SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Balloon Expandable Stent

Device Trade Name: PALMAZ MULLINS XD™ Pulmonary Stent

Device Procode: QWC

Applicant's Name and Address: Cordis US Corp.
14201 NW 60th Avenue
Miami Lakes, FL 33014

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P220004

Date of FDA Notice of Approval: 7/21/2023

II. INDICATIONS FOR USE

The PALMAZ MULLINS XD Pulmonary Stent is indicated for the non-emergency treatment of pulmonary artery stenosis in pediatric patients who are at least 10kg in weight with two ventricle anatomy.

III. CONTRAINDICATIONS

Contraindications associated with the use of the PALMAZ MULLINS XD Pulmonary Stent include:

- Active infection
- Aneurysm, dissection, or in-situ thrombus formation at the treatment site
- Inability to traverse narrowed segment safely
- Vessel too small for the delivery system

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the PALMAZ MULLINS XD Pulmonary Stent labeling.

V. DEVICE DESCRIPTION

The PALMAZ MULLINS XD Pulmonary Stent is a balloon-expandable, laser cut stent made from 316L stainless steel tubing. The PALMAZ MULLINS XD Pulmonary Stent is identical in design, stent sizes, specifications, materials, and manufacturing to the

currently marketed PALMAZ GENESIS XD Transhepatic Biliary Stent. The PALMAZ GENESIS XD Transhepatic Biliary Stent is cleared under K020809 for palliation of malignant neoplasms in the biliary tree.

The PALMAZ MULLINS XD Pulmonary Stent is supplied in both 10 mm and 12 mm nominal diameters for unexpanded lengths of 19 mm, 25 mm, 29 mm, and 39 mm and in a 10 mm nominal diameter for an unexpanded length of 59 mm. The length of each size stent after it has been expanded to its nominal diameter is shown in **Table 1**.

Table 1: PALMAZ MULLINS XD Pulmonary Stent Product Specifications

Stent Description		Stent Length	
Product Code	**Nominal Diameter and Length (mm)**	**Unexpanded (mm)**	**Expanded (mm)***
PM1910PXD	10 x 19	19	17
	12 x 19		16
PM2510PXD	10 x 25	25	23
	12 x 25		21
PM2910PXD	10 x 29	29	27
	12 x 29		25
PM3910PXD	10 x 39	39	36
	12 x 39		34
PM5910PXD	10 x 59	59	55

* Expanded stent length data are based on *in vitro* testing.

During the stent implantation procedure, after having been crimped onto a balloon catheter by the physician, the stent balloon assembly is inserted into a percutaneous long sheath and advanced to the target lesion. The balloon is then inflated to expand the stent. The expanded stent remains in place following withdrawal of the deflated balloon catheter, thus keeping the pulmonary artery open, and thereby decreasing the pressure load on the right ventricle while improving flow to the distal pulmonary arterial tree.

Figure 1: Expanded PALMAZ MULLINS XD Pulmonary Stent

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of pulmonary artery stenosis, including balloon dilation and surgical intervention. 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 PALMAZ MULLINS XD has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

- Arrhythmia
- Bleeding
- Death
- Fistula formation
- Hemoptysis
- Hypotension
- Infection
- In-stent thrombosis
- Ischemia/reperfusion injury
- Jailed side branches of the pulmonary arteries
- Myocardial infarction
- Obstruction
- Pulmonary artery aneurysm, dissection, or rupture
- Pulmonary artery thrombosis/thromboembolism
- Pulmonary edema
- Restenosis
- Stent fracture with loss of structural integrity
- Stent malposition dislodgement/migration or embolization requiring transcatheter or surgical adjustment or retrieval
- Stroke or transient ischemic attack
- Vessel perforation/injury/dissection/rupture/tear

For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

Bench testing to support clearance of PALMAZ GENESIS XD Transhepatic Biliary Stent (K020809) for the biliary indication was leveraged to support the pulmonary artery indication as the testing conducted for biliary use represents worst case conditions (e.g., pressures) compared to expected conditions of use in treating pulmonary artery stenosis. The testing conducted on the PALMAZ GENESIS XD Transhepatic Biliary Stent is representative of the PALMAZ MULLINS XD Pulmonary Stent. The tests are summarized in Table 2 below.

