SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Aortic Stent

Device Trade Name: Cheatham Platinum (CP) Stent System
(Covered CP Stent – Model 427
Covered Mounted CP Stent – Model 428)

Device Procode: PNF

Applicant's Name and Address: NuMED, Inc.
2880 Main Street
Hopkinton, NY 12965

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P150028/S001

Date of FDA Notice of Approval: October 24, 2017

The original PMA (P150028) was approved on March 25, 2016, includes covered and uncovered stent varieties and is indicated for the following:

The CP Stent and Mounted CP Stent are indicated for use in the treatment of native and/or recurrent coarctation of the aorta involving a compliant aortic isthmus or first segment of the descending aorta where there is adequate size and patency of at least one femoral artery and balloon angioplasty is contraindicated or predicted to be ineffective.

The Covered CP Stent and Covered Mounted CP Stent are indicated for use in the treatment of native and/or recurrent coarctation of the aorta involving the aortic isthmus or first segment of the descending aorta where there is adequate size and patency of at least one femoral artery associated with one or more of the following:

- Acute or chronic aortic wall injury
- Nearly atretic descending aorta of 3 mm or less in diameter
- A non-compliant stenotic aortic segment found on pre-stent balloon dilation
- A genetic or congenital syndrome associated with aortic wall weakening or ascending aortic aneurysm.

The SSED to support the indication is available on the CDRH website (https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150028b.pdf) and is incorporated by reference here. The current supplement was submitted to expand the indication for the Covered CP Stent and Covered Mounted CP Stent to include use in the right ventricular outflow tract.

II. INDICATIONS FOR USE

The Covered CP Stent and Covered Mounted CP Stent is indicated for use in the treatment of right ventricle to pulmonary artery (right ventricular outflow tract, RVOT) conduit disruptions that are identified during conduit pre-dilatation procedures performed in preparation for transcatheter pulmonary valve replacement (TPVR).

III. CONTRAINDICATIONS

1. Patients too small to allow safe delivery of the stent without injury to a systemic vein or to the right side of the heart;
2. Clinical or biological signs of infection;
3. Active endocarditis;
4. Pregnancy.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Covered CP Stent and Covered Mounted CP Stent labeling.

V. DEVICE DESCRIPTION

The NuMED Covered Cheatham Platinum (CP) Stent System includes a Covered CP Stent and a delivery catheter (BIB). Each stent is balloon expandable and intended for permanent implant. The device is available unmounted and pre-mounted on the BIB delivery catheter. Each configuration is available in the sizes listed in Table 1. Additional stent sizes were introduced in this PMA supplement and are noted as those corresponding to the 10-zig configuration in Table 1. The 10-zig variety includes an additional row of zig strut patterns to achieve a larger diameter.

Table 1. Device Size Matrix

Configuration (number of zigs)	Platinum Wire Diameter (inch)	Diameter (mm)	Labeled Stent Length (mm)								
			16	22	28	34	39	45	50	55	60
8	0.013	12	✓	✓	✓	✓	✓	✓	✓	✓	✓
		14	✓	✓	✓	✓	✓	✓	✓	✓	✓
		15	✓	✓	✓	✓	✓	✓	✓	✓	✓
		16	✓	✓	✓	✓	✓	✓	✓	✓	✓
		18	✓	✓	✓	✓	✓	✓	✓	✓	✓
		20	✓	✓	✓	✓	✓	✓	✓	✓	✓
		22	✓	✓	✓	✓	✓	✓	✓	✓	✓
		24	✓	✓	✓	✓	✓	✓	✓	✓	✓
10	0.013	26	–	–	–	–	✓	✓	✓	✓	✓
		28	–	–	–	–	✓	✓	✓	✓	✓
		30	–	–	–	–	✓	✓	✓	✓	✓

The NuMED Covered CP Stent (Figure 1) is comprised of the Bare CP Stent that is covered with an expandable sleeve of ePTFE. The sleeve covers the entire length of the stent. The sleeve is attached to each end of the stent with a cyanoacrylate adhesive on a physically etched section of the sleeve. Upon balloon expansion of the stent, the covering remains intact and expanded with the stent to create a barrier around the stent. The stent has the capability of containing the movement of blood.

Figure 1. Left: Expanded and Right: crimped Covered NuMED CP stent.

The NuMED Covered Mounted CP Stent (**Figure 2**) is the Covered CP Stent mounted on NuMED's BIB balloon expandable catheter.

