EVALUATION OF AUTOMATIC CLASS III DESIGNATION (DE NOVO) FOR NUMED NUCLEUS AND NUCLEUS-X BAV CATHETERS

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> Balloon Aortic Valvuloplasty Catheter. A catheter with a balloon at the distal end of the shaft which is intended to treat stenosis in the aortic valve when the balloon is expanded.

NEW REGULATION NUMBER: ***870.1255***

CLASSIFICATION: II

PRODUCT CODE*: OZT*

BACKGROUND

DEVICE NAME*: NuMED NuCLEUS and NuCLEUS-X BAV Catheters*

510(K)*: K082776*

DATE OF 510(K) NSE DECISION*: December 3, 2008*

DATE OF DE NOVO PETITION*: December 23, 2008*

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PETITIONER'S RECOMMENDED CLASSIFICATION*: II*

INDICATIONS FOR USE

The NuMED NuCLEUS and NuCLEUS-X BAV Catheters are indicated for Balloon Aortic Valvuloplasty.

LIMITATIONS

Please refer to the labeling for a more complete list of warnings, precautions, and contraindications.

DEVICE DESCRIPTION

The NuCLEUS BAV and the NuCLEUS-X BAV are both coaxial catheters, with the NuCLEUS-X currently cleared in the United States under K081680 for Balloon Pulmonic Valvuloplasty (BPV). The NuCLEUS BAV is currently only marketed outside of the United States.

The outer body of both devices is made of {Redacted as b4} tubing, while the inner shaft (or tubing) material is the only difference between the two devices. In the NuCLEUS-X Catheter, the inner tubing is comprised of {Redacted as b4}while in the NuCLEUS Catheter, the inner tubing is comprised of {Redacted as b4} The sponsor states that the {Redacted as b4}makes it less likely to stretch when force is used. From an engineering perspective, in terms of composition, testing, and intended use, FDA believes there is no significant difference in these technological characteristics between the inner tubing of the two catheters based upon the non-clinical performance testing results. Furthermore, these two devices would be expected to perform in a similar manner in the clinical setting during balloon aortic valvuloplasty procedures.

The catheters also feature a molded proximal end bifurcate with two distinct luminal passages. The inflation lumen terminates into a distally mounted balloon made of polyamide. The balloon is designed with a waist formed into the middle of the balloon to allow accurate balloon placement. Upon reaching a specified pressure, the waist will expand to the rated balloon diameter and dilate the valve to the rated diameter.

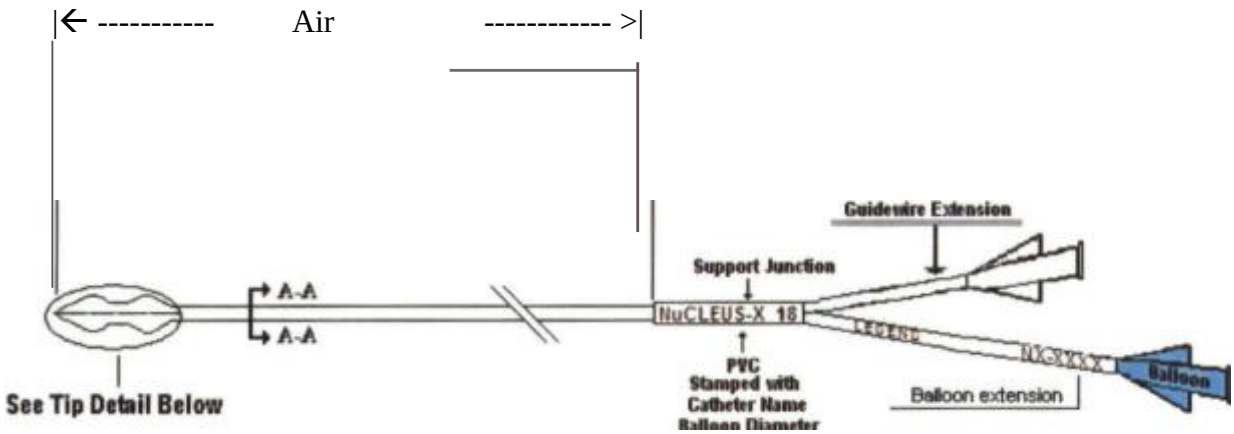
The distal lumen terminates at the tip of the catheters and will accept the passage of the 0.035" guidewire. This lumen has 3 radiopaque platinum marker bands. One under each of the balloon shoulders and one located at the "waist" or center of the balloon for placement using fluoroscopy. The catheters are packaged in a {Redacted as b4} sheath and double packed in two {Redacted as b4} sealed Tyvek pouches.