Table 2: Summary of in vitro Product Testing for PALMAZ GENESIS XD Transhepatic Biliary Stent

Test	Purpose	Acceptance Criteria	Results
Material Composition	To verify the chemical composition of the stent	Material should be 316L stainless steel	Pass
Mechanical Properties	To verify that the stent properties conform to the requirements of ASTM F138	ASTM F138	Pass
Corrosion Resistance	To evaluate the susceptibility of the stent to corrosion	Stent will be corrosion resistant	Pass
Dimensional Verification (Uniformity of Expansion)	To evaluate the stent uniformity of expansion post-deployment	≤ 10% non-uniformity	Pass
Percent Open Area	To report the percent of open, non-contact area within the stented vessel	80-90% open area	Pass
Foreshortening	To report the decrease in length of the stent between the catheter-loaded condition and the deployed diameter	≤ 20% @ 10 and 12mm diameters.	Pass
Recoil for Balloon Expandable Stents	To report the measured change in diameter of the stent between post-balloon expansion and after balloon deflation	≤ 10%	Pass
Stent Integrity	To report any defects on the deployed stent	No evidence of stent cracking after expansion and following balloon burst at 40X magnification	Pass
Radial Force/Strength	To determine the pressure at which the stent experiences permanent deformation	≥ 2.0 psi	Pass

Test	Purpose	Acceptance Criteria	Results
Fatigue Analysis	Determine Fatigue Safety Factors under physiologically relevant pulsatile loading conditions	At maximum material conditions stent does not exceed the strain limit of material. At maximum material conditions stent does not exceed the fatigue limit of material	Pass
Accelerated Durability Testing	Evaluate stent structural durability under physiologically relevant pulsatile loading conditions	No strut separation at 400MM cycles (equivalent to 10 years simulated cardiac cycles)	Pass
Particulate Evaluation	To measure the total number of particulates and size of the particulates generated and ensure the levels outlined in USP 788 are not exceeded	Per USP 788, the average number of particles present does not exceed: 6000 for size ≥ 10um 600 for size ≥ 25um	Pass
Radiopacity	To evaluate the radiopacity of the stent	Acceptable visibility under fluoroscopy	Pass
Stent Flexibility (three-point bend)	To evaluate the flexibility of the stent	Force to bend 29mm Y-stent ≤ Force to bend stent 15º Deflection	Pass
Stent Retention	To evaluate the force at which the crimped stent is dislodged from a balloon catheter	≥0.13 lbs.	Pass

Magnetic Resonance Imaging (MRI) Compatibility

Non-clinical testing has demonstrated that the device is MR Conditional. A patient with the PALMAZ MULLINS XD Pulmonary Stent can be scanned safely under the following conditions:

- Static magnetic field of 1.5 Tesla and 3.0 Tesla
- Maximum spatial gradient field of 2000 Gauss/cm (20 T/m) or less
- Maximum MRI system reported, whole body averaged specific absorption rate (SAR) of 2.0 W/kg for 15 minutes of scanning (Normal Operating Mode)

Under the scan conditions defined above, non-clinical testing and simulation results indicated the Palmaz stents are expected to produce a maximum temperature rise of 5.7°C after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends approximately 12mm from the Palmaz stent when imaged with a spin echo pulse sequence and a 3.0 T MRI System.

Biocompatibility

The biocompatibility of the PALMAZ MULLINS XD Pulmonary Stent was evaluated per the requirements of ISO 10993-1:2018 and the FDA Guidance, *Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process*. The PALMAZ MULLINS XD Pulmonary Stent is categorized as an implant device in contact with circulating blood with long-term exposure (>30 days). The PALMAZ MULLINS XD Pulmonary Stent is identical to the currently marketed PALMAZ GENESIS XD Transhepatic Biliary Stent and has the same material, same design, and manufacturing processes. Testing to address acute biocompatibility endpoints were conducted on the final finished version of the PALMAZ MULLINS XD Pulmonary Stent. Longer term endpoints were leveraged from the evaluations conducted to support the clearance of the PALMAZ GENESIS XD Transhepatic Biliary Stent (K020809). The tests are summarized in Table 3 below.

Table 3: Summary of Biocompatibility Evaluation

Biological Effect per ISO 10993-1	Test Method	Results
Cytotoxicity	Mouse Fibroblast Assay	Pass
Sensitization	Maximization Test	Pass
Intracutaneous Irritation	Intracutaneous Injection	Pass
Acute System Toxicity	Systemic Injection	Pass
Subacute/Subchronic Implantation Testing	Leveraged from 30-Day GLP Tissue Response Evaluation of PALMAZ Genesis Stents in a Porcine Iliac Model (summarized in Section B below)	Pass
Pyrogenicity	Rabbit Pyrogen Test	Pass
Hemocompatibility	Hemolysis	Pass
Hemocompatibility	Complement Activation	Pass
Hemocompatibility	In Vivo Thrombogenicity (leveraged from K020809)	Pass
Genotoxicity	AMES Test (leveraged from K020809)	Pass
Genotoxicity	MLA Assay (leveraged from K020809)	Pass
Carcinogenicity and Chronic Toxicity	Chemical Characterization/Toxicological	Pass

Biological Effect per ISO 10993-1	Test Method	Results
	Risk Assessment (leveraged from K020809)	

B. Animal Studies

Two studies, one 30-day GLP animal study and one chronic 180-day GLP animal study, were provided to evaluate *in vivo* local tissue response (safety) and assess the overall performance of the stent. The acute study was performed using the PALMAZ GENESIS Iliac Stent, which is identical to the PALMAZ MULLINS XD Pulmonary Stent with the exception of expanded diameters. A total of 10 PALMAZ GENESIS XD stents were implanted in porcine iliac arteries for 30 days. Acute performance evaluation was performed at the time of implant. The pathology results indicated complete endothelialization and the average inflammation score was low. Percent stenosis was 12% which is within an acceptable range. Overall, the results of the acute study demonstrated good healing response with no adverse effect on the tissue response.

