# NuMED
# Summary of Safety and Clinical Performance
# SSCP – Sizing

*This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device.*

*The SSCP is not intended to replace the Instructions for Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.*

*The following information is intended for users/healthcare professionals.*

| **1. Device identification and general information** | |
|---|---|
| Device trade name(s) | NuMED Sizing Family<br>PTS<br>PTS-X |
| Model Number | NuMED Sizing Family – Model 1200<br>PTS – Model 360<br>PTS-X – Model 360X |
| Manufacturer's name and address | NuMED, Inc.<br>2880 Main Street<br>Hopkinton, NY 12965<br>USA |
| Manufacturer's single registration number (SRN) | US-MF-000010948 |
| Basic UDI-DI | 08877141200SE |
| Medical device nomenclature description / text | EMDN – C0104020103 - VASCULAR OCCLUSION CATHETERS |
| Class of device | III |
| Year when first certificate (CE) was issued | 2001 – PTS<br>2004 – PTS-X |
| Authorised Representative (AR) | G. van Wageningen B.V.<br>Hallenweg 40, 5683 CT Best,<br>The Netherlands |
| AR SRN | NL-AR-000010437 |
| Notified Body | SGS Belgium NV |
| Notified Body ID number | 1639 |

| **2. Intended use of the device** | |
|---|---|
| Indications for use | Recommended for use in those patients with cardiovascular defects wherein accurate measurement of the defect is important to select the appropriately sized occluder device. |
| Contraindications and/or limitations | There are no contraindications listed for this device and indication. |

| 3. Device Description | |
|---|---|
| Description of the device | The Sizing Catheters are coaxial catheters for use in those patients with cardiovascular defects wherein accurate measurement of the defect is important to select the appropriately sized occluder device. The outer and inner body are made of polyamide tubing. The X-line version of the catheter has an inner tubing that is comprised of a multi-layer extrusion of polyamide that surrounds a braid of 304 LV Stainless Steel. The catheter features a proximal end bifurcate with two distinct luminal passages. The inflation lumen terminates into a distally mounted balloon. This balloon is of the non-compliant variety and is designed to insert through the smallest possible introducer. The through lumen terminates at the tip of the catheter and will accept the passage of the appropriate guidewire. All catheter sizes with the exception of the 1cm balloon length will have four radiopaque platinum marker bands, to aid during placement; two under the balloon shoulders and two at the balloon center, spaced at 10mm (as measured from leading edge to leading edge). The 1cm balloon length will only have the two image bands at the balloon center, spaced at 10mm (as measured from leading edge to leading edge).<br><br>The balloon is designed to inflate to the diameter and length listed on the label at a specific pressure. Thus, it is recommended that the device be used in conjunction with a mechanism to monitor pressure, an inflation device with pressure gauge. This device is also designed to be used with an appropriately sized introducer and guidewire.<br><br>The balloon size is ± 10 % at the Rated Burst Pressure (RBP) and the RBP is not to be exceeded.<br><br>The catheters are supplied sterile, by ethylene oxide gas, and are intended for single use only. The catheters are invasive and intended for transient use (continuous use of <60 minutes) on patients. |
| Reference to previous generation(s) or variants | N/A |
| Accessories which are intended to be used in combination with the device | Guidewire, introducer, balloon inflation medium, inflation device with pressure gauge, and stopcock. |
| Description of any other devices and products which are intended to be used in combination with the device | N/A |

| 4. Risks and Warning | |
|---|---|
| Residual risks and undesirable effects | Side-effects reported in the literature are inherent and common to all percutaneous sizing procedures and/or intravascular catheter procedures and are not specifically associated with the Sizing Catheter.<br><br>All risks identified in the clinical literature as well as the risks detected from the Post Market Surveillance or from clinical data have been considered by the risk management process.<br><br>All significant risks were considered, mitigated as far as possible (AFAP), and are acceptable in regard to the clinical benefit of the device.<br>**POTENTIAL COMPLICATIONS**<br>Potential balloon separation following balloon rupture or abuse and the subsequent need to use a snare or other medical interventional techniques to retrieve the pieces.<br>**NOTE:** There have been infrequent reports of larger diameter balloons bursting circumferentially, possibly due to a combination of tight focal strictures in large vessels. In <u>any</u> instance of a balloon rupture while in use, it is recommended that a sheath be placed over the ruptured balloon prior to withdrawal through the entry site. This can be accomplished by cutting off the proximal end of the catheter and slipping an appropriately sized sheath over the catheter into the entry site. For specific technique, refer to: |

