NuMED
Summary of Safety and Clinical Performance
SSCP – Stent Placement

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 Stent Placement Family BIB® (Balloon in Balloon) Stent Placement Catheter
Model Number	NuMED Stent Placement Family – Model 1500 BIB – Model 420.1
Manufacturer's name and address	NuMED, Inc. 2880 Main Street Hopkinton, NY 12965 USA
Manufacturer's single registration number (SRN)	US-MF-000010948
Basic UDI-DI	08877141500SV
Medical device nomenclature description / text	EMDN – C010402020102 – Cardiocirculatory System Devices, Stent Positioning Vascular Balloon Dilatation Catheters
Class of device	III
Year when first certificate (CE) was issued	2003
Authorised Representative (AR)	G. van Wageningen B.V. Hallenweg 40, 5683 CT Best, 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	Indicated for stent placement in vessels over 8mm in diameter.
Contraindications and/or limitations	There are no contraindications to the use of the BIB Stent Placement Catheters, except for vessels smaller than 8mm in diameter.

3. Device description	
Description of the device	The BIB Stent Placement Catheter is triaxial in construction with two lumens being used to inflate the balloon while one lumen is being used for tracking over a guidewire. The inner balloon is 1/2 of the outer balloon diameter and 1 cm shorter. The purpose of the double balloon catheter is to apply an incremental inflation for the purpose of dilating a stent. The inner balloon provides initial

	expansion of the stent and also acts as a tool to hold the stent on the catheter prior to the outer balloon being inflated. The outer balloon is then inflated, providing the remainder of the expansion. There are radiopaque platinum marker bands under the balloon shoulders, to aid during placement. The balloons are 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, and stent. Both the inner and outer balloon size is ± 10 % at the Rated Burst Pressure (RBP) and the RBP is not to be exceeded. 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	The BIB also comes in variants with a stent pre-mounted on it: Mounted CP Stent, Covered Mounted CP Stent, G-Armor Mounted Stent, and G-Armor Covered Mounted Stent. There is also a variant in which the Covered CP Stent is mounted on the BIB catheter inside a retractable introducer sheath as an all-in-one device. This variant is known as the NuDEL device. These other variants are covered by NuMED's CoA Stent, RVOT/CoA Stent, and Delivery System SSCPs.
Accessories which are intended to be used in combination with the device	There are no accessories that are intended to be used with this device.
Description of any other devices and products which are intended to be used in combination with the device	This device is designed to be used with a stent, guidewire, introducer, and an inflation device with pressure gauge.

4. Risks and Warning	
Residual risks and undesirable effects	Side-effects reported in the literature are stent flaring and stent migration. All risks identified in the clinical literature as well as the risks detected from the Post Market Surveillance or from clinical data generated and held by the Sponsor, have been considered by the risk management process. All significant risks were considered, mitigated as far as possible (AFAP), and are acceptable in regard to the clinical benefit of the device. Identified clinical residual risks/undesirable side-effects for the Stent Placement Catheters are: **POTENTIAL COMPLICATIONS/ADVERSE EFFECTS** NOTE: Circumferential tear of the delivery balloon catheter prior to complete expansion of the stent may cause the balloon to become tethered to the stent, requiring surgical removal. In case of rupture of an adequately sized balloon after stent expansion, it can be withdrawn and a new balloon catheter exchanged over a guidewire to complete expansion of the stent. Cardiac catheterization carries certain risks. Potential complications & adverse effects associated with device use and indication include: • Stent misplacement • Stent migration • Minor hematoma • Intraluminal thrombosis • Pseudoaneurysm

	• AV fistula formation • Bleeding requiring transfusion • Sepsis/infection • Distal thromboemboli • Death • Vessel rupture • Cerebrovascular incident • Hematoma requiring repair
Warning and Precautions	The following Warnings and Precautions have been identified and are called out in the Instruction for Use: **WARNINGS** • 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. • Confirm that the distal end of the introducing sheath is at least 2.5cm back from the most proximal image markers before inflating the outer balloon. Failure to do so may stretch the outer tubing and severely hinder balloon deflation. • Use two appropriate size inflation devices with pressure gauges for inflation. • 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. • When the stent is crimped onto a balloon delivery catheter, the maximum balloon inflation pressure must not exceed the recommended inflation pressure specified in the manufacturer's instructions. • This catheter is not recommended for pressure measurement or fluid injection. • Do not remove the guidewire from the catheter at any time during the procedure except when the procedure has been completed. • 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. **PRECAUTIONS** • The BIB Stent Placement balloon catheter was tested with the NuMED Cheatham Platinum (CP) Stent (bare & covered). • Dilatation procedures should be conducted under fluoroscopic guidance with appropriate x-ray equipment. • Stents are delicate devices. Care should be exercised while handling to help prevent the possibility of breakage. • Careful attention must be paid to the maintenance of tight catheter connections by aspiration before proceeding to avoid air introduction into the system. • The inflation diameter of the balloon used during stent delivery should approximate the diameter of the obstructive vessel and the intended implant site. • Under no circumstances should any portion of the catheter system be advanced against resistance. The cause of the resistance should be identified with fluoroscopy and action taken to remedy the problem. • 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. • Before removing the catheter from the sheath, it is very important that the balloon is completely deflated. • 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 BIB Stent Placement Catheter.

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

Summary of clinical data related to equivalent device:

An equivalent device was not used for the clinical evaluation.

Summary of clinical data from conducted investigations of the device:

The COAST study was specifically initiated to investigate clinical efficacy and safety of the CP Stent, with the BIB Stent Placement Catheter. The result of this study demonstrates that a double balloon significantly reduces known risks associated with single balloon stent placement procedures. Devices used in the studies were provided both in unmounted configurations.

1. Study Name: COAST

Purpose: to provide information that will support labeling of both the CP bare metal and covered stents to treat native and recurrent CoA in selected children, adolescents and adult.

Clinical Study Methodology: Single arm interventional study (open label)
Reference to the clinical study plan (and amendment) n°: NCT00552812

Investigation site: 19 pediatric cardiology centers in United States

Ethics Committee Approval: Institutional Review Board approvals from all participating institutions

Regulatory Authority Approvals: Investigational Device Exemption from US FDA (August 3, 2007)

Patient Population: Patients with native or recurrent CoA. A total of 105 patients underwent attempted implantation, median age 16 years (range from 8 to 52 years) and with 69.5% male.