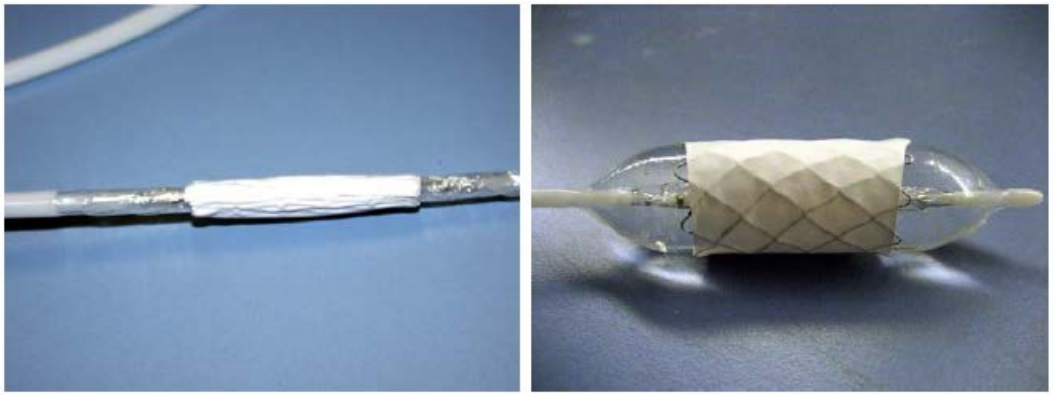

Figure 2 Left: Crimped, Right: Expanded Covered Mounted NuMED CP stent.

The NuMED BIB Stent Placement Catheter was cleared under K160889. The catheter is triaxial in construction with two lumens being used to inflate the balloons while one lumen is used for tracking over a guidewire. The double balloon catheter allows for incremental inflation for the purpose of dilating a stent. Radiopaque platinum marker bands are located under the balloon shoulders for placement using fluoroscopy. The catheter is composed of PES2, Pebax, Platinum/Iridium, and PES2 with colorants. The delivery catheter is compatible with 0.035" guidewires and 8-16 Fr introducers.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Open heart surgery provides the only alternative for the treatment of RVOT conduit disruptions that are identified during conduit pre-dilation procedures performed in preparation for TPVR. Surgical repair 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 Covered CP Stent Systems are currently marketed in the following countries:

Table 2. Device Marketing Locations

Product	Countries
Covered CP Stent	Algeria, Argentina, Australia, Bahamas, Brazil, Brunei, Canada, Chile, Columbia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, European Union, Guatemala, Honduras, Hong Kong, India, Israel, Jordan, Kenya, Kuwait, Malaysia, Mauritius Island, Mexico, Mongolia, New Zealand, Norway, Pakistan, Peru, Russia, Saudi Arabia, South Africa, Sultanate of Oman, Switzerland, Trinidad & Tobago, Turkey, Uganda, United States, Uruguay, Vietnam.
Covered Mounted CP Stent	Algeria, Argentina, Australia, Bahamas, Brazil, Brunei, Canada, Chile, Columbia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, European Union, Guatemala, Honduras, Hong Kong, India, Israel, Jordan, Kenya, Kuwait, Malaysia, Mauritius Island, Mongolia, Norway, Pakistan, Peru, Saudi Arabia, South Africa, Sultanate of Oman, Switzerland, Trinidad & Tobago, Turkey, Uganda, United States, Uruguay, Vietnam.

The device has not been withdrawn from marketing for any reason related to its safety and effectiveness.

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.

- Vessel injury, thrombosis or psuedoaneurysm
- Stent Migration
- Stent Stenosis
- Stent Fracture
- Pseudoaneurysm/aneurysm

- Vessel Ruptures
- Stent Malposition
- Hematoma
- Sepsis/infection
- Thrombosis/Thromboembolism
- AV fistula formation
- Death
- Transitory arrhythmia
- Endocarditis
- Bleeding
- Cell necrosis at the site of implant
- Cerebrovascular Incident

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

IX. SUMMARY OF NONCLINICAL STUDIES

In vitro studies were performed on the Covered CP Stent System and accessories. Testing was referenced from PMA submission P150028 for those evaluations that could be leveraged from previous testing. A summary of previously reported preclinical studies can be found in the Summary of Safety and Effectiveness Data (SSED) for the original PMA (https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150028B.pdf).

A. Laboratory Studies

1. In vitro Product Testing

Preclinical testing was repeated where applicable to support the 10-zig stent sizes as presented in **Table 3** and **Table 4** and for the BIB catheter in **Table 5**.

Table 3. Summary of *in vitro* Product Testing for 10-zig Covered CP Stent

Test	Purpose/ Objective	Test/Reference Articles	Results
Stent Dimensional And Functional Attributes			
Dimensional Verification	To ensure that all dimensional specifications do not deviate from the design specifications	Test: 29 units of each length of the CP stent. The shortest and longest stents used 29 units of each of the bare and the covered stents. Intermediate lengths used 29 units in a combination of bare and covered stents.	All stents met the acceptance criteria and the data showed no deviation from the design specifications.
Percent Stent Area	To determine the contact area of the stent structure, as a	Calculations will be performed for the shortest and longest stent lengths at	There is no established criteria for this