| | |
|---|---|
| | Tegtmeyer, Charles J., M.D. & Bezirdijan Diran R., M.D. "Removing the Stuck, Ruptured Angioplasty Balloon Catheter." Radiology, Volume 139, 231-232, April 1981.<br><br>Potential complications & adverse effects associated with device use and indication include:<br>• Trauma / Overstretching of the Septum<br>• Device Erosion<br>• Device Embolization<br>• Access Site Complications |
| Warning and Precautions | The following Warnings and Precautions have been identified and are called out in the Instruction for Use:<br><br>**WARNINGS**<br>• CAUTION: Do not exceed the RBP. An inflation device with pressure gauge is recommended to monitor pressure. Pressure in excess of the RBP can cause balloon rupture and potential inability to withdraw the catheter through the introducer sheath.<br>• Use only appropriate balloon inflation medium. Do not use air or gaseous medium to inflate the balloon.<br>• Do not advance the guidewire, balloon dilatation catheter, or any other component if resistance is met, without first determining the cause and taking remedial action.<br>• This catheter is not recommended for pressure measurement or fluid injection.<br>• Do not remove the guidewire from the catheter at any time during the procedure.<br>• This device is intended for single use only. Do not resterilize and/or reuse it, as this can potentially result in compromised device performance and increased risk of cross- contamination.<br><br>**PRECAUTIONS**<br>• One should always select a diameter larger than the unstretched defect diameter, i.e., TEE ASD size 12mm - select 20 or 25 mm PTS.<br>• Caution should be used when inflating the balloon, over inflation can cause trauma and overstretching of the septum.<br>• Sizing procedures should be conducted under fluoroscopic guidance with appropriate x-ray equipment. (PTS-X only).<br>• Sizing procedures should be conducted under fluoroscopic/MRI guidance with appropriate x-ray equipment. (PTS only)<br>• Guidewires are delicate instruments. Care should be exercised while handling to help prevent the possibility of breakage.<br>• Careful attention must be paid to the maintenance of tight catheter connections and aspiration before proceeding to avoid air introduction into the system.<br>• Under no circumstances should any portion of the catheter system be advanced against resistance. The cause of the resistance should be identified with fluoroscopy/MRI and action taken to remedy the problem.<br>• If resistance is felt upon removal, then the balloon, guidewire, and the sheath should be removed together as a unit, particularly if balloon rupture or leakage is known or suspected. This may be accomplished by firmly grasping the balloon catheter and sheath as a unit and withdrawing both together, using a gentle twisting motion combined with traction.<br>• Before removing catheter from sheath it is very important that the balloon is completely deflated.<br>• Proper functioning of the catheter depends on its integrity. Care should be used when handling the catheter. Damage may result from kinking, stretching, or forceful wiping of the catheter. |

| | |
|---|---|
| Other relevant aspects of safety, including a summary of any field safety corrective actions (FSCA including FSN) if applicable | There have not been any Field Safety Corrective Actions or Field Safety Notices for the Sizing Catheters. |

**5. Summary of clinical evaluation and post-market clinical follow-up (PMCF)**

**Summary of clinical data related to equivalent device:**

NuMED has elected not to use the clinical data from an equivalent (clinical, technical, and biological characteristics) device(s). In the event there are devices considered equivalent, their data will be considered as similar devices.

**Summary of clinical data from conducted investigations of the device :**

NuMED has not conducted any clinical investigations on the Sizing Catheters.

**Summary of clinical data from other sources:**

1. Krizanic et al. (2008)

**Safety & Performance**

**Objective:** Investigation of the usefulness feasibility and safety of the Occlutech Figulla® single layer-PFO occlude N for closure of PFO.

**Method:** Open, prospective, nonrandomized multicenter clinical study

**Follow-up:** Up to 180 days after procedure

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Open, prospective, nonrandomized multicenter clinical study | Treatment Benefit, Treatment Harms (Common) | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | 25 mm PTS NuMED Inc. to determine the size and the anatomy of the defect | **D1** | D2 | D3 |
| Application | The right femoral vein was punctured under local anesthesia and a soft-tipped 0.035'' wire was inserted and advanced through the PFO, and finally positioned within a left-sided pulmonary vein. PTS balloon sizing was used to determine the size and anatomy of the defect before implementation of PFO-occluder device. Under fluoroscopy and TEE. | **A1** | A2 | A3 |
| Patient | P1 (37 patients with PFO; mean age 57 yo (18-80); M 18, F 17) | **P1** | P2 | P3 |
| Report | The article contains sufficient information to be able to undertake a rational and objective assessment. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | **4** | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | The reported outcome measures (implantation success/complications) indirectly reflect the intended performance of the device. | **Yes 1** | No 2 |
| Follow-up | The duration of follow-up (up to 180 days after the procedure) is long enough to assess whether duration of treatment benefits/harms and identify complications. | **Yes 1** | No 2 |

**Population**: patients with PFO (7.8 ±2.5 mm defect size mean) All patients suffered from cryptogenic stroke (the origin remains unknown).

