pfmmedical

Quality and Experience

Nit-Occlud® PDA

en Instructions for Use
For USA only!

www.pfmmedical.com

GA034/Rev02_130904

Explanation of the symbols on label and packaging

REF	Reference number
LOT	Lot number
SN	Serial number
	Read Instructions for Use carefully
	Protect from direct sunlight
	Store in a dry place
	Expiry Date
	For single use only
	Do not resterilise
STERILE EO	Sterilized by Ethylene Oxide
	Do not use if packaging is damaged
	“MR conditional” = safe use of MR diagnostics under certain conditions

	Manufacturer
	Does not contain rubber latex components
	Diethylhexylphthalate (DEHP) free
℞ only	Caution: Federal law (USA) restricts this device to sale by or on the order of a physician

Instructions for Use
Nit-Occlud® PDA

Product description

Nit-Occlud® PDA is a system for transcatheter occlusion of Patent Ductus Arteriosus (PDA) with spiral coils. The system consists of the following parts:

- **Nit-Occlud® PDA**

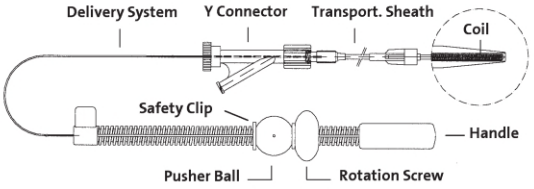


Figure 1: Nit-Occlud® PDA

The spiral coil is mounted in a straightened fashion on a flexible delivery system including a disposable handle to which it is connected by means of a patented detachment mechanism.
Nit-Occlud® PDA coils are available as Flexible and Medium type.
The flexible and medium types are pre-loaded into the transportation sheath. For insertion the transportation sheath must be connected to the implantation catheter.

The Nit-Occlud® PDA coil has a cone in cone configuration which results from the fact that the proximal windings of the coil are wound in the reverse direction (see Figure 2).

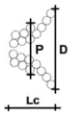


Figure 2:
Nit-Occlud® PDA spiral coils
(D=Distal diameter,
P=Proximal diameter,
Lc=Length configurated).

- **Implantation catheter**

The implantation catheter is equipped with a marker ring at its distal tip for better orientation during fluoroscopy.

Indication for Use

The Nit-Occlud® PDA coil is a permanently implanted prothesis indicated for percutaneous, transcatheter closure of small to moderate size patent ductus arteriosus with a minimum angiographic diameter less than 4 mm.

Contraindications

Medical conditions that exclude implantation of a Nit-Occlud® PDA coil include:

- Endocarditis, endarteritis or active infection at the time of the implantation
- Patients with a body weight < 5 kg
- Pulmonary hypertension (calculated PVR greater than 5 Wood Units)
- Thrombus in a blood vessel through which access to the PDA must be obtained
- Thrombus in the vicinity of the implantation site.

General Information and Warnings

These instructions for use and the information on the packaging should be read carefully before each use. The PDA coil system should be used only by physicians trained in interventional occlusion techniques.

WARNINGS

- **Do not use the product if the packaging has been opened, or is damaged, if you are not sure that it is sterile, or if the expiry date has passed.**
- **Each product is packed separately, and is delivered in an EO-sterilised and non-pyrogenic condition. It is intended for single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization of single-use devices may result in degraded performance or a loss of functionality. Reuse of single-use devices may result in exposure to pathogens such as viruses, bacteria, fungi, or prions.**
- **The product must be stored in dry conditions. Do not expose the packaged products to direct sunlight.**
- **Retrieval devices should be available during implant procedures for interventional retrieval of the coil if required.**
- **Care must be taken not to damage the coil or to dislodge it from the delivery system while unpacking or inserting it into the implantation catheter.**
- **Since the delivery system has ferromagnetic properties, implantation must not be carried out in an MR environment.**
- **The coil should not be removed from the delivery system. It should not be used with another delivery system since this may alter characteristics of configuration and detachability.**
- **A detached coil should not be remounted on the core wire of the delivery system.**
- **The configured coil should not be pulled through heart valves or ventricular chambers.**
- **The implantation catether is not suitable for application of contrast medium. It must not be connected to high pressure injectors.**
- **The Nit-Occlud® PDA coil consists of a nickel-titanium alloy, which is generally considered safe. In non-clinical testing, nickel has been shown to be released from the device in very small amounts. Patients who are allergic to nickel may have an allergic reaction to this device, especially those with a history of metal allergies. Certain allergic reactions can be serious; patients should be instructed to seek medical assistance immediately if they suspect they are experiencing an allergic reaction. Symptoms may include difficulty in breathing or swelling of the face or throat. While data are currently limited, it is possible that some patients may develop an allergy to nickel if this device is implanted.**
- **This product contains chemicals known to the State of California to cause cancer, birth defects, or reproductive harm.**

- **NOTE: Federal Law (USA) restricts this device to use by a physician.**

Product Identification

Each product label has peel-off labels, to allow the product to be identified precisely. These can be used for the patient file and the patient ID card.