The following table lists the NuCLEUS-X catheter model numbers and the corresponding sizes of the balloon component:

Catalog Number	Balloon	
	Diameter (mm)	Length (cm)
PVN400	18	4
PVN401	18	5
PVN402	18	6
PVN403	20	4
PVN404	20	5
PVN405	20	6
PVN406	22	4
PVN407	22	5
PVN408	22	6
PVN409	25	4
PVN410	25	5
PVN411	25	6
PVN412	28	4
PVN413	28	5
PVN414	28	6
PVN415	30	4
PVN416	30	5
PVN417	30	6

The following table lists the NuCLEUS catheter model numbers and the corresponding sizes of the balloon component:

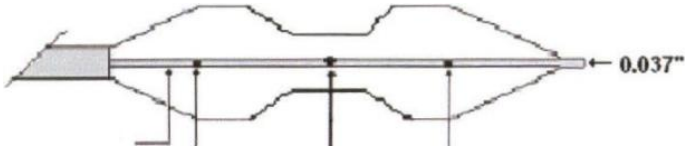
Catalog Number	Balloon	
	Diameter (mm)	Length (cm)
PVN218	10	3
PVN219	10	4
PVN220	12	3
PVN221	12	3
PVN222	12	4
PVN223	12	4
PVN224	14	3
PVN225	14	4
PVN226	16	3
PVN227	16	4
PVN228	18	3
PVN229	18	4
PVN230	20	4
PVN231	22	4
PVN232	25	4
PVN233	28	4
PVN234	28	4
PVN235	30	4
PVN236	10	5
PVN237	10	6
PVN238	12	5
PVN239	12	6
PVN240	14	5
PVN241	14	6
PVN242	16	5
PVN243	16	6
PVN244	18	5
PVN245	18	6
PVN246	20	5
PVN247	20	6
PVN248	22	5
PVN249	22	6
PVN250	25	5
PVN251	25	6
PVN252	28	5
PVN253	28	6
PVN254	30	5
PVN255	30	6



Even though the NuCLEUS-X BAV Catheter is identified above, the diagrams above and below are the same for both devices.

Tip Detail (diagram below)

| <- Variable - >|



| Inner Tubing | Imaging Bands (3) |

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

All materials used to manufacture both devices are available in other commercially available NuMED, Inc. devices (K014124, K022722, and K081680) and have passed all the relevant biocompatibility tests, including the USP Rabbit Pyrogen Test, the Intracutaneous (Intradermal) Reactivity Test, and the Systemic Injection Test. All of the tests were performed using the ISO method of testing.

NuMED has provided information describing the various balloon catheter models that they sell and the information confirms that these catheters are manufactured in the exact same way and are used in similar clinical applications as those comprising the NuCLEUS family of catheters. Therefore, no additional biocompatibility testing was conducted for the NuCLEUS-X BAV or the NuCLEUS BAV Catheters. There are no concerns with the biocompatibility of the subject devices.

SHELF LIFE/STERILITY

The sterilization processes and specifications for the NuCLEUS BAV and NuCLEUS-X BAV Catheters were validated and are the same as the sterilization process for other commercially-available NuMED products cleared under K081680 and K014124. The sterilization of the product is achieved using {Redacted as b4}. NuMED currently uses a specification limit of {Redacted as b4}, and {Redacted as b4}The maximum {Redacted as b4} are determined {Redacted as b4} post-sterilization. The sterilization cycle used to sterilize the device is validated by using the International Standard ANSU AAMUISO 11135-1194: "Medical Devices - Validation and Routine Control of Ethylene Oxide Sterilization." The sterility assurance level (SAL) is {Redacted as b4}.