Clinical Study Results: Results held on file by Sponsor

Purpose	Criteria	Results
Performance	Blood pressure gradient and coarctation minimum diameter: cardiac catheterization before and after CP Stent placement	Average systolic blood pressure difference (mmHg) changed from 29±14 mmHg at baseline to -3±15 mmHg at 24 months follow-up. The Coarctation minimum diameter reported at 7.9 ± 2.7mm at baseline to 14±3 mm after implantation.
Safety	Adverse events	No serious adverse events reported, 7% of the patients experienced somewhat serious events. Aortic aneurysms (n=6): 5 were successfully treated with covered stent placement, and 1 resolved without intervention. Stent fractures were seen in 2 patients after one year, 11 patients at two years and 12 additional fractures above 2 years.

Reference to the Clinical Study Report n°: NCT00552812
Device Used: Bare CP Stent and BIB catheter; covered stents were available in case of aortic wall injury.

Conclusion: The CP stent is safe and associated with persistent relief of aortic obstruction. Stent fracture and progression of fracture occur but have not resulted in clinically important sequelae. Reintervention is common and related to early and late aortic wall injury and need for re-expansion of small-diameter stents.

Summary of clinical data from other sources:

First Author (Year)	Appraisal/Results
1. Sohrabi et al. (2014)	**Safety & Performance**

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective randomized controlled trial.	To evaluate outcomes of treatment with Covered versus Bare NuMED CP Stents.	1	**2**	3	4	5

Suitability	Relevant Data	Grading		
Device	- NuMED CP Stent (Bare and Covered) - BIB	**D1**	D2	D3
Application	- Severe native CoA	**A1**	A2	A3
Patient	- Patients with severe native CoA - Sampling: n=120 (60 CP Stents versus 60 CP Stents, Covered) - Mean age: 23.6±10.99 (range 12 to 58) years - Sex: 79 M; 41 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Contribution	
S&P	x
SOA	

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Procedural success - Reduction in systolic blood pressure gradient - Reduction in mean diameter of coarctation segment - Adverse effects	**Yes 1**	No 2
Follow-up	- 31.1 ± 19.2 months	**Yes 1**	No 2
Statistical analysis	- A p-value <0.05 was considered significant.	**Yes 1**	No 2
Clinical significance	- Implanting CP Stent (Bare) and CP Stent (Covered) have very high success rates with remarkable hemodynamic effects in severe native CoA patients, with no significant complication during the procedure and hospitalization. - Patients undergoing CP Stent (Covered) implantation experienced a non-significantly lower re-coarctation rate and a higher occurrence of pseudoaneurysm formation with respect to CP Stent (Bare) stenting during follow-up. - In both groups, blood pressure was significantly reduced after intervention. - These findings indicate that CoA stenting is a safe procedure.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade	LOE (2) + Suitability (4) +	Disposition and Weighting (select)	**Accepted and Pivotal 9-12**

(Range 9-25)	Data Contribution (4) = 10		Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- Pseudoaneurysms: 0 (CP Stent, Bare) versus 2 (CP Stent, Covered) - Mortality: 1 (CP Stent, Bare) versus 0 (CP Stent, Covered)
Performance data	- Successful placement: successful in all patients - Mean systolic blood pressure gradient reduction: from 54.61 (CP Stent, Bare) and 54.42 (CP Stent, Covered) to 3.47 and 3.36 mmHg respectively; no significant difference between the two types of stents, P<0.001 - Mean diameter of coarctation segment reduction: From 3.34 (CP Stent, Bare) and 3.30 (CP Stent, Covered) to 16.07 and 15.82 mm respectively; no significant difference between the two types of stents, P<0.001 - Recurring coarctation: 4 (CP Stent, Bare) versus 0 (CP Stent, Covered), non-significant
Benefits/claims data	- Reduction in mean systolic blood pressure gradient - Reduction in diameter of coarctation segment
Strengths	- The CP Stent was hand-crimped down onto a balloon-in-balloon catheter (NuMED), which allows a precise and safe stent delivery
Weaknesses/ Potential bias	- Although the first randomized clinical trial in this respect, study was limited in some aspects. First, during follow-up, patients did not undergo 24-hour ambulatory blood pressure monitoring, which could have diagnosed the normotensive state more accurately. Second, evaluation of the blood pressure response during exercise testing could have been more valuable in defining the procedure outcome.

2. Vanagt et al. (2014)

Contribution	
S&P	x
SOA	

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Single-center retrospective study (CHD database of all CP Stent, Covered, during 2003-2012)	To evaluate possibilities and safety of CP Stent (Covered) in CHD.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Covered) - BIB	**D1**	D2	D3
Application	- CoA and RVOT pre-stenting for percutaneous revalvulation	**A1**	A2	A3

Patient	- Patients with CoA and RVOT pre-stenting for percutaneous revalvulation. For the RVOT group, CP Stent (Covered) was chosen for delivery balloon protection after rupture of the pre-dilation balloon in 7/37 patients (19%) and 30 (81%) because tear, rupture, or fracture of the conduit was expected, or further stent expansion following somatic growth was anticipated.
	- Sampling: n= 51 (CoA group), n=37 (RVOT group)
	- Mean age:
	  - CoA group: 19 (range from 8 to 69) years
	  - RVOT group: 16 (range from 6 to 43) years
	- Sex:
	  - CoA group: 38M; 13F
	  - RVOT group: 26M; 11F
		P1	P2	P3

Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Increase in diameter at coarctation (CoA group) - Decrease in peak to peak gradient (CoA group) - Number of procedures for pre-stenting and pulmonary valve delivery (RVOT Group) - increase in graft diameter (RVOT Group) - Adverse effects	**Yes 1**	No 2
Follow-up	- Not specified.	Yes 1	**No 2**
Statistical analysis	- Two-sided p<0.05 was considered significant.	**Yes 1**	No 2
Clinical significance	- CP Stents (Covered) can safely be applied in CHD patients. The covering allows adequate sealing of existing or expected tears, thereby increasing the safety margin with more complete dilation.	**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 (4) + Suitability (4) + Data Contribution (5) = 13	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- CoA Group:
	  - No acute bleeding, aneurysm formation or life-threatening complications.
	  - Mild procedure related-complications included groin hematoma (n = 3), transient nodal rhythm (n = 1, no wire present in left ventricle), and transient atrioventricular block with nodal escape rhythm (n = 1, while wire was present in left ventricle).
	  - During follow-up: no stent fractures, nor stent recompression occurred, and none of the patients had limb ischemia or signs of vessel occlusion at the puncture site.
	- RVOT group:
	  - No procedure-related complications and no extravasation.
	  - No embolization nor fracture of CP Stent (Covered) found on annual chest X-ray follow-up.