**Sampling**: n= 36

**Mean Age:** 50 years old (yo) (18 – 80)

**Sex:**
M - 18
F – 17

| | | | |
|---|---|---|---|
| Statistical analysis | No statistical analysis of the data has been provided. | Yes 1 | **No 2** |
| Clinical significance | The magnitude of the treatment benefit observed was clinically significant (implantation success). | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | **5** | |

**Overall S&P Appraisal, Disposition and Weighting**

| | | | |
|---|---|---|---|
| S&P Grade (Range 9-25) | LOE (3) + Suitability (4) + Data Contribution (5) = **12** | Disposition and Weighting (select) | Accepted and Pivotal **9-12**<br>Accepted but not Pivotal, 13-21<br>Excluded, 22-25 |

**Relevant S&P Results**

| Criteria | Results | P value |
|---|---|---|
| Safety data | Perioperatively:<br>No major in-hospital-AE or complications thromboembolism, occlude dislodgement, infection or myocardial infarction. | N/A |
| | Comparison to Amplatzer® PFO occluder device: See Table 1 below | N/A |
| Performance data – After implantation | One patient had transient atrial fibrillation, which terminated medically after 12 h. | N/A |
| Performance data – 60 days after procedure | TEE studies in the remaining 35 patients (one patient was unwilling to further participate) showed a residual shunt in 8.6% (3/35) and a left-to-right shunt in 2.6% (1/35) of patients | N/A |
| Performance data – 180 days after procedure | One patient with severe arteriosclerotic heart disease and aortic carotic stenosis revealed a stroke without evidence of cardioembolic origin or devices thrombosis.<br>Complete closure was achieved in 88.2% of the cases (30/34). | N/A |
| Comparison to Amplatzer® PFO occluder device | Table 1 Comparison Amplatzer vs Figulla PFO Occluder N | N/A |
| Benefits/claims data | Authors mentioned that they routinely used the sizing balloon for definition of the defect size. TEE studies could not exactly determine the defect size. Implantation by monitoring with ICE is an alternative method which was not routinely used. They generally recommend ICE or TEE monitoring during the procedure in the clinical study. For general use both methods are optional. Balloon assessment of PFOs enhances the understanding of their morphology and aids in the identification of long tunnels. De-tunnelisation using the same balloon facilitates the uncomplicated trancatheter closure of long tunnel PFOs in most patients. | N/A |
| Strengths | Comparison of results with a reference device (Amplatzer PFO occlude (n = 69)). | N/A |
| Weaknesses/ Potential bias | Low number of subjects included.<br>Study does not directly assess safety and performance of the sizing balloon but was designed for assessment of the PFO occlude device. | N/A |

| No. | Amplatzer PFO occluder *n* = 69 | Figulla PFO occluder *n* = 36 |
|---|---|---|
| Implantation success | 100% | 100% |
| Periinterventional Complications | | 1 |
| (a) minor, *n* % | 1 (1.5%) | 1 Atrial fibrillation |
| Trans. ST-elevation | 1 (1.5%) | 1 Grain bleeding |
| (b) major, *n* % | 0 | 0 |
| TIA | 0 | 0 |
| Devicedislodgement | 0 | 0 |
| Pericardial effusion | 0 | 0 |
| Arrosion of aorta | 0 | 0 |
| Death | 0 | 0 |

**State of the Art**

N/A – Articles does not contribute to SOA.

**Conclusions of the authors:** The novel Occlutech Figulla® PFO N single layer device appears to be safe, feasible and useful for PFO closure despite a 50% reduction of the meshwire, no distal hub and an improved flexibility of the left atrial disc.

**Device used:** 25 mm NuMED Inc. to determine the size and the anatomy of the defect; the correct position of the PFO-occluder was confirmed by means of fluoroscopy and TEE

2. Kutty et al. (2008)

**Safety & Performance**

**Objective:** Presentation of the results of investigations performed to determine causes of significant recurrent focal neurologic events (FNEs) in patients from a center who underwent transcatheter PFO closure over a period of 5.5 years (From March 2000 to September 2005)

**Method:** Retrospective clinical study

**Follow-up:** mean of 2.1 years (1 month to 7.1 years) for a total of 438 patient-years after closure (199/216 patients with follow-up information)