The PALMAZ GENESIS XD stent (identical to the PALMAZ MULLINS XD Pulmonary Stent) was also evaluated in a chronic GLP porcine renal artery model and evaluated at 30, 90 and 180 days (4 PALMAZ GENESIS XD stents evaluated at each time point). The histomorphometric and histopathological evaluations showed good luminal patency through the three time periods. Radiographs of the aorto-renal segment show the proper placement of the stent in the renal arteries without migration.

C. Additional Studies

Sterilization, Packaging and Shelf Life

The PALMAZ MULLINS XD Stent is sterilized using Gamma irradiation per ISO 11137-2. The sterilization process validation demonstrated a Sterility Assurance Level (SAL) of 10^{-6}.

The PALMAZ MULLINS XD stent is packaged in a blister package with a foam insert and the lid is heat sealed to the tray. The sealed blister is then placed in a Tyvek pouch and sealed.

The shelf life of the PALMAZ MULLINS XD stent is 48 months. Shelf-life testing for the PALMAZ MULLINS XD stent was leveraged from the packaging and shelf-life validation testing performed on the cleared PALMAZ GENESIS XD stent, which is identical to that of the PALMAZ MULLINS XD stent.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a retrospective clinical study to establish a reasonable assurance of safety and effectiveness of implantation of the PALMAZ GENESIS XD stent in a main branch pulmonary artery of patients with confirmed unilateral, central branch pulmonary artery stenosis and bi-ventricular circulation in the US and Canada. Data from this clinical study, titled "Implantation of Endovascular Stents for Dilation of Pulmonary Artery Branch Stenosis in Patients with Congenital Heart Disease - The Pulmonary Artery Stent Study" (PASS), were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between January 11, 2006 and September 22, 2016. The database for this PMA reflected data collected through October 2, 2019 and included 108 patients. There were 11 investigational sites.

The PASS study was a retrospective, multicenter, analysis utilizing data captured in the Congenital Cardiovascular Interventional Study Consortium (CCISC) Registry. The primary objective of this registry study was to assess safety and effectiveness outcomes associated with the real-world use of the Cordis PALMAZ GENESIS XD in a single main branch pulmonary artery of patients with confirmed unilateral, central branch pulmonary artery stenosis and bi-ventricular circulation.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the PASS study was limited to patients who met the following inclusion criteria:

   1. Males and females with biventricular circulation of an age and size sufficient to require branch pulmonary artery dilation for congenital or postoperative branch pulmonary artery stenosis
   2. Unilateral pulmonary artery stenosis involving either the right or left main branch. The stenotic segment is confined to the right or left main branch with reduction of the lumen size of the normal adjacent vessel by at least 50%
   3. Any of the following physiologic and anatomic data: a systolic pressure gradient across the stenosis of 20 mm Hg, right ventricular (RV) hypertension of at least 60% systemic pressure, stenosis diameter of half the normal adjacent vessel, objective evidence of decreased perfusion of $\leq$ 35% to the ipsilateral lung detected by a nuclear medicine perfusion study, MRI, or other imaging modalities
   4. Stenosis localized in a relatively straight segment of the central branch pulmonary artery starting from 2mm of the branch ostium and not involving the orifice of the lobar branch
   5. Patients with a previous thoracotomy which places them at unusually high risk for surgery directed at branch pulmonary stenosis relief or Patients who have had previously unsuccessful attempts at balloon dilation of branch pulmonary artery stenosis, only to have recoil of the dilated vessel with restenosis

6. Only outpatient cases

Patients were not permitted to enroll in the PASS study if they met any of the following exclusion criteria:

1. Children whose weight was ≤ 10 kg prior to the stenting procedure
2. Children with additional branch pulmonary artery stenoses located in the lobar branches or beyond, bilateral stenoses, or stenoses involving the orifices of the branch pulmonary arteries
3. Patients with a single or one and a half ventricle circulation
4. A previous attempt at balloon dilation of resistant branch pulmonary artery stenosis which could not be expanded with conventional angioplasty balloons
5. Patients in whom vascular access and/or cardiac status did not permit the implantation of the PALMAZ GENESIS XD
6. Patients with severe branch pulmonary artery stenoses such that the intended treatment plan was to implant a partially dilated stent and further dilate in a serial fashion in order to avoid vessel wall disruption
7. Patients with a previously placed pulmonary artery stent at the intended site
8. Patients who had received other types of stents in the pulmonary artery at the intended site
9. Early post-operative or urgent/emergent cases where there were compromised hemodynamics or other morbidities that might have confounded the catheterization procedure

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 1 year postoperatively.