MRI Compatibility

The Nit-Occlud® PDA coil was determined to be MR-conditional according to the terminology specified in the American Society for Testing and Materials (ASTM) International, Designation: F2503-05. Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment. ASTM International, 100 Barr Harbor Drive, PO Box C700, West Conshohocken, Pennsylvania, 2005.

Non-clinical testing demonstrated that the Nit-Occlud® PDA coil is MR conditional. A patient with this device can be scanned safely immediately after placement under the following conditions:

- Static magnetic field of 3 Tesla or less
- Maximum spatial gradient magnetic field of 720 Gauss/cm or less
- The maximum whole-body averaged specific absorption rate (SAR) shall be limited to 2.0 W/kg (normal operating mode only) for 15 minutes of scanning.

MRI-Related Heating

- In non-clinical testing, the Nit-Occlud® PDA coil produced the following temperature rise during MRI performed for 15-min in the 3-Tesla (3-Tesla/128-MHz, Excite, HDx, Software 14X.M5, General Electric Healthcare, Milwaukee, WI) MR system: Highest temperature change +1.6°C.
  Therefore, the MRI-related heating experiments for the Nit-Occlud® PDA coil at 3-Tesla using a transmit/receive RF body coil at an MR system reported whole body averaged SAR of 2.9 -W/kg (i.e., associated with a calorimetry measured whole body averaged value of 2.7-W/kg) indicated that the greatest amount of heating that occurred in association with these specific conditions was equal to or less than +1.6°C.

Artifact Information

- MR image quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the Nit-Occlud® PDA coil. Therefore, optimization of MR imaging parameters to compensate for the presence of this device may be necessary.

Pulse Sequence	T1-SE	T1-SE	GRE	GRE
Signal Void Size	369 mm^2	118 mm^2	647 mm^2	739 mm^2
Plane Orientation	Parallel	Perpendicular	Parallel	Perpendicular

Table 1: Image artifacts, results of non-clinical testing

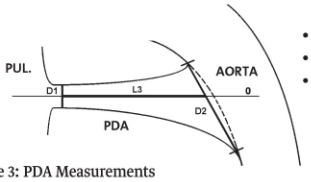
Potential Adverse Events

- Air embolism
- Allergic reaction to drug/contrast
- Apnea
- Arrhythmia requiring medical treatment or pacing
- Arteriovenous Fistula
- Bacterial Endocarditis
- Blood loss requiring transfusion
- Chest Pain
- Damage to the tricuspid or pulmonary valves
- Death
- Embolization of the occluder, requiring percutaneous or surgical intervention
- Endarteritis
- False aneurysm of the femoral artery
- Fever
- Headache/migraine
- Heart failure
- Hemolysis after implantation of the occluder
- Hypertension
- Hypotension or shock
- Infection
- Myocardial infarction
- Occluder fracture or damage
- Perforation of the heart or blood vessels
- Stenosis of the left pulmonary artery or descending thoracic aorta
- Stroke/TIA
- Thromboembolism (cerebral or pulmornary)
- Valvular Regurgitation
- Vessel damage at the site of groin puncture (loss of pulse, hematoma etc.).

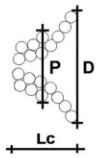
Precautionary Measures

- An angiogram must be performed prior to implantation for measuring length and diameter of the PDA.
- The implantation catheter must be flushed with heparinized saline solution prior to introduction and during the procedure, especially after angiography.
- The pfm medical implantation catheter is specifically designed for the delivery system. Other catheters should not be used to implant the device.
- Contrast media should not be injected through the implantation catheter.
- The coil should not be pulled back into the implantation catheter using strong force.
- Administration of 50 units of heparin per kg body weight is recommended after femoral sheaths are placed.
- Antibiotic coverage before (1 dose) and after implantation (2 doses) is recommended in order to prevent infection during the implant procedure. Antibiotic prophylaxis should be performed to prevent infective endocarditis during first 6 months after coil implantation.
- A suitable lateral aortogram should be performed for measurement of PDA dimensions (see Fig. PDA Measurements):