Performance data	- Diameter at coarctation (CoA group):
	  - Increased from 6 (0-15) to 14 (7-20) mm, P<0.001.
	- Peak to peak gradient (CoA group):
	  - Reduced from 23 (0-86) to 2 (0-25) mm Hg, P<0.001.
	- Number of procedures for pre-stenting and pulmonary valve delivery (RVOT Group):
	  - 22/37 single procedure and 15/37 in a second procedure.
	- Graft diameter (RVOT Group)
	  - Increased from graft stenosis diameter of 13 (5-22) mm to 22 (16-26) mm at pre-revalvulation, P<0.001.

Benefits/claims data	- Increase in luminal diameter in CoA patients.
Strengths	- CP Stent (Covered) frame is made from 90% platinum and 10% iridium 0.013” wire, welded in a zig pattern with

	additional gold soldering. The strut thickness is slightly larger than most other stents, but makes the stent edges relatively atraumatic. - CP Stent (Covered) was hand-crimped on a balloon-in-balloon (BIB, Numed). Hand-inflation of the balloon was performed with a 10 ml syringe on the inner balloon and 20 ml syringe on the outer balloon, automatically limiting inflation pressures to 4–6 atmospheres.
Weaknesses/ Potential bias	- In this retrospective study, there are no control groups with bare stents, the lack of which is inherently related to the fact that some of these procedures would have been impossible, or significantly less safe, if bare stents were used.

Safety & Performance (for safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective and observational study.	To investigate reduction in aortic wall rupture and dissection, as well as aneurysms by implanting covered stents.	1	2	3	**4**	5

3. Alcibar et al. (2013)

Contribution	
S&P	X (safety only)
SOA	

Suitability	Relevant Data	Grading		
Device	- CP Stent (Covered) - BIB	**D1**	D2	D3
Application	- CoA and re-coarctation	**A1**	A2	A3
Patient	- Patients treated for CoA and re-coarctation (2 adolescents and 15 adults treated between November 2005 and January 2012). - Sampling: n=17 (11 native CoA and 6 re-coarctation) - Mean age: 35 (range 14-65) years - Sex: 4 M; 13 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Reduction in blood pressure - Reduction in lumen diameter - Reduction of hypertensive medications at follow-up - Adverse effects	**Yes 1**	No 2
Follow-up	- 2.5 years	**Yes 1**	No 2
Statistical analysis	- Significance was considered as P<0.05.	**Yes 1**	No 2
Clinical significance	- CP Stents (Covered) are effective in treating CoA and re-coarctation in adolescents and adults, are the treatment of choice in patients with complex anatomy, and must be available in the operating room as a rescue device when implanting a conventional stent.	**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 (4) + Suitability (4) + Data Contribution (4) = 12	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21

			Excluded, 22-25

Relevant S&P Results

Safety data	- One death: patient died two days post-op due to massive hematemesis as a result of the combination of an extreme increase in blood pressure and an existing aneurysm. - No local complications occurred, except one hematoma that resolved spontaneously. - No patient had any complication at the iliac-femoral level that required stenting.
Benefits/claims data	- Increased in luminal diameter - Decreased in antihypertensive medication use
Strengths	- Having observed the case of aortic rupture, and with the aim of reducing these complications in patients who have had CoA and re-coarctation since their youth, the authors decided to electively implant a NuMED (Hopkinton, New York, United States) ePTFE CP Stent (Covered). This stent is mounted on a balloon catheter and protects the vascular wall when expanded.
Weaknesses/ Potential bias	- Retrospective and observational study with no control group of patients receiving conventional stents. Although all patients underwent clinical follow-up, this did not include an imaging study in all cases, and so authors cannot determine with certainty the incidence of potential aneurysms.

4. Chang et al. (2012)

Contribution	
S&P	x
SOA	

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Single arm interventional study.	To evaluate the use of CP Stent (Covered) as the primary modality in the treatment for native CoA.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Covered and Bare) - BIB	**D1**	D2	D3
Application	- Native CoA	**A1**	A2	A3
Patient	- Patients with native CoA without previous treatment - Sampling: n=25 - Mean age: 22.5 (range 14-46) years - Sex: 16 M; 9 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Decrease in systolic gradient - Increase in stenotic segment diameter	**Yes 1**	No 2
Follow-up	- 32 (7-72) months	**Yes 1**	No 2
Statistical analysis	- P<0.05 was set as statistically significant.	**Yes 1**	No 2
Clinical significance	- Implantation of CP Stent (Covered) as the primary modality is safe and effective in the treatment for native CoA in adolescents and adults. - Treatment modality of native CoA in adolescents and adults acquired excellent results, such as significant reduction in peak systolic gradient across CoA, successful relief of anatomic	**Yes 1**	No 2

	stenosis, and reduction of systemic hypertension. - Above all, no adverse events were encountered during the procedure or during the follow-up period of up to 72 months.		
		Data Contribution Grade (Range 4-8)	4

Overall S&P Appraisal, Disposition and Weighting

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

Relevant S&P Results

Safety data	- No acute complications were observed. - During a follow-up period of up to 72 months (median, 32 months and quartile range, 51 months), no adverse effects (e.g., dissection, aneurysm formation, stent migration, stent fracture) were encountered. - In the patient with the implantation of three CP stents, the aneurysm formation related to the bare CP stent was not encountered, the left subclavian artery crossed by the bare CP stent presented patent without thrombosis, and the left arm ischemia was not detected.
Benefits/claims data	- Reduced in peak systolic gradient. - Reduced in luminal diameter. - BIB offered precise and safe control over the stent implantation without any stent migration
Strengths	- Use of covered CP stents as the primary treatment modality may reduce the risk of significant complications related to stent implantation.
Weaknesses/ Potential bias	- Conflict of interest: not reported.

5. Erdem et al. (2011)

Safety & Performance (for safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Single arm interventional study.	To present author's institutional experience of endovascular CP Stent implantation in children and adults with native and recurrent CoA.	1	2	3	**4**	5

Contribution	
S&P	X (safety only)
SOA	

Suitability	Relevant Data	Grading		
Device	- CP Stent (16 Covered or 31 Bare) – n=47 - BIB (n=29) or single balloon catheter (n=18), Z-med (not subject device)	D1	**D2**	D3
Application	- Patients with native or recurrent CoA	**A1**	A2	A3
Patient	- Patients with native CoA (Group 1); recurrent CoA and/or aneurysm developed after either surgery or balloon angioplasty (Group 2) - Sampling: n=45 (47 CP Stents, Covered or Bare) - Median age: 11 (range: 5-33) years - Sex: 34M; 11F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3