The shelf life of both catheters is five years according to the validation performed as well as the validation that is in place at NuMED. The validation performed on NuMED products utilized the packaging configurations that are used at NuMED. One is a coiled configuration, and the other is a straight configuration. The validation lab conducted an evaluation as to which product represented the worst case scenario for each packaging configuration. This was determined by the balloon wall thickness as well as the shaft size. Final Inspection testing of all specifications were performed on these two catheters before and after accelerated aging. The specifications were determined and based on the In Vitro testing. Both configurations passed all the testing criteria. The clinical laboratory standard for determination of pyrogenicity, the {Redacted as b4} was used for validation.

There are no outstanding concerns with the sterilization or shelf life testing information provided by the sponsor.

PERFORMANCE TESTING – BENCH

Test Performed	Acceptance Criteria	NuCLEUS-X B A V Results	NuCLEUS BAV Results
Visual Inspection	The catheters shall be free from contamination, discoloration, and any form of damage that could impact the proper functioning of the device.	All catheters were visually inspected without any anomalies.	All catheters were visually inspected without any anomalies.
Balloon Preparation Test	Each catheter shall be prepped per the procedure without functional difficulties or anomalies.	All catheters tested were without functional difficulties or anomalies.	All catheters tested were without functional difficulties or anomalies.
Diameter and Profile Test	The balloon diameter at rated burst pressure shall be within+/- 10% of the labeled balloon diameter and the samples should fit through the selected introducer with no problems.	All catheters met the acceptance criteria.	All catheters met the acceptance criteria.
Balloon Distensibility	The results must demonstrate that the balloon diameter are within+/- 10% of the labeled diameter at the RBP and will not be significantly increased at increasingly higher pressures.	All data obtained demonstrated that the balloon diameter is w/in +/-100/o of the labeled diameter at the RBP. All data obtained demonstrated that the diameter of the balloons will not be significantly increased at increasingly higher pressures.	All data obtained demonstrated that the balloon diameter is within +/-10% of the labeled diameter at the RBP. All data obtained demonstrates that the diameter of the balloons will not be significantly increased at increasingly higher pressures.
Repeated Balloon Inflation (Balloon Fatigue Test)	No breaks allowed	30 Samples – no breaks	30 Samples – no breaks

Test Performed	Acceptance Criteria	NuCLEUS-X Results	NuCLEUS BAV Results

Balloon Minimum Burst Strength	The results must show statistically that with at least 95% confidence, 99.9% of the balloons will not burst at or below the maximum recommended rated burst pressure.	20 samples of smallest diameter-shortest length, smallest diameter-longest length, largest diameter-shortest length, largest diameter-longest length, and all diameters in between. 18x4-4ATM 18x6-4ATM 20x4-4ATM 22x4-3ATM 25x4-3ATM 28x4-2ATM 30x4-2ATM 30x6-2ATM	20 samples of smallest diameter-shortest length, smallest diameter-longest length, largest diameter-shortest length, largest diameter-longest length, and all diameters in between. 4x2-13 ATM 4x4-13ATM 5x2-12ATM 6 x 2-12 ATM 7x2-11ATM 8 x2-10ATM 9x2-10ATM 10x2-10ATM 11x2-8ATM 12x2-7 ATM 12 x4-7 ATM
Balloon Inflation/ Deflation Test	Inflation achieved in less than 12 seconds and deflation achieved in less than 20 seconds	Twenty samples of all Diameters. All catheters met the established acceptance criteria.	Twenty Samples of all Diameters. All catheters met the established acceptance criteria.
Balloon Inflatability Test	There should be no interference with balloon deflation	Twenty Samples of all Diameters All catheters met the established acceptance criteria.	Twenty Samples of all Diameters. All catheters met the established acceptance criteria.
Tip Pull and Torque Test	Must withstand at least 10 turns without breaking	Twenty random samples of each shaft size. No breaks reported.	Twenty random samples of each shaft size. No breaks reported
Bond Strength Test	All bonds must withstand at least 3 lbs. of pull strength.	Twenty samples of each shaft size. All bonds met the established acceptance criteria.	Twenty samples of each shaft size. All bonds met the established acceptance criteria.
Catheter Body Maximum Pressure Test	All sample must withstand 30 ATM (400psi).	Twenty samples of each guidewire size. >30ATM	Twenty samples of each guidewire size. > 400 psi