	percentage of the conceptual solid circumferential area	maximum & minimum deployed diameters	test. The percent stent area for CP8Z16 at 12mm is 49% and CP8Z45 at 24mm is 35%. CP10Z39 at 24mm diameter was 34.7% CP10Z39 at 30mm diameter was 35.8% CP10Z60 at 24mm diameter was 35.0% CP10Z60 at 30mm diameter was 35.4%
Stent Foreshortening	To demonstrate the decrease in length of the stent between the catheter loaded condition and deployment to the maximum diameter per the IFU, determining the maximum nominal diameter for which the device is designed	Test: 29 units each for: the shortest stent length at minimum and maximum inflation diameter, the longest stent length at minimum and maximum inflation diameter, and 29 units of every stent length in between.	There is no established criteria for this test, values are calculated and reported. All results can be found within the Instructions for Use.
Stent Recoil	To determine the decrease in diameter of the stent, from the maximum balloon expanded condition per IFU to the balloon deflated conditions	Test: 29 stents were tested at each diameter to report recoil values and show no differences in recoil between the stent lengths.	All stents met the acceptance criteria, namely that the stent recoil did not exceed 3.5%.
Uniformity of Expanded Diameter	To ensure that the uniformity of the expanded stent is consistent with the labeled expanded	Test: 29 units of the CP10Z60 mounted on the minimum (24mm) and maximum (30mm) diameter of balloons.	All stents deployed uniformly in each case without significant

	diameter		diameter changes along the length of the stent.
Stent Integrity	To examine deployed stents for damage (cracks/scratches) caused by manufacture, load, and crimp roll down or by deployment/expansion	Test: 29 stents inflated to maximum labeled diameter	All data demonstrated that there was no damage to the stents.

Table 4. Design Specific Testing for Covered/Covered Mounted CP Stent

Test	Purpose	Test Articles	Results
ePTFE Bond Strength	To determine the covering attachment strength	Test: 29 Covered stents of various lengths	All stent coverings remained attached to the wire framework at bond points.

Table 5. BIB Delivery Catheter Compatibility Testing

Test	Purpose	Test Articles	Results
Balloon and CP Stent Burst Pressure	To demonstrate the burst strength of the catheter	Test: (29) 10Z39 on 24 x 4 (29) 10Z60 on 24 x 6 (29) 10Z on 26 x 6 (29) 10Z on 28 x 6 (29) 10Z39 on 30 x 4 (29) 10Z60 on 30 x 6	All data supported that statistically the balloons will not burst at or below the maximum recommended rated burst pressure.
Balloon Compliance	To demonstrate the stent ID versus inflation pressure characteristics	Test: (29) 10Z39 on 24 x 4 (29) 10Z60 on 24 x 6 (29) 10Z on 26 x 6 (29) 10Z on 28 x 6 (29) 10Z39 on 30 x 4 (29) 10Z60 on 30 x 6	All data met the acceptance criteria that the inside diameter of the stent shall be +/- 10% of the rated balloon diameter at rated pressure.
Balloon Fatigue	To determine the repeatability of successful balloon inflations to the RBP	Test: (29) 10Z39 on 24 x 4 (29) 10Z60 on 24 x 6 (29) 10Z39 on 30 x 4 (29) 10Z60 on 30 x 6	All catheters passed the acceptance criteria, with no failures including loss of pressure or burst at rated burst

			pressure.
Balloon Inflation/Deflation	To ensure that the catheter inflates and deflated within a specified time	Test: (29) 10Z39 on 24 x 4 (29) 10Z60 on 24 x 6 (29) 10Z39 on 30 x 4 (29) 10Z60 on 30 x 6	All BIBs met the acceptance criteria of a 15 second inflation time and 25 second deflation time.
Balloon Deflatability	To ensure that the catheter deflates without interference	Test: (29) 10Z39 on 24 x 4 (29) 10Z60 on 24 x 6 (29) 10Z39 on 30 x 4 (29) 10Z60 on 30 x 6	All BIBs met the acceptance criteria with no interference with balloon deflation.
Catheter Bond Strength	To demonstrate the pull strength of the following: distal hub to extension, extension to "Y" connector, "Y" connector to shaft, proximal balloon bond, tip to balloon	Test: 29 units of each shaft size	All samples exceeded the minimum pull strength of 8.9 Newtons.
Crossing Profile	To measure the crossing profile as the maximum diameter over the length from the proximal end of the mounted stent to the distal tip of the delivery system	Test: 29 catheters of each rated introducer size were tested with a mounted stent of random length.	All catheters passed through the appropriate Mullins sheath.
CP Stent Securement on BIB Delivery Catheter	To ensure that the stent remains intact and is not dislodged while being passed through the tortuous pathway	Test: (29) 10Z39 on 24 x 4 (29) 10Z60 on 24 x 6 (29) 10Z39 on 30 x 4 (29) 10Z60 on 30 x 6	Samples shall not dislodge while passing through the passageway and will require an average force of at least 3.28 Newtons to initiate dislodgement from the balloon for the 10 zig.