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Retrospective clinical study | Treatment Benefit, Treatment Harms (Common) | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | PTS Sizing balloon NuMED Inc.; | **D1** | D2 | D3 |
| Application | A complete right-sided hemodynamic catheterization and right atrial angiography was performed to assess the anatomy of the PFO. A guidewire was positioned in the left upper pulmonary vein through a venous catheter advanced through the PFO.<br>PTS Sizing balloon was advanced over the guidewire and incompletely inflated (<1 atm) until a distinct indentation in the balloon and elimination of any shunting by color Doppler was identified. The balloon was not inflated fully to avoid the possibility of inadvertently enlarging the defect. The diameter of the indentation was measured angiography and by echocardiography.<br>Under general anesthesia and TEE and since 2001 ICE and conscious sedation. | **A1** | A2 | A3 |
| Patient | 216 patients with PFO; 50 yo (19 – 77); M 107/F 109 | **P1** | P2 | P3 |
| Report | The article contains sufficient information to be able to undertake a rational and objective assessment. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | **4** | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | The reported outcome measures (implantation success/complications) indirectly reflect the intended performance of the device. | **Yes 1** | No 2 |
| Follow-up | The duration of follow-up (mean 2.1 years) is appropriate to assess whether duration of treatment benefits/harms and identify complications. | **Yes 1** | No 2 |
| Statistical analysis | Statistical analysis of the data has been provided for safety data and is appropriate. | **Yes 1** | No 2 |
| Clinical significance | The magnitude of the treatment benefit observed was clinically significant (implantation success). | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | **4** | |

**Overall S&P Appraisal, Disposition and Weighting**

**Population**: patients with PFO (11 mm (4 – 24) stretch diameter)

**Sampling**: n= 216

**Mean Age:** 50 yo (19 – 77)

**Sex:** M - 107 F – 109

| | | | |
|---|---|---|---|
| S&P Grade (Range 9-25) | LOE (3) + Suitability (4) + Data Contribution (4) = **11** | Disposition and Weighting (select) | Accepted and Pivotal **9-12**<br>Accepted but not Pivotal, 13-21<br>Excluded, 22-25 |

**Relevant S&P Results:**

| Criteria | Results | P value |
|---|---|---|
| Safety data - Main results | Twenty patients had a focal neurologic event (FNE) 0.1 month to 40.2 months after PFO closure over 438 person-years of follow-up (mean 2.1 years, range 1 month to 7.1 years). There were 4 recurrent strokes, 2 likely directly device related. Ten patients had transient ischemic attack (TIA) and 6 patients had clear evidence of pathology unrelated to the device. | N/A |
| Safety data - Event rate for recurrent strokes | 0.91% per year or 9.1 per 1,000 person-years (95% CI for difference 3.4 to 24.3) | N/A |
| Safety data - Combined event-rate for stroke/transient ischemic attack (TIA) | 3.42% per year or 34.2 per 1,000 person-years (95% CI for difference 20.7 to 56.8) | N/A |
| Safety data - Comparison with other studies | The recurrent stroke rate found in this study after CardioSEAL occlusion of PFO is comparable to rates from studies that evaluated recurrence of stroke and TIA in patients with PFO and cryptogenic stroke placed on various regimen of medical prophylaxis. | N/A |
| Performance data - Successful implantation | 100% | N/A |
| Benefits/claims data | None | N/A |
| Strengths | High number of subjects included (216)<br>FU of 2.1 years (mean). | N/A |
| Weaknesses/ Potential bias | Study does not directly assess safety and performance of the sizing balloon but was designed for assessment of the PFO occlude device. | N/A |

**State of the Art**
N/A – Articles does not contribute to SOA.

**Conclusions of the authors:** In conclusion, transcatheter PFO occlusion can be accomplished as an outpatient procedure with minimal immediate morbidity. Patients may have multiple possible causes of recurrent FNE. Recurrence rate of cryptogenic FNE compares favorably with reports of medical management. Analysis of results from ongoing randomized trials of transcatheter PFO closure versus medical management may improve our ability to select the best treatment for individual patients
**Device used:** Sizing balloon NuMED Inc.; advanced over the guidewire and incompletely inflated (<1 atm) until a distinct indentation in the balloon abd elimination of any shunting by color Doppler was identified. The balloon was not inflated fully to avoid the possibility of inadvertently enlarging the defect. The diameter of the indentation was measured angiography and by echocardiography.

3. Gaspardone et al. (2020)

**Safety & Performance**
**Objective:** This study sought to assess PFO anatomy by TEE in patients undergoing percutaneous suture-mediated PFO closure to identify predictors of post-procedural residual atrial right-to-left shunt (RLS).
**Method:** Retrospective study
**Follow-up:** 12 months or later if needed

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Retrospective study | Treatment Benefit, Treatment Harms (Common) | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | PTS-X NuMED Inc. to determine the size and the anatomy of the defect | **D1** | D2 | D3 |