PERFORMANCE TESTING - IN VIVO EVALUATION

FDA believes that an in vivo evaluation of the device is necessary to demonstrate adequate

device performance. No animal testing data were provided in the petition; however, FDA determined that animal testing was not necessary because the petitioner was able to provide evidence of significant clinical *in vivo* experience with their devices as well as non-clinical performance testing. The clinical information is discussed below.

Granting the de novo petition for the NuMED NuCLEUS family of BAV catheters is based on an overall assessment of general clinical experience with BAV and clinical data available for the two devices specified in this de novo petition. NuMED has provided two clinical reports containing extensive published literature summarizing the clinical use of their subject devices for balloon aortic valvuloplasty.

The literature provided by the sponsor describes the use of both the NuCLEUS family of devices for BAV as well as the use of BAV as a palliative treatment for patients with aortic stenosis or for patients who are undergoing transcatheter aortic valve replacement (TAVR).

The documents establish that BAV has been performed for many years with a variety of devices and also establish that there has been clinical experience with use of the NuCLEUS and NuCLEUS-X Catheters for balloon aortic valvuloplasty.

The following clinical reports provided by the sponsor support the BAV procedure in general and the NuCLEUS family of catheters in particular for BAV.

Information supporting the use of the balloon aortic valvuloplasty (BAV) procedure in general

The anticipated risks associated with the use of catheters for BAV are in general not significantly different from the anticipated risks associated with balloon pulmonic valvuloplasty catheters, which have been determined to be Class II devices requiring 510(k) clearance, under the classification regulation 21 CFR 870.1250. The main difference between pulmonic balloon valvuloplasty and aortic balloon valvuloplasty is that there may be more bleeding complications with aortic balloon valvuloplasty, since vascular access to the stenotic aortic valve is usually retrograde through the arterial circulation which has a higher pressure than the venous circulation that is used to access the stenotic pulmonic valve. However, almost all of the complications associated with BAV, including the bleeding complications, are procedure-related complications rather than necessarily device-related complications. The device-related complication of balloon rupture (with possible consequent embolization of balloon material) rarely occurs and may be due to physician error in balloon inflation, which can be addressed through adequate Instructions for Use.

Although there has been no formal clinical study of BAV, FDA believes that there are enough clinical data to support approval of these devices. Given the extensive worldwide clinical experience, which includes use of the Nucleus family of catheters for BAV, the data and information provided support use of this procedure in treating severe aortic stenosis, as long as it is performed with a clear understanding of the risks associated with the procedure.

The following is a summary of the literature provided by the sponsor to support the use of the balloon aortic valvuloplasty procedure in general:

1. Gustav, R, DO. "Balloon Aortic Valvuloplasty for Aortic Stenosis Using a Novel Percutaneous Dilation Catheter and Power Injector." *Journal Of Interventional Cardiology* 24.1 (2011). Print.

   This paper describes how BAV has been advocated as palliative treatment for patients who are considered poor surgical candidates. Percutaneous aortic valve replacement is currently being investigated as a possible alternative to open surgical intervention to provide another option for patients who are not surgical candidates or prefer to avoid surgery. The proposed BAV technique in the article described using a smaller balloon catheter and power injector to achieve complete inflation quickly with a short aortic valve occlusion time. This was successfully performed in 20 consecutive, high-risk patients with severe stenosis. In all cases, NYHA class improved from IV before BAV to I or II at 30 days follow-up. At 180 days, 15 patients remained NYHA class I or II and one patient had become class III. The 3 deaths that occurred were considered unrelated to the procedure.

   FDA Comment: FDA believes this reference article provides supporting evidence of clinical use of balloon aortic valvuloplasty (BAV) as a palliative treatment for patients with severe aortic stenosis. There do not appear to be any adverse events reported that would raise concerns with BAV.