Suitability Grade (Range 4-12)	5

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Decrease in invasive and echocardiographic gradients - Increase in lesion diameter - Adverse effects	**Yes 1**	No 2
Follow-up	- 12.1±7.1 months; median 11 month (range 2-29)	**Yes 1**	No 2
Statistical analysis	- A p value <0.05 was considered statistically significant.	**Yes 1**	No 2
Clinical significance	- Early and short- term follow-up results indicate that stent implantation is safe and very effective in reducing coarctation gradient and increasing lesion diameter both in native and recurrent CoA. - Some serious complications do occur and hypertension remains in some patients. - Aortic disruption and stent displacement are potentially catastrophic complications of stenting but implanting a second covered stent can seal the ruptured wall and parking in a safe area or replacement of displaced stent carried by half-inflated balloon could solve the problem.	**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 (4) + Suitability (5) + Data Contribution (4) = 13	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- No procedure related death.
	- Two immediate complications relating to stenting:
	  - One an acute wall rupture, successfully managed immediately in the same session with implantation of a second covered stent
	  - One stent was displaced before it was completely opened. It was carried with support of partially inflated balloon and long sheath, and repositioned into the correct place.
	- No femoral arterial complications
	- No difficulty in catheter manipulation.
	- None of the patients required intensive care following the procedure, and all were discharged home the following day except the patient with aortic rupture and after stenting with covered stent this patient was followed two days in intensive care unit.

Benefits/claims data	- Increase in luminal/lesion diameter.
Strengths	- CP stent is the one of the most commonly used stent in pediatric cardiology - This stent has excellent radial strength even at larger diameters and also has brilliant visibility on fluoroscopy.

Weaknesses/
Potential bias
	- Some limitations have to be noted about this study:
	  - Firstly, there is a need a greater number of patients have undergone stent implantation and their long-term results.
	  - Secondly, population included both children and adult.
	  - Thirdly, this was a single-center report and patients were not compared with surgery or balloon angioplasty

	alone. - Fourthly, 24-hour ambulatory blood pressure monitoring before stenting was not performed in any patients. - Finally, radiologic imaging for aneurysm was done in limited number of patients after procedure. - Conflict of interest: None declared.

6. Butera et al. (2011)

Contribution	
S&P	X (safety only)
SOA	

Safety & Performance (for safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective single arm interventional study.	To evaluate the management of aneurysms associated with CoA by covered stent deployment.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Covered) - BIB or Crystal balloon (not subject device)	D1	**D2**	D3
Application	- Patients with native CoA associated with aortic wall aneurysm	**A1**	A2	A3
Patient	- Patients with CoA associated with aortic wall aneurysm - Sampling: n=11 (3 native CoA, 3 with previous surgical repair, 3 with previous balloon angioplasty, and 2 with previous bare stent implantation) - Median age: 13 (range: 6-66) years - Sex: Not reported	P1	**P2**	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	6		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Systolic pressure gradient reduction - Increase in aortic diameter - Adverse effects	**Yes 1**	No 2
Follow-up	- Median follow-up 50 (16-61) months	**Yes 1**	No 2
Statistical analysis	- P-value less than 0.05 was considered to be statistically significant	**Yes 1**	No 2
Clinical significance	- CP Stent (Covered) are a safe and effective treatment with low risk of complication for the treatment of CoA associated with aortic wall aneurysm. - CP Stents (Covered, e-PTFE) may be considered the treatment of choice for native CoA associated with aortic wall aneurysm.	**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 (6) + Data Contribution (4) = 13	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- No early complications observed.
Benefits/claims data	- Increase in luminal diameter

	- Reduce systolic pressure gradient - Reduce/prevent aortic wall injury (patients associated with aortic wall aneurysm)
Strengths	- Covered CP stents are manufactured with an alloy of 90% platinum and 10% iridium. Theoretically, this combination is more malleable and with good radial strength, which is enhanced by being designed in a ''zig'' pattern. The CP stent has rounded edges, decreasing the risk of balloon rupture or injury to the vessel wall and, in addition, the platinum component makes it more radio-opaque. Furthermore, the e-PTFE protects the stenotic and diseased segment.
Weaknesses/ Potential bias	- No conflict of interest reported.

7. Moltzer et al. (2010)

Contribution	
S&P	x
SOA	

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective observational study.	To evaluate the intermediate-term outcome of stent implantation for CoA in adults.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Bare and Covered) - BIB	**D1**	D2	D3
Application	- Native CoA and re-coarctation	**A1**	A2	A3
Patient	- Patients with native CoA and re-coarctation - Sampling: n=24 - Mean age: 36 (18-60) years - Sex: 12 M; 12 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Decrease in systolic gradient - Increase in minimum aortic diameter - Adverse effects	**Yes 1**	No 2
Follow-up	- 24 hours post intervention and 33 (8-77) months	**Yes 1**	No 2
Statistical analysis	- All statistical tests were two-sided and a p-value <0.05 was considered statistically significant	**Yes 1**	No 2
Clinical significance	- Stenting in adults results in significant blood pressure gradient decrease and increase in vessel diameter. However, serious complications do occur and hypertension remains in the majority of patients.	**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** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- One death due to aorta ruptured. - Two groin hematoma post-op.
Performance data	- Systolic gradient: Decreased to < 10 mmHg in 21 patients, P<0.001 - Minimum aortic diameter: Increased from median 10 (2-17) to 16 (10-28) mm, P<0.001
Benefits/claims data	- Reduced in systolic gradient - Increased in minimum aortic diameter
Strengths	- N/A
Weaknesses/ Potential bias	- Only a small number of patients have undergone stent implantation since the authors started this procedure in 2003. This was a single-center report and patients were not compared with surgery or balloon angioplasty alone. Finally, 24-hour blood pressure monitoring before stenting was not performed in the majority of the patients. Post-stent 24-hour ambulatory blood pressure monitoring is therefore difficult to translate in terms of blood pressure reduction.