2. MRI Compatibility

Nonclinical testing and modeling of this device in magnetic fields of 1.5 and 3.0 Tesla showed that the device is MR Conditional. The Covered CP stent, and Mounted Covered CP stent can be scanned safely under the following conditions:

- Static magnetic field of 1.5 T and 3 T
- Maximum spatial gradient magnetic field of 2500 gauss/cm (25 T/m)
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2.0 W/kg for 15 minutes of scanning (Normal Operating Mode)

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed a clinical study, the Pulmonary Artery Repair with Covered Stents (PARCS) study, to establish a reasonable assurance of safety and effectiveness of implantation of the Covered CP Stent System in the treatment of right ventricle to pulmonary artery (RV-PA) conduit disruptions that are identified during conduit pre-dilation procedures performed in preparation for transcatheter pulmonary valve replacement. The study was conducted in the US under IDE # G120188. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between April 19, 2013 and September 11, 2014. The database for this Panel Track Supplement reflected data collected through January 30, 2017 and included 50 patients. There were 39 investigational sites.

The study was a prospective, multi-center, – single arm, non-randomized clinical study. The study compared stent treatment of RVOT conduit disruption to a performance criteria of 80% derived from clinically meaningful expectations for safety and effectiveness for this treatment method. This approach was taken due to the lack of literature observations for related event rates. All subjects who received a stent were treated with the 8-zig configuration.

The study used a Data Coordinating Center (DCC) that was responsible for database development, data management, monitoring data quality, monitoring adherence to the protocol by each site, monitoring device accountability, coordinating flow of information to and from the angiographic core laboratory, coordinating activities of the Data and Safety Monitoring Board (DSMB), directing data analysis and complying with FDA regulatory reporting requirements.

1. Clinical Inclusion and Exclusion Criteria

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

   Pre-catheterization Inclusion Criteria:

   a. Patient meets institutional criterion for placement of Melody® TPV

b. Patient size adequate to receive Melody® TPV implantation via venous access using the Ensemble® Transcatheter Delivery System
c. RV-PA conduit original size ≥ 16mm diameter
d. Patient age between 7 and 75 years

Catheterization Inclusion Criteria:

a. Angiographic evidence for RV-PA conduit disruption including: dissection, aneurysm, pseudo-aneurysm, tears or rupture
    - Recognition and treatment of conduit disruption may occur before, during or after implantation of the Melody® TPV
    - Conduit disruption related to prior intervention, identified angiographically before conduit dilation is performed during the Melody® implant procedure, can be eligible for CCPS implantation and study inclusion.

Patients were <u>not</u> permitted to enroll in the PARCS study if they met any of the following exclusion criteria:

Pre-catheterization Exclusion Criteria:

a. Patient size too small for transvenous placement of the Melody® TPV
b. Bloodstream infection, including endocarditis
c. Pregnancy
d. Prisoners and adults lacking the capacity of give consent

Catheterization Exclusion Criteria:

a. Conduit size is not suitable (too small or too large) for a Melody® TPV
b. Risk of coronary compression has been identified
c. Lack of angiographic evidence for RV-PA conduit disruption, Prophylactic use of study CCPS was prohibited
d. Vessel injury occurring in either the right or left branch pulmonary arteries
    - If injury to branch pulmonary arteries occurs during the catheterization and covered stent usage is indicated, Emergency Use guidelines must be employed.

2. <u>Follow-up Schedule</u>

All patients were scheduled to return for follow-up examinations at 6 months postoperatively. The preoperative and postoperative assessments are listed in **Table 6**.

Table 6. Follow-up Schedule

	Pre-Implant (within 8 weeks prior to implant)	Intraoperative	Pre-discharge	6 month (4-8 months post-implant)
Screen	X			

Informed Consent	X			
Cardiac history / Physical Exam	X			X
Echo/Doppler	X			X
Angiographic and hemodynamic result		X		
Adverse Events		X	X	X

Adverse events and complications were recorded at all visits.

The key time-points are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

With regards to safety, the following criteria were evaluated:

Primary Safety Endpoint #1*:* Patient must have successful coverage of conduit disruption defined as either no residual disruption or contained disruption, followed by successful implantation of the Melody® valve.

Hypothesis: At least 80% of patients will have successful implantation of the Melody® TPV following repair of the RV-PA conduit to a post-procedure Severity of Illness Score (SIS) level of 0 or 1, using the Covered CP Stent.

Primary Safety Endpoint #2: Patient must not have any adverse event attributed to the Covered CP Stent within 30 days of the catheterization procedure, as adjudicated by the Data and Safety Monitoring Board.

Hypothesis: At least 80% of patients will be free of an adverse event attributed to the Covered CP Stent within 30 days of the catheterization procedure.

With regards to effectiveness, the following criteria were evaluated:

Primary Effectiveness Endpoint #1: Improvement in the Severity of Illness Score is defined as pre-implantation SIS minus post-procedure SIS assessed after Melody Valve insertion (e.g., a change from level 3 at baseline to level 2 post-procedure would represent an improvement of 1 level in SIS).

The scale used for the clinical study was pre-specified and developed by the Principal Investigator specifically for the PARCS trial and is shown in **Table 7** for baseline and post-implant assessments. A higher level of security indicates a poorer physiological condition.

