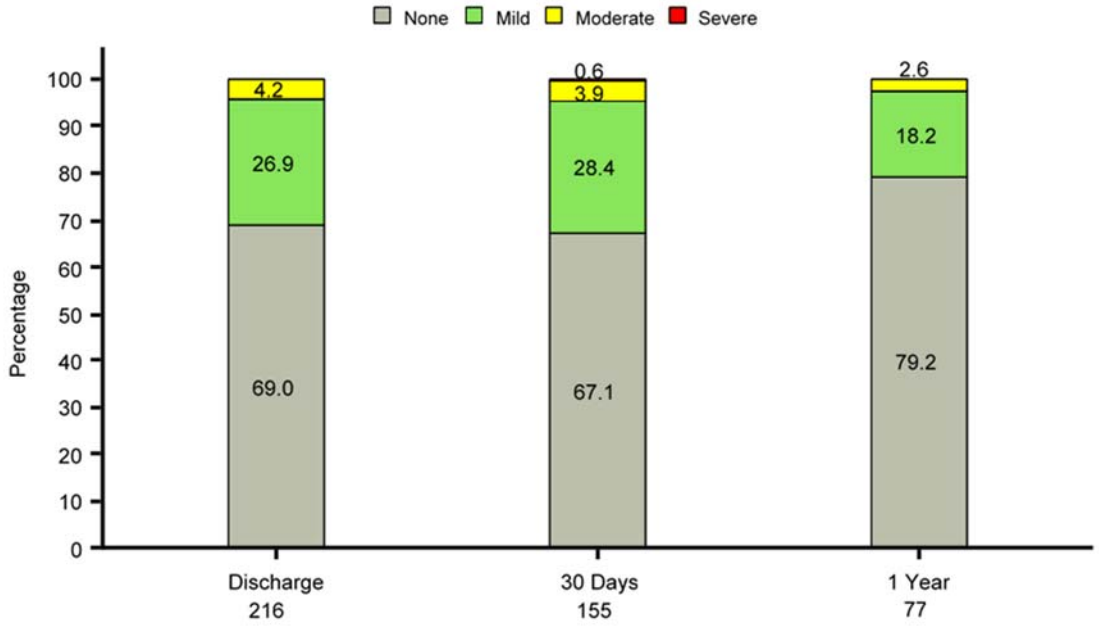


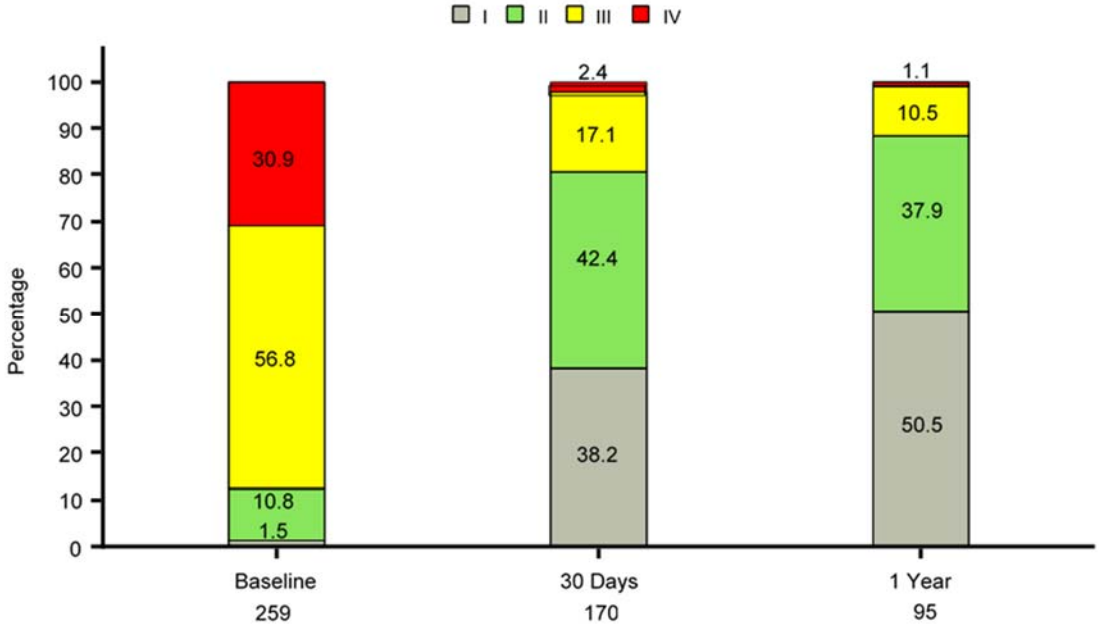
Figure 11: Paravalvular Regurgitation (VI Population)



NYHA Functional Class

The NYHA functional class distributions by visit are presented in Figure 12. At baseline, 87.7% of patients were in NYHA III/IV. At 1 year, the majority (88.4%) of patients were in NYHA I/II.