Preoperatively, pre-catheter history and physical data were collected for each subject. Postoperatively, the objective parameters measured during the study included: pre- and post-catheterization minimum diameters of the stented vessel, pressure gradient, and right ventricle to systemic pressure ratio at the time of the procedure. At 1-year follow up, clinical status post-procedure and echocardiogram were measured, and additional studies including MRI, lung perfusion scan, CT angiogram, or cardiac catheterization with angiography were recorded if available and obtained during the 1-year time period. Adverse events and complications were recorded at all visits.

3. Clinical Endpoints

With regards to safety, the following criteria were evaluated.

> The **primary safety endpoint** was the occurrence of any somewhat serious or serious adverse event (SAE) attributed to the stent or implantation procedure within 12 months of the procedure. “Somewhat Serious” was defined as any event which resulted in significant transient impairment of a body function or transient damage to a body structure;

required significant intervention to prevent permanent impairment of a body function or damage to a body structure. "Serious" was defined as any event which was life-threatening; resulted in permanent impairment of a bodily function or permanent damage to a body structure; necessitated major intervention to prevent permanent impairment of a body function or permanent damage to a body structure.

With regards to effectiveness, the following criteria were evaluated.

The **primary effectiveness endpoint** was defined as an increase in the stented vessel minimum pulmonary artery diameter by ≥ 50% of the pre-stent diameter, as determined by post-implant catheterization angiography.

The **secondary effectiveness endpoint** was defined as the ability to maintain relief of stenosis (includes planned re-dilatation or re-dilatation due to somatic growth) in the stented pulmonary artery at 12 months post-stent implantation by follow-up echocardiogram, catheterization angiography or CT based on at least one of the criteria below:

- Maintenance of stented vessel minimum pulmonary artery diameter by ≥ 50% vs. original baseline (pre-stent implant)
- Maintenance of decreased systolic gradient by ≥ 50% vs. original baseline or maintenance of gradient < 20mmHg (when applicable – i.e., when the pre-stent gradient was ≥ 20 mmHg across stenotic vessel)
- Maintenance of RV/FA (right ventricle/femoral artery) systolic pressure ratio to ≤ 50% vs. original baseline (when applicable - i.e., when pre-stent RV/FA ratio was > 50%)

Technical success was achieved if ALL of the following criteria were met:

- Subject was alive
- Successful access, delivery, and retrieval of the investigational device delivery system
- Deployment and correct positioning of the investigational device in the intended location
- No need for additional unplanned surgery or re-intervention related to the investigational device or access procedure

With regard to success/failure criteria, this study was descriptively evaluated for clinically meaningful safety and effectiveness.

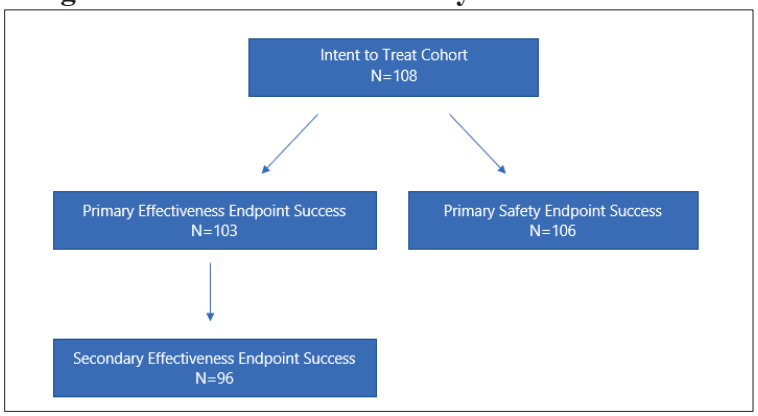
B. Accountability of PMA Cohort

At the time of database lock, of 108 patients enrolled in the PMA study, 89.8% (97) of patients were available for analysis at the completion of the study, the 1 year post-operative visit.

The accountability and breakdown/flow of all subjects in the total enrolled cohort is summarized as follows and diagrammed in Figure 2.

- Total ITT Cohort (N=108 subjects)
  - Failed implant (surgical removal) of the study stent due to complications/SAEs in two (2) subjects: technical and primary safety outcome failures and non-evaluable for primary effectiveness outcome 1.8%; 2/108)
  - Successful implant (technical success) in 106 subjects 98.1%; 106/108)
    - Primary effectiveness outcome failure in three (3) subjects
    - Primary effectiveness outcome success in 103 subjects (95.4%; 103/108)
      - Inadequate follow-up data for secondary effectiveness outcome evaluation in six (6) subjects
      - Adequate follow-up data for secondary effectiveness outcome obtained in 97 subjects 94.2%; 97/103)

Figure 2: Patient Accountability in the ITT Cohort



C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a retrospective study performed in the US.