**Population**: 230 consecutive patients underwent percutaneous suture-mediated PFO closure

**Sampling**: n= N/A

**Mean Age:** mean 46 ±

| | | | | |
|---|---|---|---|---|
| Application | Placement in the superior pulmonary vein; TEE monitoring in 27 patients (in the remaining patients the procedure was carried out in local anesthesia without TEE or intracardiac echo monitoring) | **A1** | A2 | A3 |
| Patient | 230 consecutive patients underwent percutaneous suture-mediated PFO closure; mean 46 ± 13, range 15 to 76); M:84/F:146 | **P1** | P2 | P3 |
| Report | The article contain sufficient information to be able to undertake a rational and objective assessment. | **R1** | R2 | R3 |
| Suitability Grade (Range 4-12) | | **4** | | |

13, range 15 to 76)

**Sex:**
M – 84
F – 146

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | The reported outcome measures (closure (RLS grade)/complications) indirectly reflect the intended performance of the device. | **Yes 1** | No 2 |
| Follow-up | The duration of follow-up (up to 12 months after the procedure) is acceptable to assess whether duration of treatment benefits/harms and identify complications. | **Yes 1** | No 2 |
| Statistical analysis | Statistical analysis of the data has been provided. | **Yes 1** | No 2 |
| Clinical significance | The magnitude of the treatment benefit observed was clinically significant (closure grade). | **Yes 1** | No 2 |
| Data Contribution Grade (Range 4-8) | | **4** | |

**Overall S&P Appraisal, Disposition and Weighting**

| | | | |
|---|---|---|---|
| S&P Grade (Range 9-25) | LOE (3) + Suitability (4) + Data Contribution (4) = **11** | Disposition and Weighting (select) | Accepted and Pivotal **9-12**<br>Accepted but not Pivotal, 13-21<br>Excluded, 22-25 |

**Relevant S&P Results**

| Criteria | Results | P value |
|---|---|---|
| Safety data | No procedural complications. | N/A |
| Performance data | At maximum follow-up, TTE evaluation showed a complete closure (RLS grade 0) in 142 (62%) patients and an effective closure (RLS ≤ 1grade) in 193 (84%) patients. | N/A |
| Benefits/claims data | None | N/A |
| Strengths | Large population studied (230) | N/A |
| Weaknesses/ Potential bias | Retrospective analysis with obvious intrinsic limitation and potentially leads to biases.<br>The study is focused on the assessment of the safety and performance of the PFO occlude device and not of the NuMED, Inc. sizing balloon. | N/A |

**State of the Art**
N/A – Articles does not contribute to SOA.

**Conclusions of the authors:** Percutaneous suture-mediated PFO closure is feasible in the majority of septal anatomies; however, PFO >5 mm in width and spontaneous large RLS are less likely to be closed with 1 stitch only.
**Device used:** PTS-X NuMED, Inc. for contrast-enhanced sizing-balloon PFO anatomy assessment; TEE monitoring in 27 patients (in the remaining patients the procedure was carried out in local anesthesia without TEE or intracardiac echo monitoring).

4. Karagiannni et al. (2020)

**Safety & Performance**
**Objective:** This study aimed to investigate the risk factors for recurrent cryptogenic cerebrovascular events (rCVEs) after closure of PFO during long-term follow-up.
**Method:** Retrospective study
**Follow-up:** 8.4 (± 2) years from PFO closure
**Appraisal**

**Population**: 282 consecutive patients underwent percutaneous PFO closure

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Retrospective study | Treatment Benefit, Treatment Harms (Common) | 1 | 2 | **3** | 4 | 5 |

**Sampling**: n= N/A

**Mean Age:** mean 48 ± 11.7, range not reported

**Sex:**
M – 176
F – 106

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | The size and anatomy of the PFO were determined by gentle inflation of a compliant-sized balloon PTS NuMED, Inc. until a waist was apparent. | **D1** | D2 | D3 |
| Application | PFO closure was performed in a catheterization laboratory under general anesthesia with fluoroscopy and TEE imaging. | **A1** | A2 | A3 |
| Patient | 282 consecutive patients underwent percutaneous PFO closure; mean 48 ± 11.7, range not reported; M: 176/F: 106. | **P1** | P2 | P3 |
| Report | The article contains sufficient information to be able to undertake a rational and objective assessment. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | **4** | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | The reported outcome measures (closure (RLS grade)/complications) indirectly reflect the intended performance of the device. | **Yes 1** | No 2 |
| Follow-up | Long-term duration of follow-up (up to 8.4 years from PFO closure) to assess whether duration of treatment benefits/harms and identify complications. | **Yes 1** | No 2 |
| Statistical analysis | Statistical analysis of the data has been provided. | **Yes 1** | No 2 |
| Clinical significance | The magnitude of the treatment benefit observed was clinically significant (closure grade). | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | **4** | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (3) + Suitability (4) + Data Contribution (4) = **11** | Disposition and Weighting (select) | Accepted and Pivotal **9-12**<br>Accepted but not Pivotal, 13-21<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| Criteria | Results | P value |
|---|---|---|
| Safety data – Complications (0 – 6 months) | Intra-operative complications:<br>- Temporary ST-elevation: 4 (1.4%)<br>- Thrombus on catheter during operation: 4 (1.4%)<br>- Device thrombus: 1 (0.7%)<br>- Pericardial effusion: 1 (0.7%)<br>Complications post-operative:<br>- Major bleeding: 0<br>- Minor bleeding: 5 (1.8%)<br>- Stroke first 48 hours: 1 (0.4%)<br>- Device dislocation: 5 (1.8%) | N/A |
| Performance data – rCVEs after PFO closure | 14 (5%) out of the 282 consecutive patients who underwent PFO closure suffered from rCVEs during a mean FU of 8.4 years (1.7 rCVEs per 1000 patient-years). | N/A |
| Benefits/claims data | None | N/A |
| Strengths | Large population studied (282); long-term FU (8.4 years) | N/A |
| Weaknesses/ Potential bias | Retrospective analysis with obvious intrinsic limitation and potentially leads to biases.<br>The study is focused on the assessment of the safety and performance of the PFO occluder device and not of the NuMED, Inc. sizing balloon. | N/A |