Figure 12: NYHA Class by Visit (VI Population)



Length of Stay

The mean index hospitalization stay was 4.9 days, which included an average of 1.7 days in the intensive care unit (ICU), as summarized in Table 7.

Table 7: Index Hospitalization (AI Population)

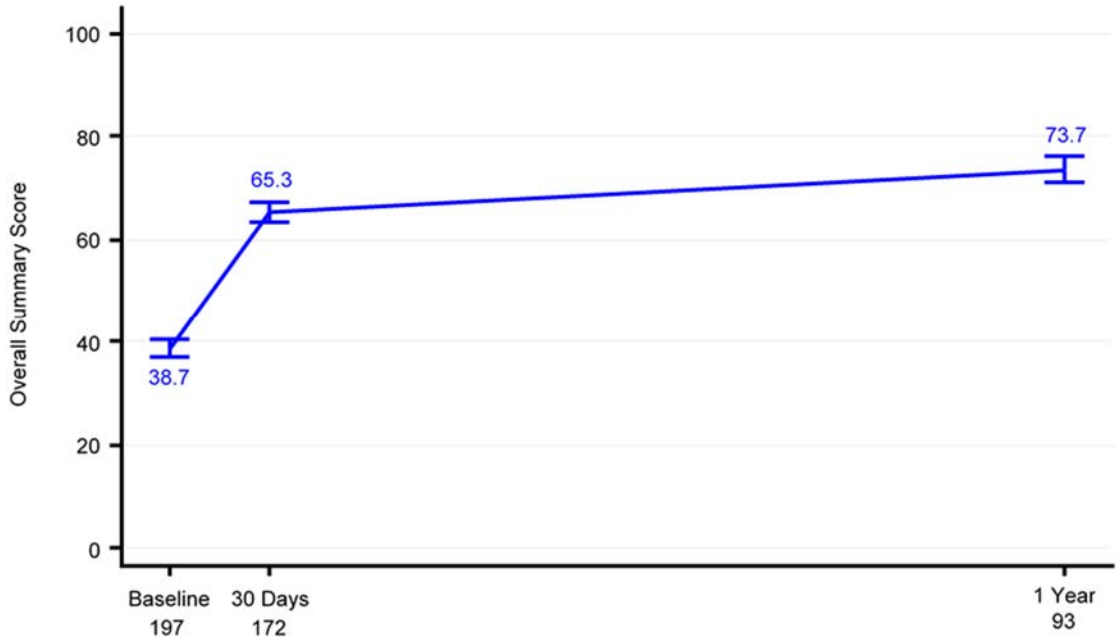
	Length of Stay (days)*
Index hospitalization duration	4.9 ± 0.3 (263)
Intensive care stay	1.7 ± 0.2 (255)

*Mean ± SE (Total no.)

Quality of Life

The results for the KCCQ overall summary score are presented in Figure 13. The mean score increased from 38.7 at baseline to 65.3 and 73.7 at 30 days and 1 year, respectively.

Figure 14: KCCQ Overall Summary Score (VI Population)



Note: Line plot with mean and standard error. The total number of patients at each visit time point only counted patients with valid values.

3. Other Study Observations

Procedural Information

The procedural information is summarized in Table 9. General anesthesia was used in the majority (70%) of patients. Conversion to open heart surgery occurred in two patients due to ventricular rupture and annulus rupture, respectively.

Table 9: Procedural Data Summary (AI Population)

Procedural Data	Summary Statistics*
Operator reason for procedure	
Inoperable/extreme risk	20.8% (54/259)
High risk	69.1% (179/259)
Intermediate risk	9.7% (25/259)
Low risk	0.4% (1/259)
Implant approach	
Transfemoral	95.8% (252/263)
Transapical	1.1% (3/263)
Transaortic	0.8% (2/263)
Subclavian/axillary	0.8% (2/263)
Transseptal	0.4% (1/263)
Transcarotid	1.1% (3/263)
Valve size	
20 mm	2.3% (6/263)
23 mm	35.0% (92/263)
26 mm	30.8% (81/263)
29 mm	31.9% (84/263)
Cardiopulmonary bypass	0.4% (1/263)
Cardiopulmonary bypass status	
Emergent	100.0% (1/1)
Cardiopulmonary bypass time, minutes	254.0 ± NA (1)
Type of anesthesia	
General anesthesia	70.0% (184/263)
Moderate sedation	29.7% (78/263)
Combination	0.4% (1/263)
Total procedure time, minutes	108.5 ± 4.3 (263)
Device implanted successfully	98.9% (260/263)
Procedure aborted	0.0% (0/263)
Conversion to open heart surgery	0.8% (2/263)
Ventricular rupture	1
Annulus rupture	1
Mechanical assist device in place at start of procedure	0.4% (1/263)