Table 4: Demographics and Baseline Characteristics

Characteristics	N=108
Age (years)	
Mean ± SD	17.7 ± 9.5
Median	16.5
Range (Min, Max)	(0.9, 65.3)
Female %)	51.9% (56/108)
Weight (kg)	
Mean ± SD	32.9 ± 22.0
Median	24.9
Range (Min, Max)	(10.1, 122)

Characteristics	N=108
Prior History of Surgery %)	92.6% (100/108)
Primary Diagnosis (%)	
Tetralogy of Fallot	54.6% (59/108)
Pulmonary atresia with ventricular septal defect (VSD)	15.7% (17/108)
Transposition of the Great Arteries	1.9% (2/108)
Patent Ductus Arteriosus with Pulmonary Artery Stenosis	3.7% (4/108)
Right Ventricular Conduit with Pulmonary Artery Stenosis	4.6% (5/108)
Truncus	10.2% (11/108)
Unknown	9.3% (10/108)

The distribution of enrolled subjects by weight and age are further shown in Table 5 below.

Table 5: Age and Weight Distribution of Enrolled Subjects

Age Range	Weight Range	N
>1 month to 2 years	11-13kg	3
>2 years to 12 years	10.1-32kg	24
>12 years to 21 years	11-77.4kg	53
>21 years	18.8-122kg	28

D. Safety and Effectiveness Results

1. Safety Results

   The analysis of safety was based on the retrospective cohort of 108 patients undergoing an implant procedure with the PALMAZ GENESIS XD stent. Of the 108 ITT subjects, 2 experienced primary safety events through 12 months post-implantation. Stent malposition in one subject and stent embolization in the other subject resulted in surgical removal of the study stent in both subjects during the implantation procedure. All other subjects achieved technical success (98.1%, 106/108); six subjects were treated with a second study stent during the procedure in order to cover the initial lesion or due to initial stent malposition. The observed primary safety event rate was 1.9% (2/108). Adverse effects (AEs) are reported in Tables 6 and 7.

Table 6: Observed Serious Adverse Events

Adverse Event	Number of Events (Rates)
Stent malposition	1 (0.9%)
Stent embolization	1 (0.9%)

Table 7: Observed Non-Serious Adverse Events

Adverse Event	Number of Events (Rates)
Jailing of the contralateral (right) pulmonary artery without flow obstruction beyond the study stent	1 (0.9%)
Non-sustained supra-ventricular tachycardia resulting in overdrive pacing	1 (0.9%)
Non-sustained ventricular fibrillation/ventricular tachycardia requiring shock and pacing	1 (0.9%)
Reperfusion injury of the intervened vessel which required prolonged ventilation of 24 hours	1 (0.9%)

The above events were all anticipated. No stent fractures, aneurysms, dissections, somewhat serious adverse events, or unanticipated AEs were reported for any of the subjects in the study cohort.

2. Effectiveness Results

The analysis of primary effectiveness was based on the 106 evaluable patients who achieved technical success and for whom pre-stent and post-stent pulmonary artery diameters were obtained by cardiac catheterization at post-stent implantation. The analysis of secondary effectiveness was based on the 97 evaluable patients who met the primary effectiveness outcome and had adequate and applicable follow-up data for comparison with baseline data. Key effectiveness outcomes are presented in Tables 8 to 12 and Figures 3 to 6.

Primary Effectiveness Outcome:

The primary effectiveness endpoint (increase in the stented vessel minimum pulmonary artery diameter by ≥ 50% of the pre-stent diameter, as determined by post-implant catheterization angiography) was achieved in 95.4% (103/108) of all ITT subjects. Of the five subjects who did not achieve the primary effectiveness endpoint, two (2) subjects were technical failures (Table 6) and three (3) additional subjects did not experience at least a 50% increase in minimum diameter of the stented pulmonary artery post-intervention.

The mean value for the diameter of the stenotic segment of the pulmonary artery (i.e., minimum diameter) in subjects pre-procedure was 5.3 ± 2.1 mm and increased to 11.0 ± 3.1 mm post-procedure. The post-procedure mean vessel diameter favorably compared with the mean diameter (11.3 ± 3.9 mm) of the adjacent, anatomically normal segment of the pulmonary artery measured pre-procedure (Figure 3 and Table 8).

The mean percentage increase in the diameter of the stenotic segment of the pulmonary artery was 142.5 ± 87.8% (Table 9). The lower bound of the 95% confidence interval was 125.6%.