Table 7. PARCS Severity of Illness Scale (SIS) at baseline and post-implant

	SIS baseline Assessment	SIS Post-Implant Assessment
Level of Security - 0	No injury or conduit wall disruption: No contrast seen extending more than 2 mm outside of or extravasating (leaking) outside of the longitudinal plane of the vascular lumen. (does not indicate the need for CCPS implantation)	No residual disruption: Total occlusion of conduit disruption without contrast seen outside of the longitudinal plane of the vascular lumen.
Level of Security - 1	Contained disruption: Small collection of contrast seen extending outside of the longitudinal plane of the vascular lumen ≤ ½ the diameter of the adjacent conduit, indicating the occurrence of an aneurysm, pseudo-aneurysm or well contained tear. This category can also be used to describe the unlikely occurrence of a dissection with contrast held in a contained space within the conduit lumen.	Contained disruption: Small collection of contrast extending outside longitudinal plane of vascular lumen ≤ ½ the diameter of the adjacent conduit, c/w persistence of an aneurysm, pseudo-aneurysm or well contained tear. This category describes leak into original or new injury. This category should only be used for disruption judged unlikely to need further intervention or surgery.
Level of Security - 2	Partially Contained disruption: Large collection of contrast seen outside the wall of the RV-PA conduit ≥ ½ the diameter of the adjacent conduit.	Partially Contained disruption: Large collection of contrast seen outside the wall of the RV-PA conduit > ½ the diameter of the adjacent conduit.
Level of Security - 3	Uncontained conduit disruption: Extravasation of contrast into the mediastinum or pleural cavity.	Uncontained conduit disruption: Extravasation of contrast into the mediastinum or pleural cavity (likely to require further intervention or surgery).
Level of Security - 4	N/A	Emergent conduit rupture: Severe conduit rupture resulting in the immediate need for surgery or resulting in death.

Hypothesis: Patients will demonstrate a median improvement by at least 1 level from baseline to post-procedure on the severity of illness scale.

Primary Effectiveness Endpoint #2: Procedure Success – defined as device and lesion success with the Covered CP Stent implantation without intra

procedural or post-catheterization somewhat serious or serious adverse events attributable to CCPS implantation. Procedure success will be determined 6 months after the implantation procedure, enabling inclusion of repeat cardiac catheterization or surgery to repair a pseudo-aneurysm or conduit tear related to incomplete repair of the conduit wall disruption.

Hypothesis: The procedure will be successful in at least 75% of patients.

Secondary Effectiveness Endpoints:

1. Device Success defined as successful implantation of a Covered CP Stent, either providing complete repair of a conduit disruption or placement in preparation for a second Covered stent overlapping in tandem without adverse event

2. Lesion Success defined as complete repair of a conduit disruption with a single Covered CP Stent or via planned, tandem covered stent implantations. Patient must have successful coverage of conduit disruption, defined as either no residual disruption or contained disruption with the first covered CP stent, or no residual disruption or contained disruption with a subsequent covered CP stent, as long as the use of a second CCPS was planned.

Continued Access Protocol (CAP)

Data was also obtained and separately analyzed for 70 subjects within a continued access protocol (CAP) which used the same protocol as was followed during the PARCS pivotal study.

B. Accountability of PMA Cohort

At the time of database lock, of 50 patients enrolled in the PMA study, 90% (45) of patients were available for analysis at the completion of the study (the 6 month post-operative visit). Study accountability is detailed in **Table 8**.

Table 8. PARCS Accountability

	Eligible/total[3] N (100%)	6 Month Visit N (%)
PARCS Patients Safety Cohort[1, 2]	50/50 (100%)	47 (94%)
Effectiveness Cohort[1, 2]	50/50 (100%)	45 (90%)
CAP Patients[3]	48/65[4] (74%)	42 (88%)

[1] Two pivotal patients (023-102 and 028-101) had CCPS surgically removed after implant. These patients were followed for safety only at the 6-month visit.

[2] Three pivotal patients have been declared lost to follow-up at the 6-month visit (001-101, 004-102, and 036-102).

[3] Number of eligible patients at time of data lock

[4] Five CAP subjects did not receive a Melody Valve during the catheterization procedure

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a RVOT conduit disruption study performed in the US. The PARCS demographics are shown in **Table 9.** Medical History and procedural indication for study subjects are presented in **Table 10.**

Table 9. PARCS Pivotal Cohort – Patient Characteristics

	Pivotal Trial Number (Percent) or Median (Range) Total (n=50)	CAP Number (Percent) or Median (Range) Total (n = 70)
Gender		
Male	28 (56%)	40 (57%)
Female	22 (44%)	30(43%)
Age, years[1]	17 (6 to 44)	16 (7 to 49)
Age Group, years		
<10	5 (4%)	7 (10%)
10 to 13	11 (17%)	19 (27%)
14 to 17	12 (29%)	14 (20%)
18 to 29	18 (28%)	19 (27%)
>30	4 (4%)	11 (16%)
Weight, kg[2]	57.9 (19 to 116)	61.6 (19.3 to 108.6)

[1] Patient 021-101 was 6 years old at the time of implant. Inclusion criteria require patients to be at least 7 years old.
[2] Patient 015-102 was 19 kg and patient 023-204 was 19.3kg at the time of implant. Inclusion criteria require patients to be at least 20 kg.