Directions for Use



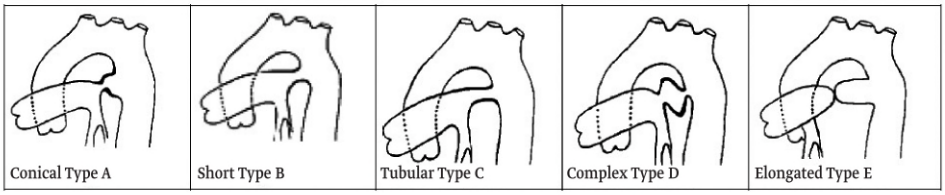
- D1 = Narrowest diameter
- D2 = Aortic Ampulla diameter
- L3 = PDA length



- D = Distal diameter
- P = Proximal diameter
- Lc = Length configurated

Figure 3: PDA Measurements

When defining the paramaters of your measurements, please consider that the anatomy of the PDA may differ among patients. According to Krichenko et al. there are five different types of PDAs (see device performance by PDA anatomy in clinical study section below).



Conical Type A	Short Type B	Tubular Type C	Complex Type D	Elongated Type E

Figure 4: Types of PDAs According to: Krichenko et. al. 1989, AmJ Cardiol; 63:877-880

Coil Selection

According to the measurements, the ductus type and the following recommendations, an appropriate coil should be selected:

- The distal coil diameter D should be no more than 2 mm larger than D2.
- The distal coil diameter D should be at least 3 to 4 mm larger than D1.
- Length of the configured coil Lc (see product label) should be not longer than L3.

D1	D2	Device
1mm	≤ 3mm	4x4
1mm	4mm	5x4
1mm	≥ 5mm	6x5
2mm	≤ 5mm	6x5
2mm	6-7mm	7x6
2mm	≥ 8mm	9x6

D1	D2	Device
3mm	≤ 7mm	7x6
3mm	8-9mm	9x6
3mm	≥ 9mm	9x6 or 11x6
<4mm	9mm	11x6
<4mm	10-11mm	11x6
<4mm	≥ 12mm	11x6

Table 2: Selection of the Nit-Occlud® PDA (according to angiographic PDA dimensions)

Coil Implantation Sequence

Step: 01

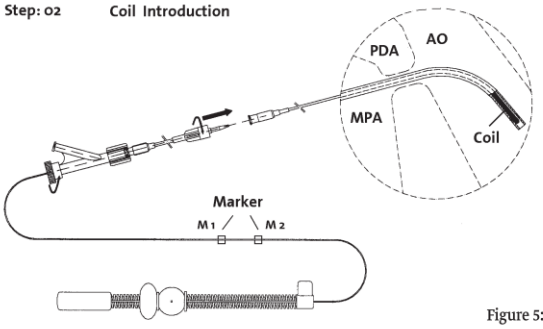
- Unpack the Nit-Occlud® PDA consisting of coil with disposable handle and implantation catheter under sterile conditions.

WARNING

Do not pull on the delivery system. If the coil is withdrawn into the Y connector, there is a danger that the system can no longer be loaded. Check all screw connections. Some screw joints may have been loosened by the sterilization process.

- Flush the system carefully through the side access of the Y connector with heparinized saline solution, and ensure that there is no air remaining anywhere in the system.
- Check the coil position inside the transparent transportation sheath. The coil should be inside the sheath. When it is in this position, it is essential not to pull on the delivery system. If the coil is not positioned inside the transportation sheath, or shows visible signs of damage, it must be replaced with a new coil.

Step: 02 Coil Introduction



MPA: Main Pulmonary artery
AO: Aorta

Figure 5: Coil Introduction

- Using a soft guide wire, advance the implantation catheter from the right femoral vein through the right heart, across the PDA into the descending thoracic aorta.
- Remove the guide wire from the implantation catheter and flush the catheter with a heparinized saline solution.
- Attach the luer lock connector of the transportation sheath to the implantation catheter.
- Open the hemostatic valve of the Y connector. The coil is now free for advancement.

WARNING

Do not pull on the delivery system in this position!

- Advance the coil into the implantation catheter.

Step: 03 Coil Configuration

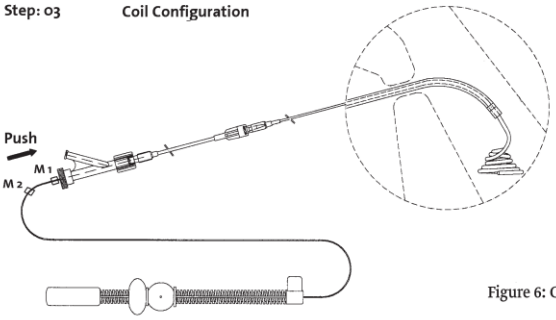


Figure 6: Coil Configuration

- Under fluoroscopic control advance the coil carefully through the implantation catheter into the aorta. This is done by moving the delivery system forward while arresting the implantation catheter.