Figure 3: Stenotic Pre- and Post-Stent Pulmonary Artery Diameters Relative to Normal Pre-Stent Diameter by Catheterization (n=106)

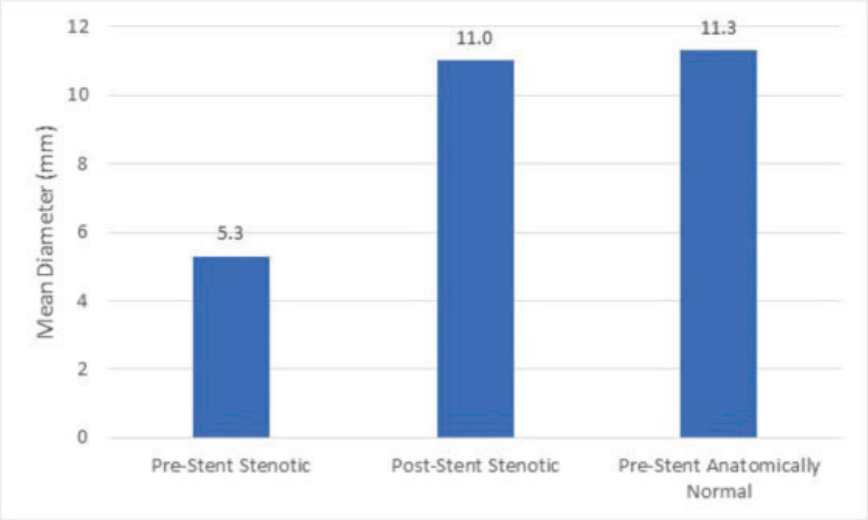


Table 8: Summary of Pre-Stent and Post-Stent Pulmonary Artery Diameter Measurements (n =106)

Diameter Measurement	Mean	SD	Median	SD Error Mean	Range
Pre-Stent Stenotic Pulmonary Artery Diameter (mm)	5.3	2.1	5.0	0.2	1.0 - 11.0
Post-Stent Stenotic Pulmonary Artery Diameter (mm)	11.0	3.1	10.0	0.3	5.1 - 18.2
Pre-Stent Anatomically Normal (Largest) Pulmonary Artery Diameter (mm)	11.3	3.9	11.2	0.4	4.0 - 22.5

Table 9: Percentage Increase in Stenotic Pulmonary Artery Diameters from Pre- to Post-Stent Implant by Catheterization (n=106)

Variable	Percentage (%)
Mean	142.5
Standard Deviation	87.8
Median	117.2

Variable	Percentage (%)
95% Confidence Interval (Lower)	125.6
95% Confidence Interval (Upper)	159.4
Minimum	28.6
Maximum	500.0

Secondary Effectiveness Outcome: Of the 97 total subjects evaluated for the secondary effectiveness outcome, 96 met at least one of the three criteria, thereby meeting the secondary effectiveness outcome:

- 57 subjects met one (1) criterion
- 30 met two (2) criteria
- 9 met all three (3) criteria

Evaluation by Pulmonary Artery Diameter at 1 year: In the 94 of 97 subjects with echocardiographic measurements at baseline and 1-year follow-up, there was clinically meaningful improvement in the mean diameter from 5.2 ± 1.8 mm at baseline to 10.1 ± 2.9 mm at 1-year follow-up (Figure 4 and Table 10). A ≥ 50% increase in diameter from baseline to 1-year follow-up was observed in 91 of these 94 subjects.

Figure 4: Mean Stenotic Pulmonary Artery Diameters Pre-Procedure and at 1-Year Follow-Up by Echocardiography (n=94)

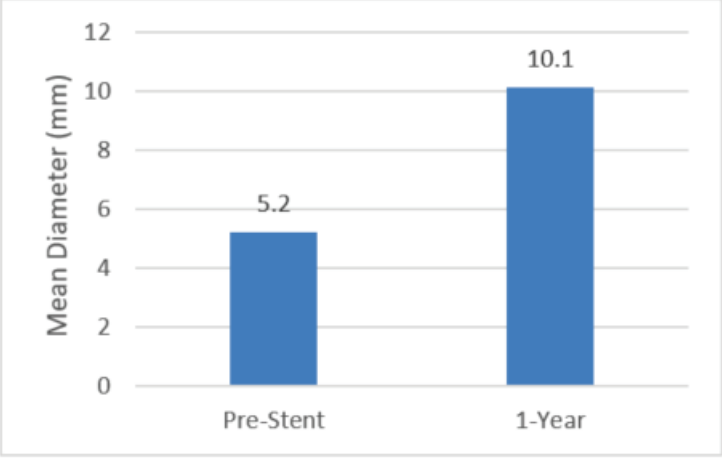


Table 10: Summary of Pre-Procedure and 1-Year Pulmonary Artery Diameter Measurements (n=94)

Vessel Diameter Measurement	Mean	SD	Median	SD Error Mean	Range
Pre-Procedure Echo Stenotic Vessel Diameter (mm)	5.2	1.8	5.1	0.2	2.0-10.5

Vessel Diameter Measurement	Mean	SD	Median	SD Error Mean	Range
1-Year Echo Stenotic Vessel Diameter (mm)	10.1	2.9	9.1	0.3	7.0-18.0

Evaluation by Systolic Gradient at 1 year: Of the 46 of 97 subjects with echocardiographic measurements at baseline and 1-year follow-up and for whom evaluation of this endpoint was applicable, there was a clinically meaningful decrease observed in the mean systolic gradient from 33.8 ± 11.7 mmHg at baseline to 18.0 ± 10.8 mmHg at 1-year follow-up (Figure 5 and Table 11). The 1-year gradient was ≥ 50% lower than the baseline gradient and/or < 20mmHg in 32 of these 46 subjects.