2. Rajesh, M. Dave, MD, FACC. "Aortic Valvuloplasty." *Cardiac Interventions To*day, (June 2007). Print.

   This paper documents clinical use of the 22-mm X 60 mm Z-MED II balloon catheter in 212 consecutive, nonsurgical aortic stenosis (AS) patients ranging in age from 59 to 104 years. The study objective was to determine the symptom relief and survival rate with single or repeat BAV in a patient population having a prohibitive risk for surgical AVR. BAV was performed at the index procedure to obtain a post-procedure transaortic pressure gradient at least 30% lower than the baseline gradient. All patients in the study were at least 60 years of age, with a mean age of 81 ±10 years; 23% of the patients were over the age of 90 years. Patients having more than moderate aortic regurgitation were excluded from the study. Repeat BAV was required in several patients, and the long-term survival was followed for a mean of 3±2 year.

   FDA Comment: This article explains that BAV should be considered as a viable treatment option for the high-risk surgical patient with AS or the patient who declines conventional AVR. The symptom relief is immediate, and short- to long-term palliative results are certainly acceptable from a perspective of improved quality-of life assessments.

3. Vasilis C. Babaliaros. "Use of Balloon Aortic Valvuloplasty to Size the Aortic Annulus Before Implantation of a Balloon-Expandable Transcatheter Heart Valve." *Journal of American College of Cardiac Interventions* 3 (2010): 114-118. Print.

   The aim of the study was to describe the use of the NuMED Z-MED balloon aortic valvuloplasty (BAV) catheter to select proper transcatheter heart valve (THV) size. Twenty-

seven patients undergoing transfemoral implantation of a THV for aortic stenosis were studied from January 2008 to April 2009. All patients were part of the PARTNER (Placement of AoRTic TraNscathetER Valve Trial, Edwards Lifesciences) trial to study the efficacy of a balloon-expandable THV (Edwards SAPIEN valve) in non-operable or high-risk surgical candidates. All patients had BAV performed using the NuMED Z-MED balloon catheter before THV implantation. In addition to dilating the native valve, BAV was used to size the aortic annulus.

FDA Comment: This reference discusses the use of BAV prior to TAVR to dilate the native valve and as a method of sizing the aortic annulus for the implant. FDA has no concerns with this reference which supports use of BAV.

FDA Summary Comment: The information provided by the sponsor documents the well-accepted use of balloon catheters to perform balloon aortic valvuloplasty, primarily as a palliative procedure in high-risk surgical patients with severe aortic stenosis but also as a preparatory step prior to transcatheter aortic valve replacement and a method for measuring the size of the aortic annulus. Additional justification for the procedure is described in the references below that justify the use of the NuMED NuCLEUS family of catheters for BAV.

Information supporting the specific use of the NuMED NuCLEUS family of catheters (NuCLEUS and NuCLEUS-X) for balloon aortic valvuloplasty (BAV)

1. Hasan Jilaihawi. "Prosthesis-patient mismatch after transcatheter aortic valve implantation with the Medtronic-CoreValve bioprosthesis." *European Heart Journal* 31 (2010): 857–864. Print.

   The article describes patients with severe calcific aortic stenosis that received TAVI with the CoreValve bioprosthesis via the transfemoral route. The pre-dilatation balloon used was the NuCLEUS Catheter, filmed in the same projection that was used for calibration, its markers 20 mm apart for all 50 patients. Following TAVI, moderate prosthesis-patient mismatch was defined as indexed aortic valve effective orifice area (AVAi) 0.85 cm^2/m^2 and severe P-PM as AVAi 0.65 cm^2/m^2. Clinical, echocardiographic, and procedural factors relating to P-PM were studied. Optimal device position was defined on fluoroscopy as final position of the proximal aspect of the CoreValve stent frame 5–10 mm below the native aortic annulus. Between January 2007 and January 2009, 50 consecutive patients underwent TAVI in a single centre with the CoreValve bioprosthesis. Mean age was 82.8 years (SD 5.9; 70–93) and 48% were male. P-PM occurred in 16 of 50 cases (32%). Optimal position was achieved in 50% of cases. P-PM was unrelated to age, annulus size, LVOT size, CoreValve size, aortic angulation, ejection fraction, and sex. It was inversely correlated to optimal position. Those with optimal positioning had a 16% incidence of P-PM relative to 48% of those with suboptimal positioning. The incidence of P-PM following TAVI with the CoreValve bioprosthesis is compared favorably with that seen after AVR with conventional open stented bioprosthesis and its occurrence is influenced by device positioning.