8. Kische et al. (2010)

Contribution	
S&P	x
SOA	

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Technical review.	To report the technique of interventional repair in adult CoA.	1	2	3	4	**5**

Suitability	Relevant Data	Grading		
Device	- BIB	**D1**	D2	D3
Application	- CoA	**A1**	A2	A3
Patient	- Patients with CoA. - Sampling: Not reported. - Mean age: adult CoA patients, specific age not reported. - Sex: Not reported.	P1	**P2**	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	5		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Stent placement (delivery of large-diameter stents). - Safety.	**Yes 1**	No 2
Follow-up	- Not applicable.	Yes 1	**No 2**
Statistical analysis	- Not applicable.	Yes 1	**No 2**
Clinical significance	- Not applicable.	Yes 1	**No 2**
	Data Contribution Grade (Range 4-8)	7	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (5) + Suitability (5) + Data Contribution (7) = 17	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- BIB catheters require a larger arterial sheath for introduction, however, which needs to be upsized by 1F if a hand-crimped balloon is mounted on the balloon. Thus, although BIB catheters prevent stent flare and offer more precise control over stent placement, single-balloon catheters are still sometimes preferable in smaller patients to reduce the risk of femoral artery injury at the access site. - The use of a BIB catheter will generally prevent technical complications such as balloon rupture and stent migration.
Performance data	- One of the most important technical refinements for delivery of large-diameter stents has been the NuMED Balloon-in-Balloon (BIB) catheter. - These catheters have an inner balloon and a longer outer balloon that is double the diameter of the inner balloon and are available in outer-balloon sizes of up to 24 mm. - The inner balloon of the BIB catheter is inflated, and an angiogram can be performed through the sheath or through an anterograde catheter in the proximal aorta to confirm position of the stent. With the stent in the desired position, the outer balloon is inflated to fix the stent in the lesion. Once the stent is expanded, both the outer and inner balloons are deflated as rapidly as possible.
Benefits/claims data	- BIB catheters offer more precise control over stent placement
Strengths	- BIB offers the important advantage of opening the stent more uniformly along its length, thereby eliminating the risk of unintended stent protrusion that has been documented by the use of single balloons.
Weaknesses/ Potential bias	- No conflict of interest reported.

9. Agnoletti et al. (2009)

Contribution	
S&P	X (safety only)
SOA	

Safety & Performance (for safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Two arms comparative interventional study.	To compare the CP Stent and the Palmaz stent for treatment of native and postoperative lesions of CHD patients.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Bare & Covered), crimped on BIB - Palmaz stent, crimped on BIB and simple balloons	**D1**	D2	D3
Application	- Patients with CHD (including CoA/re-coarctation, RVOT)	A1	**A2**	A3

Patient	- Patients with CHD (including CoA/re-coarctation, RVOT and other CHD conditions, such as transposition of the great arteries, ventricular septal defect, single ventricle, etc.)
	- Sampling: n= 153
	  - 89 CP Stents (crimped on 77 BIB & 12 other balloons)
	  - 64 Palmaz Stents (crimped on 23 BIB and 41 simple balloons)
	- Mean age:
	  - CP Stents: 15.4 (SD: 9.2) years
		P1	**P2**	P3

	- Palmaz Stents: 11.6 (SD: 8.1) years - Sex: Not reported			
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	6		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Blood pressure gradient reduction - Vessel diameter reduction - Adverse effects	**Yes 1**	No 2
Follow-up	- Not reported.	Yes 1	**No 2**
Statistical analysis	- A P-value less than 0.05 was considered statistically significant for stent group comparison.	**Yes 1**	No 2
Clinical significance	- The use of the CP Stents to treat stenotic lesions of CHD is effective and relatively safe. The overall efficacy of CP Stents for the treatment of stenotic lesions is superior to that of the Palmaz stent. - CP Stents' overall safety is higher than that of the Palmaz stent; but Palmaz stents have a lower profile when inserted.	**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 (6) + Data Contribution (5) = 14	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- Stent-related complications:
	  - CP Stents (n=89 patients): 4 mild, 1 moderate, 1 severe.
	  - Palmaz (n=64 patients): 10 mild, 2 moderate, 2 severe.
	- Stent migration:
	  - CP Stents: 7.
	  - Palmaz: 4.
	- Non stent related complications:
	  - CP Stents: 1 mild, 2 moderate.
	  - Palmaz: 1 mild, 2 moderate, 5 severe.
	- Urgent surgery:
	  - CP Stents: 2 due to homograft rupture and stent migration.
	  - Palmaz: 1 for aortic dissection.
	- Balloon related complications: Balloon burst
	  - CP Stents: 0.
	  - Palmaz: 7 (3 in BIB, 3 with simple balloons, and 1 on pre-mounted stent).

Benefits/claims data	- Decreased in blood pressure gradient. - Increased in vessel diameter.
Strengths	- Efficacy of CP Stents was similar to that of Palmaz stent for stenting of the right ventricular outflow, and higher than

	that of Palmaz for the stenting of aorta, but the difference was not statistically.
Weaknesses/ Potential bias	- Study presented retrospective results obtained in 153 consecutive patients. - CP stents were used for patients weighing more than 15 kg; and thus two populations were different concerning age, weight, indication for stenting; however, none of these differences were related to occurrence of complications. - Subgroup analyses were not performed.

10. Peters et al. (2009)

Contribution	
S&P	x
SOA	

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Technical review.	To discuss the available stents and balloons in stenting in regard to their advantages and disadvantages for common applications in CHD.	1	2	3	4	**5**

Suitability	Relevant Data	Grading		
Device	- CP Stent and BIB	**D1**	D2	D3
Application	- Stenting in CoA	**A1**	A2	A3
Patient	- Patients with CoA - Sampling: Not reported. - Mean age: Not reported. - Sex: Not reported.	P1	P2	**P3**
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	6		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Design advantages or disadvantages (technical description) - Safety	**Yes 1**	No 2
Follow-up	- Not applicable.	Yes 1	**No 2**
Statistical analysis	- Not applicable.	Yes 1	**No 2**
Clinical significance	- Large-diameter single-balloon catheters tend to expand first at their ends and thereby evert the stent ends such that they protrude radially from the stent center. Deploying a stent in this orientation can cause injury to the vessel wall and may be a risk factor for development of aneurysm or dissection. One of the most important developments in equipment for the delivery of large-diameter stents has been the Balloon-in-Balloon (BIB; NuMED) catheter, the first balloon specifically designed for stent delivery in the CHD population.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	6	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (5) + Suitability (6) + Data Contribution (6) = 17	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- BIB:

	- Stent foreshortening can be much higher if stents are expanded with a single large balloon directly to 15 or 18 mm. The reason for this is that the ends of the stent are compressed toward each other due to the typical "dumb-belling" of the balloon at the end of inflation while the center of the stent is expanding to its full diameter. This results in significant shrinkage of the overall length of the stent. Thus, if final length is critical, the delivery requires sequential balloon dilatation with increasing diameters or, even better, the use of a Balloon-in-Balloon (BIB™ catheter; NuMED). - Balloon rupture with inadequate stent expansion may be prevented by avoiding kinking of the balloon/stent assembly by the use of newer stents with softer ends and by the use of BIB systems.
Performance data	- BIB: - These catheters have an inner balloon and a longer outer balloon that is double the diameter of the inner balloon. The BIB catheters offer the important advantage of opening the stent more uniformly along its length but require a larger arterial sheath for introduction. - While BIB catheters prevent stent flare and offer more precise control over stent placement, single-balloon catheters are still sometimes preferable in smaller patients to reduce risk of injury to the femoral artery at the access site.
Benefits/claims data	- BIB offers more precise control over stent placement
Strengths	- CP Stent: - These stents have excellent visibility on fluoroscopy and maintain excellent radial strength even at larger diameters.
Weaknesses/ Potential bias	- No conflict of interest reported.