Table 10. Medical History and procedural indication for PARCS study patients

	PARCS Implanted (n=50)[2]	CAP Implanted (n=70)[1,2]
Primary Cardiac Diagnosis		
Tetralogy of Fallot with Pulmonary Atresia	26 (52)	27 (39)
Aortic Stenosis	13 (26)	15 (21)
Truncus arteriosus	7 (14)	9 (13)
Transposition of the Great Arteries	2 (4)	6 (9)
Double Outlet Right Ventricle	1 (2)	8 (11)
Other	1 (2)	5 (7)
Prior RVOT Surgery		

Pulmonary homograft	36 (72)	39 (57)
Aortic homograft	9 (18)	18 (26)
Unspecified homograft	1 (2)	0 (0)
Contegra	2 (4)	3 (4)
Dacron/Hancock	2 (4)	1 (1)
Bioprosthetic valve	0 (0)	1 (1)
Sorin Mitroflow	0 (0)	0 (0)
Other	0 (0)	6 (9)
Original Prosthesis Diameter (mm)	19 (7, 28)	20 (14, 27)
Prior Pulmonary Artery Implants		
Any stents	10 (20)	19 (27)
Any additional conduits	8 (16)	15 (21)
Pulmonary Stenosis (Echo)		
Peak Pressure Gradient (mmHg)	63 ± 23	66 ± 26
Mean Pressure Gradient (mm Hg)	35 ± 13	39 ± 15
Primary Melody TPV Indication		
Pulmonary regurgitation	9 (18)	6 (9)
Pulmonary stenosis	31 (64)	61 (88)
Both PR and PS	9 (18)	2 (3)
Other	0 (0)	0 (0)

[1] Prior RVOT surgery data not reported for 2 CAP implanted patients
[2] Original prosthesis diameter not reported for 1 pivotal implanted patient and 3 CAP implanted patients
[3] Peak Gradient not reported for 2 pivotal implanted patients and 8 CAP implanted patients
[4] Mean Pressure Gradient not reported for 12 pivotal implanted patients and 17 CAP implanted patients
[5] Primary Melody TPV indication not reported for 1 pivotal implanted patient and 1 CAP implanted patient

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the implanted cohort of 50 patients/procedures available for the 6 month evaluation. The key safety outcomes for this study are presented below in **Table 11**. Adverse effects are reported in **Table 12** and **Table 13**.

Table 11. Primary Safety Endpoints

	Pivotal Implanted (n=50[2])		CAP Implanted (n=70[3])	
	Number (%)	95% CI	Number (%)	95% CI

Patients with successful coverage of conduit disruption followed by successful implantation of Melody Valve[1]	46 (93.9%)	(83.1, 98.7)	62 (89.8%)	(80.2, 95.8)
Patients with any Adverse Event attributed to the Covered CP Stent within 30 days of implant[4]	1 (2.0%)	(0.1, 10.7)	2 (2.9%)	(0.4, 9.9)

[1] Successful coverage defined as no residual disruption or contained disruption
[2] Results not reported for 1 pivotal patient
[3] Results not reported for 1 CAP patient
[4] Two adverse events were attributed to CCPS in 1 pivotal patient (stent malposition, embolism)

The PARCS primary safety endpoints were met with at least 80% of patients having successful coverage of conduit disruption followed by successful implantation of Melody Valves and at least 80% of patients had freedom from adverse events attributed to the device within 30 days of the catheterization procedure.

Adverse effects that occurred in the PMA clinical study:

Adverse events observed in the PARCS and CAP studies are presented in **Table 12** and **Table 13**, respectively. The overall incidence and types of adverse events were within expected ranges. Regarding the PARCS study, one stent embolization and one stent malposition were observed (2% each) and attributed to the covered stent implant procedure. An additional stent malposition and one instance of AV block were observed in the CAP study and attributed to the covered stent implant procedure.

Table 12. Adverse Events reported throughout the PARCS study

Pivotal Cohort Adverse Events (n=50)	Number of Events Degree of Seriousness			
	Serious	Somewhat Serious	Not Serious	Total
Due to CCPS Position:				
Stent embolization	1	0	0	1
Total	1	0	0	1
Due to CCPS Implant Procedure:				
Stent malposition	0	1	0	1

Total	0	1	0	1
Due to Melody TPV Implant Procedure:				
Access site pain	0	0	1	1
Total	0	0	1	1
Due to Pre-existing or Independent Condition or Unknown:				
Fever	0	0	1	1
Left flank pain	0	0	1	1
Non-sustained tachycardia	0	0	1	1
Post procedural vomiting	0	0	1	1
Total	0	0	4	4