FDA Comment: This reference specifically mentions the use of the NuMED NuCLEUS Catheter for balloon aortic valvuloplasty (BAV) prior to placement of the CoreValve implant in all 50 patients involved in the study. This demonstrates clearly that the NuCLEUS catheter has been used for BAV as part of transcatheter aortic valve replacement procedures. Furthermore, the successful TAVI procedures performed using the NuCLEUS Catheter for the BAV component of the procedure demonstrates that the use of the NuCLEUS Catheter was effective and allowed successful accomplishment of the TAVI procedure.

2. Rosa Ana Hernandez-Antolin. "Findings of a Mixed Transfemoral Aortic Valve Implantation Program Using Edwards and CoreValve Devices." *Revista Espanola de Cardiogia* 64.1 (2011): 35-42. Print.

   This article discusses the transfemoral implantation of an Edwards-SAPIEN (ES) and the Medtronic CoreValve (MCV) aortic valve prosthesis as an alternative to surgical replacement for patients with severe aortic stenosis and a high surgical risk. The study's aim was to compare results obtained with these two devices. Balloon valvuloplasty was performed using the NuCLEUS Catheter (NuMED) during high-frequency ventricular pacing.

   FDA Comment: While this reference paper compares the results of transfemoral aortic valve implants by two different companies, the reference does specifically mention the use of the NuMED NuCLEUS Catheter for balloon aortic valvuloplasty (BAV) prior to TAVI. The paper demonstrates that the NuCLEUS catheter has been used clinically for BAV. Moreover, the successful TAVI procedures performed using the NuCLEUS Catheter for the BAV component of the procedure demonstrates that the use of the NuCLEUS Catheter was effective and allowed successful accomplishment of the TAVI procedure.

3. Giuseppe Bruschi. "Percutaneous Implantation of CoreValve Aortic Prostheses in Patients with a Mechanical Mitral Valve." *Annals of Thoracic Surgery* 88(2009): 50-52. Print.

   The article describes the concerns that exist in the field of transcatheter aortic valve implantation regarding the treatment of patients with mechanical mitral valve for possible interference between the percutaneous aortic valve and the mechanical mitral prosthesis. The authors report experience with percutaneous aortic valve implantation in 4 patients with severe aortic stenosis, previously operated on for mitral valve replacement with a mechanical prosthesis. All of the patients underwent uneventful percutaneous retrograde CoreValve implantation (CoreValve Inc, Irvine, CA). A totally percutaneous retrograde CoreValve implantation was performed with all patients awake with local anesthesia and mild sedation and continuous systemic arterial pressure control. After placing a temporary pacing lead through a femoral vein in the patients without permanent pacemaker, the best femoral artery was accessed by a single-wall puncture under fluoroscopic and angiographic guidance. A

Prostar XL 10F suture mediated closure device (Abbott Vascular Devices Laboratories, Redwood City, CA) was placed in the femoral artery (Preclosure technique). A Cook 30-cm Check-Flo Performer 18F introducer was then inserted over an Amplatz super stiff guidewire and the native aortic valve was pre-dilated with a 22-mm NuMED NuCLEUS balloon in all patients.

FDA Comment: This reference mentions the use of the NuMED NuCLEUS Catheter for balloon aortic valvuloplasty (BAV) as being performed prior to the TAVI performed on the four patients discussed in the paper. The use of BAV can be considered an integral part of TAVI. Without a satisfactory initial treatment with BAV of the aortic stenosis that is present, the successful performance of TAVI may not occur. A successful TAVI procedure done using the NuCLEUS Catheter for the BAV component of the procedure demonstrates that the use of the NuCLEUS Catheter was effective and allowed successful accomplishment of the TAVI procedure.