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Single arm interventional study.	To evaluate the use of Covered CP Stents in treatment of CoA.	1	2	3	**4**	5

11. Tzifa et al. (2006)

Contribution	
S&P	x
SOA	

Suitability	Relevant Data	Grading		
Device	- CP Stent (Covered) - BIB	**D1**	D2	D3
Application	- CoA	**A1**	A2	A3
Patient	- Patients with CoA (fully grown patients) - Sampling: n=30 - Mean age: 28±17.5 (range 8 to 65) years - Sex: not reported	**P1**	P2	P3
Report	- High quality.	R1	**R2**	R3
	Suitability Grade (Range 4-12)	5		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Reduction in blood pressure gradient - Reduction in coarctation diameter	**Yes 1**	No 2

Follow-up	- 11 months	**Yes 1**	No 2
Statistical analysis	- Statistical significance was defined as P<0.05.	**Yes 1**	No 2
Clinical significance	- CP Stents (Covered) may be used as the therapy of choice in patients with complications after CoA repairs, whereas they provide a safe alternative to conventional stenting in patients with severe and complex CoA lesions or advanced age.	**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 (4) + Suitability (5) + Data Contribution (4) = 13	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- Two stent fractures in the "old" design of the stent, no fractures in the "new" stent design Note: Since May 2002, the CP Stents (Covered) have been produced with reinforced golden soldering joints as the "new" stent design
Performance data	- Blood pressure gradient: From 36 + 20 mmHg to 4 + 4 mmHg, P<0.0001 - Diameter at coarctation: From 6.4 +3.8 mm to 17.1 + 3.1 mm, P<0.0001
Benefits/claims data	- Reduction in blood pressure gradient - Reduction in coarctation diameter - BIB allows readjustment of position after inflation of the inner balloon.
Strengths	- Covered stents were chosen: 1) as a rescue treatment in patients with CoA aneurysms or previous stent-related complications; and 2) in patients at risk of complications because of complex CoA anatomy or advanced age (defined as >65 years) - Covered CP stents are made of a framework of platinum iridium wire welded in a zig pattern. The addition of a gold soldering to each weld spot fills any voids caused by the welding and transfers the stresses to a larger area of the stent. The gold also serves to encapsulate the welded area, once again adding to the total strength of the weld. The stent is then fitted with a covering of ePTFE to achieve a solid tubular structure that retains fluid. The ePTFE covering is initially approximately 7 mm in diameter and will stretch over the range of diameters of expansion (usually from 12 to 24 mm diameter), and will always be taut over the stent when expanded. When the covering is mounted, it is folded over the crimped stent and expands uniformly when the balloon is inflated. - The BIB allows for readjustment of position after inflation of the inner balloon.
Weaknesses/ Potential bias	- Not reported.

12. Cheatham et al. (2001a)

Contribution	
S&P	x
SOA	

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Comparative, two single arm interventional study (CP Stent/BIB versus Palmaz stent/single balloon).	To demonstrate effectiveness of CP Stent, in combination with BIB, for treating aortic coarctation in comparison with the Palmaz stent.	1	2	**3**	4	5

Suitability	Relevant Data	Grading

Device	- CP Stent and BIB. Note: D1 for subject device (CP Stent and BIB). - Palmaz stent and single balloon.	**D1**	D2	D3
Application	- CoA and re-coarctation	**A1**	A2	A3

Patient	- Patients with CoA and re-coarctation
	- Sampling: n=46 (21 Palmaz Stent, 25 CP Stent)
	- Mean age:
	  - Palmaz Stent: 12 (range: 4.5 to 16) years old
	  - CP Stent: 24.1 (range: 10.5 to 60) years old
	- Sex: M;F
	  - Palmaz Stent: 15M; 6F
	  - CP Stent: 15M; 10F
		P1	P2	P3

Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Decrease in peak systolic gradient - Safety	**Yes 1**	No 2
Follow-up	- Limited follow-up because of the relatively short-elapsed time and multiple, out of country institutions involved	Yes 1	**No 2**
Statistical analysis	- Statistically significant achieved when P<0.05.	**Yes 1**	No 2
Clinical significance	- Both the Palmaz and the NuMED CP Stents offer an effective, nonsurgical treatment for both native and recurrent CoA, regardless of site or severity of obstruction. - Native CoA tends to be more severe, with tighter stenosis and higher gradients compared to recurrent coarctation. Aneurysm development may occur in these patients after Palmaz stent implantation. Therefore, graduated serial stent dilation and/or covered stent implantation should be considered in high-risk patients.	**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** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- Intraoperative complications:
	  - Two cases of stent embolization in Palmaz Stent group versus one case of left hemothorax in CP Stent (Covered) group
	- Late complications:
	  - Aortic aneurysm in Palmaz Stent Group (n=3)
	  - 9/21 (43%) continued to require antihypertensive medication
	- Adverse effects:
	  - Flaring of the Palmaz Stent as a result of the single balloon that first expands at the ends, not from the middle.

	- Premature BIB rupture reported using Palmaz stent, believed to be due to inadvertent puncture of outer balloon by the sharp-edged Palmaz stent during hand crimping.

Performance data	- Peak systolic gradient
	  - Palmaz Stent
	  - Native coarctation: 46.8 to 1.5 mmHg (P<0.05)
	  - Recurrent coarctation: 35 to 1.2 mmHg (P<0.05)
	  - CP Stent
	  - Native coarctation of the aorta: 53 mmHg to 2 mmHg (P<0.001)
	  - Recurrent coarctation: 41 mmHg to 1.2 mmHg (P<0.001)

Benefits/claims data	- BIB significantly improves stent delivery and final deployment of any stent. The inner balloon is always inflated first, partially expanding the stent without flaring and allows repositioning of the stent before final deployment, when the outer balloon is inflated.
Strengths	- The zig design of the NuMED CP Stent improved strength and flexibility while minimizing stent shortening and vessel/balloon trauma. - The tempered platinum/iridium wire and zig design of the NuMED CP Stent improved strength, flexibility, and radiopacity while minimizing stent shortening and vessel/balloon trauma. - The NuMED CP stent offers a wider range of expanded diameters and lengths than the Palmaz stent, which is necessary to ensure an adequate adult vessel diameter in growing children and young adults and reduces the need for multiple stents in long segment obstruction. - The BIB catheter is selected so that the inner balloon is always shorter than the stent while the outer balloon is slightly longer. The BIB delivery catheter significantly improves stent delivery and final deployment of any stent while minimizing stent migration and flaring. This in turn decreases the incidence of ventricular tachycardia in interventional pediatric cardiologists.
Weaknesses/ Potential bias	N/A