Table 13. Adverse events observed in the CAP

Continued Access Patient Adverse Events	Number of Events Degree of Seriousness			
(n=70)	Serious	Somewhat Serious	Not Serious	Total
Due to CCPS Implant Procedure:				
AV Block	0	0	1	1
Stent malposition	0	0	1	1
Total	0	0	2	2
Due to Melody TPV Implant Procedure:				
Pulmonary edema	3	0	0	3
Atrial flutter	0	1	0	1
Fever	0	1	0	1
Access site bleeding	0	0	1	1

Shoulder pain	0	0	1	1
Total	3	2	2	7
Due to Pre-existing or Independent Condition or Unknown:				
Thrombus	0	1	0	1
Fever	0	0	2	2
Non-sustained tachycardia	0	0	1	1
Rash	0	0	1	1
Total	0	1	4	5

One unanticipated adverse event was observed in the PARCS trial which included dislodgement of the stent covering at one attachment point. Two unanticipated adverse events were observed within CAP subjects. First, deformation/disruption of the stent cover occurred during one attempted delivery. Secondly, one instance of stent entanglement occurred when the physician attempted to remove the BIB catheter balloon after stent deployment. None of the three unanticipated adverse events resulted in patient injury or death, procedural goals were accomplished in all cases, and none of the events required emergent operations.

2. Effectiveness Results

The analysis of effectiveness was based on the 50 evaluable patients and compared baseline assessments to those at the 6-month time point. Key effectiveness outcomes are presented in **Table 14** and **Table 15**.

Table 14 Primary Effectiveness Endpoints

Improvement in SIS, from Pre-Implantation Baseline to Post-Procedure, Assessed after Melody Valve Insertion[1]	Pivotal Implanted of n=50[1], number (%)		CAP Implanted of n=70[2], number (%)	
-1	3 (6%)		3 (5%)	
0	8 (17%)		8 (12%)	
1	31 (66%)		47 (71%)	
2	3 (6%)		7 (11%)	
3	2 (4%)		1 (2%)	
Procedural Success	Pivotal Implanted n = 50[3]		CAP Implanted n =70[4]	
	Number (%)	95% CI	Number (%)	95% CI

Both Device and Lesion Success, with No Adverse Event Attributed to the Covered CP Stent [2]	40 (81.6%)	(68.0, 91.2)	54 (78.3%)	(66.7, 87.3)

[1] Post-procedure SIS not reported for 3 pivotal patients
[2] Baseline and post-procedure SIS not reported for 2 CAP patients;
[3] Results not reported for 1 pivotal patient
[4] Results not reported for 1 CAP patient

Table 15. Secondary Effectiveness Endpoints

Device Success	Number (%)	
	Pivotal Implanted (n=50[1])	CAP Implanted (n=70[2])
Successful Implantation of First CCPS, Either Providing Complete Repair of Conduit Disruption or Placement in Preparation for Overlapping Tandem Stents, with No Adverse Event Attributed to the Covered CP Stent[1]	46 (93.9%)	66 (95.7%)
Successful Coverage of Conduit Disruption[3] with First CCPS or with Subsequent Planned CCPS	42 (85.7%)	56 (81.2%)

[1] Results not reported for 1 pivotal patient
[2] Results not reported for 1 CAP patient
[3] Successful coverage defined as no residual disruption or contained disruption

Patients within the PARCS trial demonstrated a median improvement in SIS of 1 level and therefore the first primary effectiveness endpoint was met. Based on the lower bound of the 95% confidence interval, procedural success was achieved in 68% of subjects. As such, the primary effectiveness endpoint for 75% procedural success was not met.

Procedural data for the Covered CP stent is presented in **Table 16.** Results indicate that primarily one covered stent was used per case which was well positioned with either no residual disruptions or only contained disruptions.

Table 16. Procedural data for the Covered CP stent Implantation

	Number (%)	
	Pivotal Implanted (n=50[1])	CAP Implanted (n=70[2])
Total Number of CCPS Implanted		
1	40 (80)	51 (73)
2	7 (14)	16 (23)
3	3 (6)	3 (4)

Post-Implant Stent Position, First Stent		
1 Well-positioned	47 (96)	67 (97)
2 Malposition	2 (4)	1 (1)
3 Major malposition	0 (0)	1 (1)
Second CCPS Planned or Unplanned (n=10,19)		
Planned	4 (40)	8 (42)
Unplanned	6 (60)	11 (58)
Coverage of Conduit Disruption Prior to Melody Valve Implantation		
0 No residual disruption	30 (61)	51 (74)
1 Contained	17 (35)	15 (22)
2 Partially contained	1 (2)	2 (3)
3 Uncontained	1 (2)	0 (0)
4 Emergent conduit rupture	0 (0)	1 (1)
Only one CCPS:		
0 No residual disruption	23	41
1 Contained	15	7
2 Partially contained	1	1
3 Uncontained	0	0
4 Emergent conduit rupture	0	1
Second CCPS planned:		
0 No residual disruption	3	6
1 Contained	1	2
2 Partially contained	0	0
3 Uncontained	0	0
4 Emergent conduit rupture	0	0
Second CCPS unplanned:		
0 No residual disruption	4	4
1 Contained	1	6
2 Partially contained	0	1
3 Uncontained	1	0
4 Emergent conduit rupture	0	0