4. Liang, Michael. "The Incidence of Transcatheter Aortic Valve Implantation-Related Heart Block in Self-Expandable Medtronic CoreValve and Balloon-Expandable Edwards Valves." *Journal of Invasive Cardiology* 24.4 (2012):173-176. Print.

   This article describes the transcatheter aortic valve implantation (TAVI) that has been performed at Waikato Hospital for high-risk severe symptomatic aortic stenosis patients, who are considered unsuitable for conventional cardiac surgery for the last 3 years. The Medtronic CoreValve (MCV) is a self-expandable device, while the Edwards SAPIEN valve (EV) requires the use of a balloon to expand the device. This observational study reports and compares the incidence of heart block in both Medtronic and Edwards' transcatheter valves. Balloon aortic valvuloplasty was performed before device implantation to facilitate device delivery and prepare the bed for full frame expansion. A 20-25 mm x 4 cm NuCLEUS balloon (NuMED Inc) was used for MCV and 20-23 mm x 3 cm Edwards balloon (Edwards Lifesciences) was used for the EV.

   FDA Comment: This reference mentions the use of the NuMED NuCLEUS Catheter for balloon aortic valvuloplasty (BAV) prior to TAVI for 60 patients receiving the Medtronic CoreValve over a period of three years. This paper further illustrates the fact that the NuCLEUS catheter continues to be used for BAV, especially as a pre-dilatation step prior to transcatheter aortic valve implantation. Moreover, the successful TAVI procedures performed using the NuCLEUS Catheter for the BAV component of the procedure demonstrates that the use of the NuCLEUS Catheter was effective and allowed successful accomplishment of the TAVI procedure.

FDA Summary Comment: The information provided by the petitioner demonstrates the documented use of their NuCLEUS and NuCLEUS-X catheters for BAV both as a palliative

treatment and, more recently, as an important step in transcatheter aortic valve replacement (TAVR) procedures. Based on our review, a majority of the available clinical data on balloon aortic valvuloplasty is based on the use of the NuCLEUS catheter. However, given the similarity in design between the NuCLEUS and NuCLEUS-X catheters, FDA believes that these data are equally applicable to the NuCLEUS-X catheter. For additional information regarding a comparison of these two devices, please refer to the above sections.

LABELING

The following are the labeling requirements for balloon aortic valvuloplasty catheters:

- The indications for use need to clearly state that the devices are for use in balloon aortic valvuloplasty;
- The inclusion of a Balloon Sizing Chart that represents the respective device's balloon diameters at their Rated Burst Pressure (RBP);
- The inclusion of clinical literature references or other clinical references (e.g., non-published data) that support the use of the device for the stated indication for use;
- The detailed Instructions-for-Use of the device, including related Precautions and Warnings;
- The inclusion of a detailed summary of the device related and procedure related complications pertinent to the use of the device; and
- A statement that the device is available for use only as a prescription use device.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of balloon aortic valvuloplasty catheters and the measures recommended to mitigate these risks.

Identified Risk	Recommended Mitigation Measure
Adverse tissue reaction	Biocompatibility Testing Labeling
Infection	Sterility Shelf Life Testing
User Error	Labeling
Valve Leaflet Perforation	Non-clinical Performance Evaluation In Vivo Evaluation Labeling
Perforation of Vascular or Cardiac Tissue	Non-clinical Performance Evaluation In Vivo Evaluation Labeling
Procedural Complications, including Bleeding, Cardiac Tamponade, Calcium Embolic Events, Valvular Regurgitation, and Death	Non-clinical Performance Evaluation In Vivo Evaluation Labeling
Balloon Burst	Non-clinical Performance Evaluation In Vivo Evaluation Labeling
Inability for Balloon Deflation	Non-clinical Performance Evaluation In Vivo Evaluation
Increased Balloon Inflation and Deflation Times	Non-clinical Performance Evaluation In Vivo Evaluation Labeling
Inability to Steer Towards Valve of Interest	Non-clinical Performance Evaluation In Vivo Evaluation