**State of the Art**
N/A – Articles does not contribute to SOA.

**Conclusions of the authors:** This study indicates that residual shunting and choice of the device may be the major reasons for rCVEs.
**Device used:** PTS NuMED, Inc. used to determine the size and anatomy of the PFO; general anesthesia; fluoroscopy and TEE imaging.

5. Stapleton et al. (2020)

**Safety & Performance**

**Objective:** Describe experience utilizing long Gore DrySeal (GDS) sheaths (WL Gore and Associates, Flagstaff, AZ) to protect the tricuspid valve during advancement of the Commander delivery system for deployment of the SAPIEN 3 valve in the pulmonary position.

**Method:** Retrospective review

**Follow-up:** post-procedural

**Appraisal**

| Level of Evidence | Study Method/Design | Question Applied | Oxford LOE 2011 | | | | |
|---|---|---|---|---|---|---|---|
| | Retrospective study | Treatment Benefit, Treatment Harms (Common) | 1 | 2 | **3** | 4 | 5 |

| Suitability | Relevant Data | Grading | | |
|---|---|---|---|---|
| Device | 30 or 40mm diameter PTS-X sizing balloon NuMED, Inc. inflated in the right ventricular outflow tract (RVOT) to determine the minimum diameter of the location that could be used as a landing zone. | **D1** | D2 | D3 |
| Application | Internal jugular or femoral vein | **A1** | A2 | A3 |
| Patient | 48 patients; mean age between 23.2 and 25.9; 24 males | **P1** | P2 | P3 |
| Report | The article contains sufficient information to be able to undertake a rational and objective assessment. | **R1** | R2 | R3 |
| | Suitability Grade (Range 4-12) | **4** | | |

| Data Contribution | Relevant Data | Grading | |
|---|---|---|---|
| Outcomes/Endpoints | The reported outcome measures (procedural success) indirectly reflect the intended performance of the device. | **Yes 1** | No 2 |
| Follow-up | The duration of follow-up (post-procedural) seems acceptable to assess whether duration of treatment benefits/harms and identify complications. | **Yes 1** | No 2 |
| Statistical analysis | Statistical analysis of the data has been provided. | **Yes 1** | No 2 |
| Clinical significance | The magnitude of the treatment benefit observed was clinically significant (procedural success). | **Yes 1** | No 2 |
| | Data Contribution Grade (Range 4-8) | **4** | |

**Overall S&P Appraisal, Disposition and Weighting**

| S&P Grade (Range 9-25) | LOE (3) + Suitability (4) + Data Contribution (4) = **11** | Disposition and Weighting (select) | Accepted and Pivotal **9-12**<br>Accepted but not Pivotal, 13-21<br>Excluded, 22-25 |
|---|---|---|---|

**Relevant S&P Results**

| Criteria | Results | P value |
|---|---|---|
| Safety data – | Not reported | N/A |
| Performance data – Severe tricuspid valve injury | Group I: 2/25 (8%) vs. Group II: 0/23 | N/A |
| Benefits/claims data | None | N/A |
| Strengths | Comparative study | N/A |

**Population**: 48 patients underwent transcatheter placement of a SAPIEN valve in the pulmonary position

**Sampling**: Group I (without using a long delivery sheat): n=25
Group I (with): n=23

**Mean Age:**
Group I: mean 25.9 ± 15.5, range not reported
Group II: mean 23.2 ± 16.5, range not reported

**Sex:**
Group I: M: 15 (60%)
Group II: M: 9 (39%)

| | | |
|---|---|---|
| Weaknesses/ Potential bias | Retrospective analysis with obvious intrinsic limitation and potentially leads to biases.<br>The study is focused on the assessment of the safety and performance of the Gore sheath and not of the NuMED, Inc. sizing balloon. | N/A |

**State of the Art**
N/A – Articles does not contribute to SOA.

**Conclusions of the authors:** Use of a long GDS may protect the tricuspid valve from injury during implantation of the S3 valve in the pulmonary position, and is technically feasible in smaller patients.
**Device used:** 30 or 40mm diameter PTS-X sizing balloon NuMED, Inc. inflated in the RVOT to determine the minimum diameter of the location that could be used as a landing zone.