Procedural Data	Summary Statistics*
Catheter-based assist device	100.0% (1/1)

*Continuous measures - mean ± SE (n); categorical measures - % (no./Total no.)

4. Pediatric Extrapolation

   In this premarket application, existing clinical data were not leveraged to support approval of a pediatric patient population.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(2) of the Act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM THE PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The patients who underwent aortic THV-in-THV procedures captured in the TVT Registry overall demonstrated clinically significant improvements in valve hemodynamics from baseline to 1 year. On average, the aortic valve pressure gradient decreased from 29.4 mmHg at baseline to 13.3 mmHg at 1 year. The proportion of patients with moderate or severe total aortic regurgitation decreased from 79.3% at baseline to 3.4% at 1 year.

The improvements in clinical outcomes were demonstrated in patients' functional status and quality of life. The majority (88.4%) of patients were in NYHA I/II at 1 year as compared to 12.3% at baseline. Similarly, clinically significant improvement was observed in the KCCQ overall summary score, which increased from 38.7 at baseline to 73.7 at 1 year on average.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory studies and clinical data collected in the TVT Registry to support PMA approval as described above.

The Kaplan-Meier estimate of the all-cause mortality rate was 5.8% at 30 days (compared to a mean STS score of 10.2) and 18.2% at 1 year. The Kaplan-Meier estimates of all stroke, conduction/native pacer disturbance requiring pacer, and valve-related readmission were 2.8%, 10.6%, and 8.6%, respectively, at 1 year.

C. Benefit-Risk Determination

The probable benefits of the aortic THV-in-THV treatment with the SAPIEN 3 THV include

improved valve hemodynamic performance, improved functional status as measured by the NYHA classification, and improved quality of life as measured by the KCCQ.

The probable risks of the aortic THV-in-THV treatment with the SAPIEN 3 THV include procedural and late complications such as death, stroke, and conduction/native pacer disturbance requiring pacer.

1. Patient Perspectives

   This submission did not include specific information on patient perspectives for this device. However, since transcatheter valve replacement with an Edwards SAPIEN 3 THV provides a less invasive alternative to surgical valve replacement, FDA believes many patients and their physicians would prefer the transcatheter valve replacement therapy as an alternative.

In conclusion, given the available information above, the data support that for patients with a failing (stenosed, insufficient, or combined) previously implanted transcatheter bioprosthetic aortic valve who are at high or greater risk for reoperative surgical aortic valve replacement, the probable benefits of implanting an Edwards SAPIEN 3 THV outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the SAPIEN 3 THV in treating patients with symptomatic heart disease due to failing of a transcatheter 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. FDA has determined this conclusion is also applicable to the SAPIEN 3 Ultra THV.

XIII. CDRH DECISION

CDRH issued an approval order on September 9, 2020. The final conditions of approval cited in the approval order are described below.

The applicant must participate in and support continued surveillance of the Edwards SAPIEN 3 and SAPIEN 3 Ultra THV System used for the aortic THV-in-THV treatment:

1. **SAPIEN 3 and SAPIEN 3 Ultra Aortic THV-in-THV Surveillance**: The applicant has agreed to work with the TVT Registry to ensure that FDA surveillance occurs for commercial uses of the Edwards SAPIEN 3 and SAPIEN 3 Ultra THV System for the aortic THV-in-THV indication. The surveillance is to continue to monitor the performance of the Edwards SAPIEN 3 and SAPIEN 3 Ultra THV System in the real-world setting. It will involve all consecutive patients treated within the first 3 years after the PMA approval that are entered into the TVT Registry (enrollment period). The applicant has also agreed to link the data to the Centers for Medicare and Medicaid Services (CMS) claims database for long-term surveillance of these patients through 10 years post implantation (follow-up duration). 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 2-10 year post implantation.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See final approved labeling (Instructions for Use).

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the final labeling (Instructions for Use).

Post-approval Requirements and Restrictions: See Approval Order.