13. Cheatham et al. (2001b)

Contribution	
S&P	x
SOA	

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Report results collected 45 patients underwent CP stent implantation from August 1998 through August 1999.	To report the CP Stent and BIB development, including results from clinical study conducted from August 1998-August 1999.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	- CP Stent - BIB	**D1**	D2	D3
Application	- CoA and other conditions.	A1	**A2**	A3

Patient	- Patients with CoA and other conditions:
	  - CoA (n=25; 17 native CoA and 8 Re-coarctation),
	  - Right pulmonary artery (RPA) stenosis (n=5),
	  - Isolated left pulmonary artery (LPA) stenosis (n=2),
	  - Bilateral branch stenosis (n=6),
		P1	**P2**	P3

	- Recurrent right ventricle to pulmonary artery (RV-PA) homograft stenosis (n=4), - Blalock-Taussig shunt stenosis (n=1), - Multiple sites of left-to-right shunt inside a lateral tunnel Fontan repair (n=1), - Obstructed superior vena cava (SVC) baffle limb after Mustard repair for transposition of the great arteries (n=1) - Sampling: n=45 patients (CP Stent, n=57) - Mean age: 19 (range 1.8-60) years - Sex: 25 M; 20 F			
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	6		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Peak systolic gradient reduction - Procedural complications	**Yes 1**	No 2
Follow-up	- Minimal follow-up due to short study period and large number of institutions involved	Yes 1	**No 2**
Statistical analysis	- P-values reported.	**Yes 1**	No 2
Clinical significance	- NuMED CP stent (placed by BIB stent placement catheter) offers an effective, non-surgical treatment for a wide variety of vascular obstructions associated with congenital heart disease. - The NuMED BIB catheter is an innovative concept that has significantly improved operator control during intravascular stent delivery. It minimizes stent flaring, migration, and shortening, while effectively eliminating catheter movement during deployment. It also allows the partially expanded stent to be repositioned before final expansion, which is a significant benefit to the interventionalist to maintain control and precisely position the stent. We currently use the BIB catheter for all stents. Although more data and longer follow-up are required, the NuMED CP stent and BIB delivery catheter offer great promise in the future treatment of children and adults with congenital heart disease.	**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 (4) + Suitability (6) + Data Contribution (5) = 15	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- Two procedural complications, both considered avoidable and there were no further sequelae - One with severe native CoA requiring a covered stent, there was transient left hemothorax. - One traumatic stent fracture during attempted entry of the long, covered CP stent in the Fontan patient using a modified 'front-load' technique. The stent was inadvertently pushed out of the delivery sheath in the groin with the first row of 10 zigs being traumatized and fractured. - Follow-up: - Stent fatigue fracture and fragment embolization in two patients - Two patients with severe native CoA and stenoses <2 mm had immediate residual gradients of 20 and 25 mmHg

	secondary to limited stent expansion to avoid excessive vessel trauma and possible aneurysm formation with planned stent re-dilation later. - One patient had a 30 mmHg residual aortic gradient 10 months post implant secondary to an intimal flap that was successfully treated with a second CP stent
Performance data	- Peak systolic gradient was reduced in 17 patients with native CoA from 56.2 mmHg to 4.6 mmHg, while in the 8 patients with recurrent aortic obstruction, the gradient was reduced from 41.8 mmHg to 0.9 mmHg, both statistically significant at P<0.001 using paired t-tests - Isolated RPA and LPA stenoses were also effectively treated with peak systolic gradient reductions from 54.6 to 5 mmHg and 52.5 to 6.5 mmHg respectively P<0.001 - In the six children with combined RPA and LPA stenoses, 'kissing stents' reduced the peak systolic gradients from 43.5 and 45 mmHg to 6.8 and 6.0 mmHg, respectively P<0.01. - The four patients with recurrent RV-PA homograft obstruction also had effective relief of their - gradients from 55 to 14.3 mmHg P<0.01. - After stenting the stenotic right Blalock-Taussig shunt in the young man with complex cyanotic congenital heart disease, O2 saturations increased from 78 to 88%. The implantation of the long covered CP stent was also clinically effective in treating the young man with multiple leaks in the lateral tunnel by improving resting O2 saturations from 80 to 96%. - Finally, the 9 mmHg mean gradient across the obstructed SVC baffle after Mustard's repair was completely eliminated.
Benefits/claims data	- The BIB effectively eliminating catheter movement during deployment. It also allows the partially expanded stent to be repositioned before final expansion, which is a significant benefit to the interventionalist to maintain control and precisely position the stent.
Strengths	- CP Stent versus Palmaz Stent - The advantages of the NuMED CP stent compared to the Palmaz stent are as follows: (1) superior radiopacity secondary to the platinum composition; (2) superior 'compression' or radial hoop strength secondary to the tempered wire and zig design; (3) less rigidity because of the malleability of the tempered platinum-iridium wire; (4) less potential trauma to the delivery balloon and target vessel secondary to the rounded edges of the zig pattern; (5) wider range of expanded diameters from 8 to 24 mm (10 zig can be expanded to 30 mm) while maintaining ≤20% stent shortening; (6) superior selection of stent lengths to meet the demands of a wide range of target lesions; and (7) maximal stent shortening of <20% will minimize chances of missing the target site or need of multiple serial stents. - BIB versus single balloon catheter: - Careful observation of how a single balloon catheter may actually create significant problems during any stent deployment, but is exaggerated in the aorta. Conventionally, the balloon is chosen to be longer than the stent to avoid stent migration during delivery or deployment. Unfortunately, the proximal and distal ends of the balloon catheter expand first and well before the stent. This leads to flaring of the edges of the stent, which in the Palmaz stent's case is dangerous because of the sharp leading and trailing edges approaching the vessel wall and balloon leading to trauma of both. In addition, the partially expanded balloon acts as a floatation catheter, allowing catheter and stent movement prematurely during deployment. Finally, there is no ability to reposition the stent during deployment. - In November 1997, the NuMED Balloon In Balloon (BIB) catheter was designed with an inner Tyshak balloon and an outer Z-Med balloon. The inner balloon is very low profiled and expands to half the outer balloon diameter,

		while the length is 1 cm shorter than the outer balloon. The inner balloon is always inflated first using a twisting action of the locked endoflator that expands the stent to 0.5 of the target vessel diameter without flaring of ends of the stent, since the balloon is shorter than the stent. Because the stent is still in contact with the unexpanded outer balloon material, the entire stent-balloon delivery catheter system can be repositioned before final deployment by expanding the outer balloon.
	Weaknesses/ Potential bias	A Tower, DJ Villnave and R Normile (NuMED) provided technical support for this publication.