**An overall summary of the clinical performance and safety:**

A comprehensive, systematic, and critical evaluation of the pertinent clinical data and pre-clinical study data in relation to the Sizing Catheters has been carried out and documented in accordance with MEDDEV 2.7/1 Rev 4. Based on the results of the evaluation, it is considered that:

1. Conformity with relevant general safety and performance requirements set out in MDR Annex I under the normal conditions of the intended use of the device has been confirmed.
2. Undesirable side-effects and acceptability of the benefit-risk ratio have been evaluated and are acceptable according to the current knowledge/the state of the art in the medical fields concerned and according to available medical alternatives.
3. The information materials supplied by NuMED and the risk reduction measures are adequate taking into account the intended purpose of the device.
4. Usability aspects have been adequately considered and the Sizing Catheters, including the IFU, are suitable for the intended users.
5. The claims foreseen in the information materials provided with the CER are adequate taking into account the intended purpose of the device.
6. The information materials supplied and the RM documentation for the device under evaluation are consistent with the clinical data and pre-clinical study data presented in the CER and with the current knowledge/state of the art.

Overall, it is concluded that the risks associated with the use of the Sizing Catheters are acceptable when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety; that the intended clinical performances are achieved by the device; and that known and foreseeable risks and undesirable side-effects are considered acceptable when weighed against the benefits from performances achieved by the device.

**Ongoing planned post-market clinical follow-up:**

The following is data from the completed PMCF Study on the Sizing Catheter.

Purpose: The objective of the Post Market Clinical Follow-up (PMCF) study is to capture data on the 110cm useable length PTS & PTS-X catheters in actual practice. As there are no identified residual risks for these devices, based on catheter design and historical adverse events, this study will focus on clinical performance of the devices.

Clinical Study Methodology: Information will be collected from treating physicians, which will include patient specifics and status post-procedure. Collected information will also include all device and/or procedure complications. The chosen design for this study is a form / questionnaire for each treating physician to complete. These forms will be included as an insert in the Instructions for Use. The form will also be emailed to all NuMED distributors. The distributors will then be able to follow-up with hospitals on the use of these devices. NuMED feels this is the best option for collecting feedback.

The target study size will be 59 patients, based on confidence intervals, in order to guarantee a 95% confidence level, 95% of the time. The study will include all patients for which a 110cm useable length PTS and/or PTS-X catheter with a CE Marked IFU is supplied.

Reference to the clinical study plan (and amendment) number: Post Market Clinical Follow-up Study PMCF-360 / 360X Rev. 01 PTS & PTS-X Catheters – 110cm Useable Length

Investigation Site: Selection of sites / investigators will include any / all orders for which a 110cm useable length PTS and/or PTS-X catheter with a CE Marked IFU is supplied.

Regulatory Authority Approvals: N/A – the studied devices are CE-marked devices and are used according to the indications covered by current CE marking. Notified Body reviewed the clinical plan of this study.

Patient Population: Study cohort will include all patients whom undergo an interventional procedure with the 110cm useable length PTS and/or PTS-X catheter.

Clinical Study Results: NuMED has received the required (59) applicable PMCF forms, which meets the sample size criteria established for this specific study. A target study size of 59 patients was chosen, based on confidence intervals, in order to guarantee a 95% confidence level, 95% of the time.

There were zero (0) complaints received during the PMCF study time frame, related to applicable PMCF sales. The overall complaint rate for the Sizing Catheters is extremely low (0.045%). The PMCF Study forms have not shown any increase in the complaint rate or introduced any new risks associated with the additional useable length of the device.

Of the (61) applicable forms returned, 58 resulted in the physician marking that it was a successful procedure (95.1%). The remaining 3 forms were left blank in this section; however, no device or procedural complications were reported.

The Sizing Catheters have been on the worldwide market for over 20 years, allowing the devices to be used on a variety of patients and populations. In 2017, an additional useable length of 110cm was added to the product line. The overall complaint rate for the Sizing Catheters is 0.045% (broken down in Section C). Based on the PMCF study findings, NuMED concludes the long-term safety and clinical performance of these devices has been well established via substantial clinical evidence demonstrated during the study. NuMED has determined the Sizing Catheters to be safe and effective when used as indicated, at both useable lengths. No changes are required to the risk analysis or the instructions for use at this time. Any PMCF forms and/or complaints received in the future will continue to be evaluated. Established post market surveillance activities will be followed with the conclusion of the PMCF Study.