WARNING

Ensure that the pigtail aortography catheter does not become entangled with the loops of the coil.

- Advance the coil until the first marker M1 is positioned close to the Y connector. At this position, all but one loop is configured outside the implantation catheter.

Step: 04 Coil Positioning

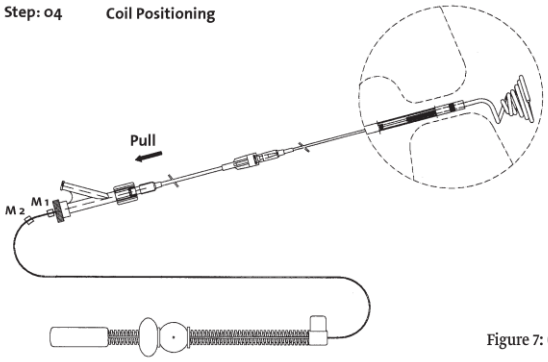


Figure 7: Coil Positioning

• Retract the entire system (implantation catheter, delivery system) under fluoroscopic control until the configured coil is positioned in the ampulla of the ductus (close hemostatic valve of Y connector or fix implantation catheter against delivery system).

NOTE: For longer ductus types, coil configuration inside the ductus ampulla is recommended. Here, 2–3 windings of the coil must first be configured in the aorta. Then the entire system is pulled into the ductus ampulla for further configuration of the coil.

Step: 05 Final Coil Adjustment

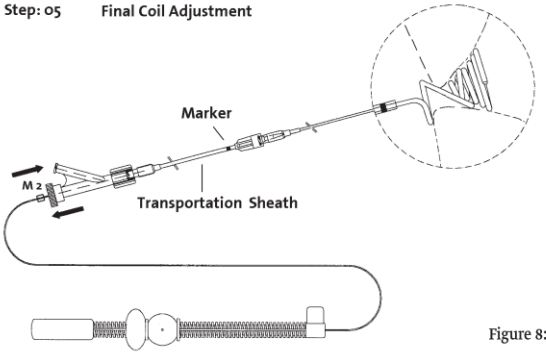


Figure 8: Final Coil Adjustment

• Open the hemostatic valve of the Y connector.
• Configure the last 1 or 2 loops on the pulmonary side of the ductus by simultaneously pulling back the implantation catheter (with your left hand) and pushing the delivery system (with your right hand). Advance the delivery system until the second marker M2 is close to the Y connector. At this position the coil is outside the catheter.
• Perform an aortogram to confirm that the coil is in the correct position.

NOTE: If the position or size of the coil is not satisfactory, it should be repositioned or exchanged at this point.

Repositioning

• To reposition the coil, pull it back into the implantation catheter by pulling the delivery system.

WARNING

Close the gap between delivery system and coil before you retrieve the coil into the implantation catheter.

• To do so, hold the handle with one hand and move the delivery system gently forward while holding it between 2 fingers of the same hand. This movement closes the gap between coil and delivery system and should be done under fluoroscopic control. Once the gap is closed the coil can be pulled smoothly into the implantation catheter.

WARNING

If a strong resistance is encountered while pulling the delivery system into the catheter, do not pull the system very hard because you risk a premature release of the coil.

- To reposition the implantation catheter, the coil should be pulled back into the transportation sheath, carefully and under visual control, until the tip of the coil is in line with the marker at the distal end of transportation sheath. Fix the coil position by closing the Y connector.

WARNING

If the coil is pulled back too far, there is the risk that it may not be possible to reload it into the delivery system.

- Then flush the implantation catheter with heparinized saline solution and repeat the procedure from Step 02.

Step: 06 **Coil Release**

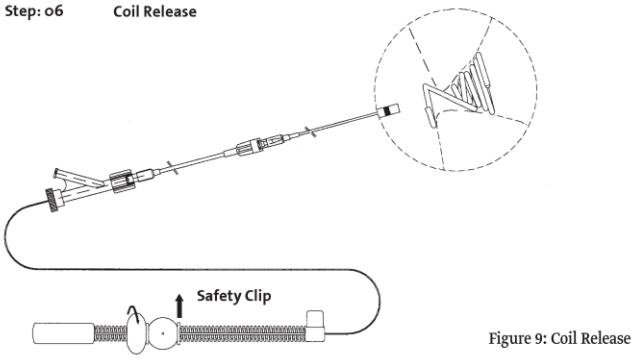


Figure 9: Coil Release

- When the coil is properly positioned, it should be released. The rotation screw should lie directly against the pusher ball. If there is any gap between the two, it must be closed.