Figure 5: Mean Vessel Gradients Pre-Procedure and at 1-Year Follow-Up by Echocardiography (n=46)

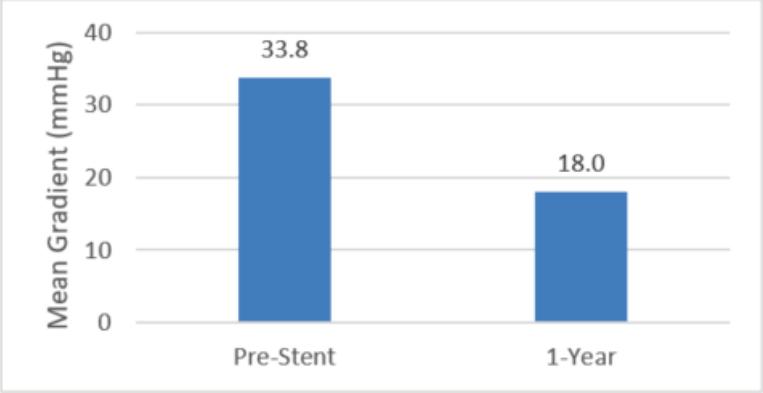


Table 11: Summary of Pre-Procedure and 1-Year Vessel Gradients (n=46)

Vessel Gradient Measurement	Mean	SD	Median	SD Error Mean	Range
Pre-Procedure Echo Vessel Gradient (mmHg)	33.8	11.7	31.0	1.7	20.0-62.0
1-Year Echo Vessel Gradient (mmHg)	18.0	10.8	16.0	1.6	4.0-54.0

Evaluation by RV/FA Systolic Pressure Ratio at 1 year: Twenty-eight of the 97 evaluable subjects had evaluable echocardiographic measurements at baseline and 1-year follow-up. There was a clinically meaningful decrease observed in the mean RV/FA systolic pressure ratio from 0.63 ± 0.1 at baseline to 0.40 ± 0.15 at 1-year follow-up (Figure 6 and Table 12). The 1-year RV/FA ratio was ≤ 50% in 21 of these 28 subjects.

Figure 6: Mean RV/FA Pressure Ratios Pre-Procedure and at 1-Year Follow-Up by Echocardiography (n=28)

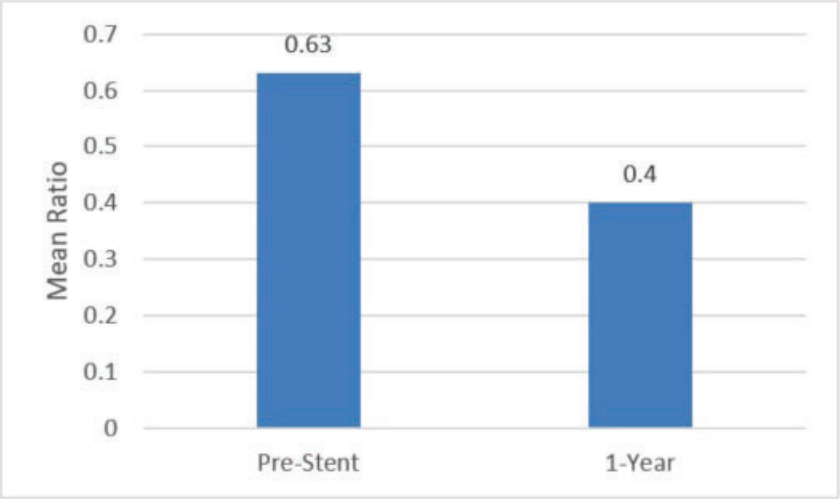


Table 12: Summary of Pre-Procedure and 1-Year Echo RV/FA Pressure Ratios (n=28)

RV/FA Pressure Ratio	Mean	SD	Median	SD Error Mean	Range
Pre-Procedure Echo RV/FA Pressure Ratio	0.63	0.1	0.63	0.02	0.51-0.96
1-Year Echo RV/FA Pressure Ratio	0.4	0.15	0.37	0.03	0.2-0.73

3. Re-Intervention

The observed proportion of subjects with a successful initial stent implant who underwent re-intervention during 1-year follow-up was 0.9% (1/108); the re-intervention in this subject was performed due to intimal proliferation.