Purpose Criteria: The objective of the PMCF study is to determine if there is an increase in complications and / or complaints associated with the 110cm useable length PTS and/or PTS-X catheters through actual clinical use, as compared to the 80cm useable lengths or if any new risks are introduced. All returned PMCF forms, sales & complaint data, as well as any applicable literature will be reviewed. The review of the PMCF forms, and sales and complaint data will take place each month during the quality meeting. The results will also be reviewed against the current Failure Modes, Effects and Criticality Analysis (FMECA) in order to determine if any new risks have been introduced.

**6. Possible diagnostic or therapeutic alternatives**

Alternatives to the use of sizing balloons would be to not use them; in this case, the size of the defect would only be estimated based on diagnostic and pre-procedure imaging. It was reported by the ASE Guideline (2015) that some operators might not perform balloon sizing because of the dimensions of the effect (small defect). Not sizing the cardiac defect before transcatheter closure would be inconsistent with ASE recommendations and standard-of-care.

Alternatives to the use of transcatheter cardiac occluder devices to which sizing balloons are associated would be to not proceed with a therapeutic intervention and establish a continuous follow-up or to provide medical treatments with dedicated drugs or to proceed with an open surgery of the heart. AHA/ACC and ESC Guidelines offers recommendations and algorithms on how to proceed based on the patient's medical history and disease conditions. However, it is generally accepted that compared to open surgery a percutaneous approach offers a shorter hospital length of stay and a faster recovery, with similar long-term outcomes.

**7. Suggested profile and training for users**

Users of percutaneous sizing balloons are qualified cardiac surgeons trained to the stop-flow technique.

**8. Reference to any harmonised standards and CS applied**

There are no Common Specifications for this type of device.

The following harmonised standards are followed for this device:

- EN ISO 10993-10: 2023 – Biological Evaluation of Medical Devices – Part 10: Tests for Skin Sensitization
- EN ISO 10993-23: 2021 – Biological Evaluation of Medical Devices – Part 23: Tests for Irritation

- EN ISO 11135: 2014 / A1:2019 – Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation and routine control of a sterilization process for medical devices.
- EN ISO 11737-1: 2018 / A1:2021 – Sterilization of medical devices – Microbiological methods – Part 1: Determination of a population of microorganisms on products
- EN ISO 13485: 2016 / A11:2021 – Medical devices – Quality management systems – Requirements for regulatory purposes
- EN ISO 14971: 2019 / A11:2021 – Medical Devices – Application of Risk Management to Medical Devices
- EN ISO 15223-1: 2021 – Medical devices – Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements

## 9. References

1. Krizanic F, Sievert H, Pfeiffer D, Konorza T, Ferrari M, Figulla HR. Clinical evaluation of a novel occluder device (Occlutech) for percutaneous transcatheter closure of patent foramen ovale (PFO). Clinical Research in Cardiol. 2008 Dec;97(12):872-7.
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3. Gaspardone A, Sgueglia GA, De Santis A, D'Ascoli E, Iamele M, Piccioni F, Giannico B, D'Errico F, Gioffrè G, Summaria F, Gaspardone C, Versaci F. Predictors of Residual Right-to-Left Shunt After Percutaneous Suture-Mediated Patent Fossa Ovalis Closure. JACC Cardiovasc Interv. 2020 Sep 28;13(18):2112-2120. doi: 10.1016/j.jcin.2020.06.004. PMID: 32972572.
4. Karagianni, Alexia & Mandalenakis, Zacharias & Dellborg, Mikael & Mirzada, Naqibullah & Johansson, Magnus & Eriksson, Peter. (2020). Recurrent cerebrovascular events in patients after percutaneous closure of patent foramen ovale. Journal of Stroke and Cerebrovascular Diseases. 29. 104860. 10.1016/j.jstrokecerebrovasdis.2020.104860.
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## 10. Revision History

| SSCP revision number | Date Issued | Change Description | Revision validated by Notified Body |
|---|---|---|---|
| 00 | 21 June 2022 | Initial implementation | ☐ Yes<br>Validation Language: English<br>☒ No |
| 01 | 18 November 2022 | Update due to new CER. Change in warnings to separate the one warning for PTS and PTS-X due to MRI, update for PMCF Study completion | ☐ Yes<br>Validation Language: English<br>☒ No |
| 02 | 03 August 2023 | Updated - **Ongoing planned post-market clinical follow-up** – section to change the word in the first sentence from ongoing to completed. Updated Section 8 for the additional harmonized standards. | ☐ Yes<br>Validation Language: English<br>☒ No |
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