SPECIAL CONTROLS:

In combination with the general controls of the FD&C Act, the NuMED NuCLEUS and NuCLEUS-X BAV Catheters are subject to the following special controls:

1. The device should be demonstrated to be biocompatible;

2. Sterility and shelf life testing should demonstrate the sterility of patient-contacting components and the shelf-life of these components;

3. Non-clinical performance evaluation of the device should demonstrate substantial equivalence in terms of safety and effectiveness for device delivery, inflation, deflation, and removal;

4. In vivo evaluation of the device should demonstrate device performance, including the ability of the device to treat aortic stenosis; and

5. Labeling must include a detailed summary of the device-related and procedure-related complications pertinent to the use of the device.

BENEFIT/RISK DETERMINATION

Significant benefit has been demonstrated over many years worldwide by numerous BAV clinical studies as well as BAV clinical experience gathered outside of formal trials. These studies and experience have included the NuMED NuCLEUS family of valvuloplasty catheters. The benefits of BAV consist of the stabilization or improvement of heart failure, the stabilization, improvement, or resolution of cardiac ischemia or angina, and the resolution of syncope or near syncope. These benefits significantly improve the quality of life of patients.

The probability of the patient experiencing durable significant benefit generally depends on the age of the patient, with a high probability of durable significant benefit in young adult patients, initially significant but only palliative benefit in adult patients who are at high or prohibitive risk for AVR surgery because of serious comorbid conditions, and significant benefit lasting at least 1 year in adult patients undergoing TAVI.

The probability of the usual BAV device-related adverse event of balloon rupture is usually related to whether the cardiologist performing the BAV overinflates the balloon, or related to the patient/clinical factor of laceration or puncture of the balloon by sharp calcium deposits in the aortic valve leaflets or annulus. The rate of BAV balloon rupture according to the literature ranges from ~15% to 33% of patients undergoing BAV. The probability of the BAV device-related adverse event of catheter leak is rare.

Most of the complications associated with BAV are procedure-related complications. The probability of a BAV procedure-related adverse event is mainly related to the experience of the cardiologist performing the BAV and to a lesser extent related to patient/clinical factors, and also depends on the type of adverse event. The most common procedure-related complications are vascular complications, including bleeding.

It is clinically appropriate to perform BAV as long as it is performed according to the guidelines and indications published by professional clinical cardiology organizations and with a clear understanding of the risks associated with the procedure. It is also important to note that much worldwide clinical experience with the use of balloon valvuloplasty catheters for BAV, including the use of the NuMED NuCLEUS family of valvuloplasty catheters for BAV, has accumulated over many years.

Based on the available information and considerations as outlined above, the benefits of the NuMED NuCLEUS family of valvuloplasty catheters outweigh its risks for the BAV indication. It is recommended that this De Novo petition, K082776, for the NuMED

NuCLEUS family of valvuloplasty catheters for the BAV indication and the request for a Class II device designation be granted.

RECOMMENDATION

The recommendation for granting approval for this De Novo petition for the NuMED NuCLEUS family of catheters indicated for BAV is based on overall clinical experience with BAV. The specifically-cited clinical experience using the NuMED NuCLEUS family of catheters for BAV is a scientifically sound approach that was agreed upon by the scientific and clinical reviewers of this de novo. Furthermore, the De Novo approval of the NuMED NuCLEUS Catheter, which is very similar to the NuMED NuCLEUS-X Catheter, is justifiable and supported based on this very large amount of worldwide clinical experience in conjunction with the supporting non-clinical performance data that indicates similar performance as well.

General and special controls do appropriately mitigate the risks associated with the NuCLEUS and NuCLEUS-X BAV catheters. The Circulatory Support and Prosthetics Branch within the Division of Cardiovascular Devices recommends that the de novo petition be granted.

CONCLUSION

The de novo petition for the NuMED NuCLEUS-X PTV Catheter is granted and the device is classified under the following:

Product Code: OZT
Device Type: Balloon Aortic Valvuloplasty Catheter
Class: II
Regulation: 21 CFR 870.1255