14. Meadows et al. (2015) Contribution: S&P x; SOA	**Safety & Performance** This publication presents the results from the COAST trial for CP Stent (Bare and Covered) to treat native and recurrent CoA in selected children, adolescents and adult (NCT00552812). Please refer information presented in **Table G-1** for safety and performance of the subject devices, Study no. 1.

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 BIB Stent Placement catheter has been carried out and documented in the clinical evaluation report. Based on the results of the clinical evaluation report, it is considered that:

a) 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.
b) 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.
c) The information materials supplied by NuMED, and the risk reduction measures are adequate taking into account the intended purpose of the device.
d) Usability aspects have been adequately considered and the BIB, including the IFUs, is suitable for the intended users.
e) The claims foreseen in the information materials provided with the CER are adequate taking into account the intended purpose of the device.
f) 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 BIB Stent Placement catheter are acceptable when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art; 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 performance achieved by the device.

Ongoing planned post-market clinical follow-up:

The BIB Stent Placement Catheter has been commercialized since December 2003 in the EU. Since then, the device is likely to have been used in a variety of patients and populations. A PMCF Study is not warranted at this time due to the fact that long-term safety and clinical performance has been established via device use and ample clinical experience. Continued post-market surveillance activities will provide sufficient data to adequately address clinical risks, and detect emerging risks on the basis of evidence.

The addition of the 26mm, 28mm, and 30mm size in 2014 warranted a PMCF Study just for those sizes. The study investigated procedural and device complications and compared that with currently available data from the use of the smaller BIB Stent Placement Catheter sizes. Based on the findings from the PMCF study, NuMED determined the BIB Stent Placement Catheter (larger sizes) to be safe and effective when used for the approved indication. No changes were required to the risk analysis as there were no new risks identified, and no changes were required to the instructions for use based on the results of the PMCF Study.

6. Possible diagnostic or therapeutic alternatives

Alternative therapies to balloon dilatation / stenting include balloon angioplasty without a stent and surgical intervention.

7. Suggested profile and training for users

The device is intended to be used by trained cardiology and surgical professionals undertaking stent implantation.

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. Sohrabi B, Jamshidi P, Yaghoubi A, Habibzadeh A, Hashemi-Aghdam Y, Moin A, Kazemi B, Ghaffari S, Abdolahzadeh BM, Mahmoody K, Comparison between covered and bare Cheatham-Platinum stents for endovascular treatment of patients with native post-ductal aortic coarctation: immediate and intermediate-term results. *JACC. Cardiovascular interventions* **7(4)**, 416-423 (2014).
2. Vanagt WY, Cools B, Boshoff DE, Frerich S, Heying R, Troost E, Louw J, Eyskens B, Budts W, Gewillig M, Use of covered Cheatham-Platinum stents in congenital heart disease. *International Journal of Cardiology* **175**, 102-107 (2014).
3. Alcibar J, Blanco R, Fernandez L, Arriola J, Garcia K, Pena N, Inguanzo R, Voces R, Castellanos E, Montes PM, Elective implantation of covered stents for coarctation and recoarctation in adolescents and adults. *Revista espanola de cardiologia (English ed.)* **66**, 443-449 (2013).
4. Chang ZP, Jiang SL, Xu ZY, Zhang GJ, Huang LJ, Zhao SH, Ling J, Zheng H, Jin JL, Wu WH, Hu HB, Li SG, Yu JH, Yan CW, Use of covered Cheatham-Platinum stent as the primary modality in the treatment for native coarctation of the aorta. *Chinese medical journal* **125**, 1005-1009 (2012).
5. Erdem A, Akdeniz C, Sarıtaş T, Erol N, Demir F, Karaci AR, Yalçın Y, Celebi A, Cheatham-Platinum stent for native and recurrent aortic coarctation in children and adults: immediate and early follow-up results. *Anadolu Kardiyol Derg.* **Aug;11(5)**, 441-449 (2011).
6. Butera G, Heles M, MacDonald ST, Carminati M, Aortic coarctation complicated by wall aneurysm: the role of covered stents. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions* **78**, 926-932 (2011).
7. Moltzer E, Roos-Hesselink JW, Yap SC, Cuypers JA, Bogers AJ, de Jaegere PP, Witsenburg M, Endovascular stenting for aortic (re)coarctation in adults. *Netherlands heart journal : monthly journal of the Netherlands Society of Cardiology and the Netherlands Heart Foundation* **18**, 430-436 (2010).
8. Kische S, Schneider H, Akin I, Ortak J, Rehders TC, Chatterjee T, Nienaber CA, Ince H. Technique of interventional repair in adult aortic coarctation. *J Vasc Surg* **Jun;51(6)**,1550-1559 (2010).
9. Agnoletti G, Marini D, Ou P, Vandrell MC, Boudjemline Y, Bonnet D, Cheatham platinum (CP) and Palmaz stents for cardiac and vascular lesions treatment in patients with congenital heart disease. *EuroIntervention* **4**, 620-625 (2009).
10. Peters B, Ewert P, Berger F, The role of stents in the treatment of congenital heart disease: Current status and future perspectives. *Ann Pediatr Cardiol* **Jan;2(1)**, 3-23 (2009).
11. Tzifa A, Ewert P, Brzezinska-Rajszys G, Peters B, Zubrzycka M, Rosenthal E, Berger F, Qureshi SA, Covered Cheatham-platinum stents for aortic coarctation: early and intermediate-term results. *J Am Coll Cardiol* **47**, 1457-1463 (2006).
12. Cheatham JP, Stenting of coarctation of the aorta. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions* **54**, 112-125 (2001a).

13. Cheatham JP, Improved stents for pediatric applications. *Progress in Pediatric Cardiology*, **14**, 95-115 (2001b).
14. Meadows J, Minahan M, McElhinney DB, McEnaney K, Ringel R, Intermediate Outcomes in the Prospective, Multicenter Coarctation of the Aorta Stent Trial (COAST). *Circulation* **131**, 1656-1664 (2015).

10. Revision History

SSCP revision number	Date Issued	Change Description	Revision validated by Notified Body
00	21 June 2022	Initial implementation	☐ Yes Validation Language: English ☒ No
01	07 July 2023	Updated sections 5, 8, and 9 for CER Update.	☐ Yes Validation Language: English ☒ No