Although patients were only followed for 1 year, additional data about re-interventions beyond 1 year was available for nine subjects. In these nine subjects, re-interventions were necessary to accommodate normal somatic growth and involved successful re-dilation and expansion of the study stents beyond their nominal diameters to match somatic growth.

The following characteristics are associated with the re-interventions in these 10 subjects:

- The mean timeframe for re-intervention was 40.1 months (range 10 to 84 months) after initial stent implant.
- For the nine (9) subjects who underwent re-intervention due to somatic growth:

    - The mean age was 13.8 years (range 7 to 20.8 years).
    - The mean post-re-intervention pulmonary artery diameter was 13.1 mm (range 10.8 to 16 mm).
- All subjects who underwent re-intervention met the original primary effectiveness outcome of the study based on pre-procedure and post-procedure pulmonary artery diameter measurements obtained by cardiac catheterization.
- No stent fractures were reported.

4. Subgroup Analyses
   Subgroup analyses were not performed.

5. Pediatric Extrapolation
   In this premarket application, existing clinical data was leveraged to support the reasonable assurance of safety and effectiveness of the proposed device in pediatric patients. The clinical study data collected for this PMA included patients across the pediatric age range.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 12 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

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

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Systems Device 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 PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The assessment of effectiveness for the PASS retrospective study was based on the evaluation of increase in the stented vessel minimum pulmonary artery diameter at post-implantation. An increase in diameter of at least 50% of the pre-stent diameter was achieved in 95.4% of all subjects based on measurements obtained by cardiac catheterization. The lower bound of the 95% confidence interval for mean percentage

increase in pulmonary artery diameter after stenting was 125.6%, which represents a clinically meaningful benefit.

The PASS study also assessed effectiveness at 1 year post-stent implantation based on maintenance of the increase in stented vessel minimum pulmonary artery diameter by ≥50%, maintenance of decreased systolic gradient by ≥50%, and maintenance of RV/FA systolic pressure ratio to ≤50%, all compared to pre-stent baseline measurements. Ninety-seven subjects had evaluable data for at least one of the above criteria at 1 year. Of those 97 evaluable subjects, 99% (96/97) met at least one of the above criteria. The pulmonary artery diameter outcome is a reliable metric for clinical success and was met in 91 of 94 evaluable subjects for that outcome (96.8% .

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in a clinical study conducted to support PMA approval as described above. The results from the non-clinical laboratory and animal studies performed on the PALMAZ GENESIS family of stents are appropriately leveraged to support the PALMAZ MULLINS XD stent and demonstrate that this device is suitable for long-term implant.

The primary safety assessment for the PASS retrospective study was based on the occurrence of any serious or somewhat serious adverse events through 12 months post-implantation with the study stent. The observed rate of primary safety endpoint events was 1.9% 2/108). The rate of serious adverse events observed in literature for patients undergoing placement of pulmonary artery stents to treat pulmonary artery stenosis is 9%. Four patients experienced a non-serious adverse event through 12 months. These adverse events did not raise significant safety concerns about the study device or procedure.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The probable benefits of the PALMAZ MULLINS stent include reduction in right ventricular systolic pressure as well as improvement in pulmonary artery obstruction in patients receiving the PALMAZ MULLINS XD stent.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The risks associated with the device include complications such as stent migration, stent fracture, hematoma, thrombosis, stent stenosis, pulmonary artery aneurysm/dissection/rupture, jailed side branches of the pulmonary arteries, bleeding, and death.

1. Patient Perspective

This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for non-emergency treatment of pulmonary artery stenosis in pediatric patients who are at least 10kg in weight with two ventricle anatomy, the probable benefits outweigh the probable risks when used according to its labeling.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. Preclinical and clinical studies provided in the PMA application demonstrate reasonable assurance that the PALMAZ MULLINS XD Pulmonary Stent is safe and effective for non-emergency treatment of pulmonary artery stenosis in pediatric patients who at least 10kg in weight with two ventricle anatomy.

XIII. CDRH DECISION

CDRH issued an approval order on 7/21/2023. The final clinical conditions of approval cited in the approval order are described below.

PALMAZ MULLINS XD Stent Real-World Use: The applicant has agreed to conduct a prospective, single-arm, multi-center study of consecutive patients treated with the PALMAZ MULLINS XD Pulmonary Stent. This study will be carried out to characterize clinical outcomes and to assess the real-world use of the commercial PALMAZ MULLINS XD Stent. The study will enroll a minimum of 35 subjects and will continue until the enrollment of 75 subjects or two years from the time of study activation, whichever comes first. This study will monitor key data points related to the device and accessories and procedure (including: technical success rate, intra-procedural increase in the stented vessel minimum pulmonary artery diameter, device and procedure related adverse events through hospital discharge, and the delivery system(s) model numbers used in the procedure). Data will be descriptively assessed and compared to the premarket cohort.

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 device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.