[1] Post-implant position of first stent and coverage of conduit disruption prior to Melody not reported for 1 pivotal patient
[2] Post-implant position of first stent and coverage of conduit disruption prior to Melody not reported for 1 CAP patient

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 39 investigators of which none were full-time or part-time employees of the sponsor and 2 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: None
- Significant payment of other sorts: 1
- Proprietary interest in the product tested held by the investigator: 2
- Significant equity interest held by investigator in sponsor of covered study: None

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. 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 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 PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The assessment of effectiveness for the PARCS trial was based on an improvement in Severity of Illness Score. For pivotal patients, there was a median improvement in SIS of 1 level ($p<0.001$, Wilcoxon signed-rank test). The median improvement in Severity of Illness Score was also 1 Level for CAP cohort. Effectiveness was also based on procedural success which assessed incidence of both device and lesion success, with no adverse event attributed to the Covered CP Stent. Based on the lower bound of the 95% confidence interval, this endpoint was achieved in only 68% of the PARCS subjects and 66.7% of the CAP patients. However, observed rates for this criterion surpassed the pre-established criterion of 75% (PARCS: 81.6% and CAP: 78.3%).

B. Safety Conclusions

The risks of the device are based on non-clinical 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 Covered CP Stent Systems demonstrate that this device is suitable for long-term implant.

The safety assessments for the PARCS trial was based on the successful coverage of the conduit disruption which was defined as either no residual disruption or contained

disruption, followed by successful implantation of the Melody valve. Successful implantation of the Melody valve was achieved in 93.9% of patients. The safety assessment was also based on the patient not experiencing adverse event attributed to the Covered CP Stent within 30 days of the procedure. Approximately 98% of the patients were free of an adverse event attributed to the Covered CP Stent within 30 days of the procedure. As such, the PARCS study met both primary safety endpoints. Similar results were observed for data acquired under the CAP.

The risks associated with the use of the device include complications common to cardiac catheterization procedures and those related to adverse effects associated with the implant as discussed in section VIII of this document. As discussed above, the adverse events observed during the PARCS trial were typical in rate and type as what is to be expected for similar treatments.

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 Covered CP Stent include an alternative to surgery in the event of conduit disruptions during balloon dilatation during a transcatheter pulmonary valve implantation procedure. Patients with catastrophic tears experience benefit from this device in the event where the surgeon may contain the conduit disruption with the covered stent and transcatheter pulmonary valve implantation may continue without surgery. Additionally, benefits of this device include prevention of late complications of conduit disruption such as pseudo-aneurysm.

Additional factors to be considered in determining probable risks and benefits for the CP Covered Stent included the lack of a non-surgical treatment alternative and the low tolerance for the patient population to withstand internal bleeding or emergent surgery.

1. Patient Perspectives
   Patient perspectives considered during the review included the preference of a pediatric population to avoid invasive surgical procedures in the event of conduit rupture prior to transcatheter pulmonary valve implantation. Given that patients within this population are likely to have undergone multiple prior surgical procedures, avoidance of unnecessary surgical intervention is a considerable benefit. Overall, patients valued the availability of the CP Covered stent to provide a secondary plan in the event of conduit disruption that did not require surgical intervention.

In conclusion, given the available information above, the data support that for treatment of RVOT conduit disruptions that are identified during conduit pre-dilatation procedures performed in preparation for transcatheter pulmonary valve replacement (TPVR), the probable benefits outweigh the probable risks.

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. As discussed above the benefits of access to a non-surgical treatment method provided by the Covered CP Stent outweigh the risk associated with use of this device. The data provided in this PMA support that a significant portion of the patient population at risk for RVOT conduit rupture prior to Melody Valve implantation will experience a clinically significant benefit.

XIII. CDRH DECISION

CDRH issued an approval order on October 24, 2017. The final conditions of approval cited in the approval order are described below.

ODE Led Post-Approval Surveillance: PARCS continued follow-up survey
The objective of this surveillance is to characterize longer-term safety and effectiveness of the CP Covered Stent when used for treatment of right ventricular outflow tract (RVOT) conduit disruptions that are identified during conduit pre-dilatation procedures performed in preparation for transcatheter pulmonary valve replacement (TPVR).

Subject follow-up will be conducted via distribution of an annual survey to investigators who participated in the PARCS pivotal study and PARCS Continued Access Protocol (CAP). The investigational sites will be provided with the CASE ID numbers for all living subjects who were enrolled under the PARCS pivotal study or PARCS CAP to assist with acquisition of follow up status. The survey distributed to the sites will request information on patients treated with a CP Covered Stent during transcatheter pulmonary valve implantation including: need for catheter or surgical reintervention for a new or enlarging RVOT aneurysm/pseudo-aneurysm, instances of progression of aneurysm or pseudo-aneurysm, instances of structural failure (fracture), or need for device explantation. Survey distribution will continue annually until all patients reach 10 years post-implant. The sponsor will acquire this information from PARCS investigators/hospitals and report results to FDA on an annual basis.

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.