WARNING

Final release should only be performed if the coil is properly positioned in the PDA. Otherwise, the coil must either be retrieved and repositioned or replaced by an appropriate substitute. Before the coil is finally released, proper position of the coil should be confirmed by angiography.

- Remove the safety clip from the handle.
- Turn the rotation screw under fluoroscopy clockwise until the coil is released. Note that depending on the coil type between 8 - 15 rotations are needed to release the coil. You will feel an increase in resistance immediately prior to release.
- Remove the delivery system and implantation catheter.
- Perform a final aortogram about 10 minutes later to document position of the coil and PDA occlusion.
- Remove the aortography catheter.

WARNING

Ensure that the catheter does not touch the coil.

Technical Complications and how to avoid them

Complications may be avoided or ameliorated by the following:

- Use of venous access for implants.
- Flushing all components with heparinized saline.
- Keeping delivery system and catheter straight, avoiding loops and curves on the catheterization table.
- Coil recapture in the pulmonary artery or aorta, avoiding pulling the exposed coil across heart valves or through the right ventricle.

Failure of detachment:

Complications may arise if the coil is not released successfully. "Sticking" may occur if positioning of the coil is very time-consuming and/ or if the delivery system does not protrude far enough from the end of the implantation catheter. The distal part of the delivery system must be placed outside of the implantation catheter immediately before release. If, however, the coil "sticks", the device must be retrieved and exchanged. As done with all interventional instruments, prior to implantation of the exchanged device the catheter should be flushed thoroughly to prevent coagulation, thus avoiding elevated friction or "sticking" of the system.

Device Embolization/ Premature release

The coil may embolize into the pulmonary artery if the aortic cone is too small or the coil fit is too loose. This can be prevented by accurate measurement of the PDA dimensions and choice of an appropriate coil for the PDA. Correct calibration of the angiographic measurement is a very important factor. In case of coil embolization, interventional retrieval should be performed using a snare or a bioptome.
In the event that the coil embolizes and interventional retrieval is unsuccessful, surgical retrieval should be considered.

Protrusion/ Obstruction

Protrusion of the windings into the aorta and/ or into the pulmonary artery may cause blood flow disturbances or vessel stenosis. This is avoidable by choosing an appropriate coil with a configured length (Lc) equal to or less than the PDA length (L3). The recoil force of the coil tends to return the device to its original configuration whenever possible and will retract the windings into the ampulla and/ or against the vessel wall. Pulmonary artery protrusion may be avoided by correct coil positioning during implant.

Late complications

Delayed complications such as migration or protrusion with a significant blood flow disturbance may require surgical removal of the coil.

Clinical Studies

Study description

A prospective, non-randomized, multi-center, single-arm Study and a continuing access study were performed using the same protocols at 15 centers in the United States of America to assess the safety and effectiveness of the Flex and Medium Nit-Occlud® PDA coil for occlusion of Patent Ductus Arteriosus (PDA) with minimum angiographic diameter of less than 4 mm. The primary effectiveness endpoints were echocardiographic and clinical closure rates at 12 months. The primary safety endpoint was the serious adverse event rate at 12 months. The endpoint rates were compared to an Objective Performance Criteria as follows:

- Echocardiographic closure (absence of detectable residual PDA flow on echocardiogram) greater than 85% at 12 months
- Clinical closure (absence of heart murmur) greater than 95% at 12 months
- Serious adverse event rate of less than 1% at 12 months

The following criteria were considered for their inclusion:

Inclusion criteria	Exclusion criteria
• PDA with 4 mm or smaller minimum diameter by color Doppler • Patient weight ≥ 5 Kg, age 6 months to 21 years (Patients older than 21 years may have device implanted and be included in a study registry.) • Previous treatment by surgery or Nit-Occlud device with residual PDA noted at least 6 months after the procedure	• Associated cardiac anomalies requiring surgery • Known bleeding or blood clotting disorders • Ongoing febrile illness • Pregnancy • Pulmonary hypertension/increased pulmonary vascular resistance (>5 Wood Units) • Known hypersensitivity to contrast medium

Table 3: Inclusion/Exclusion Criteria

Study results

A total of 378 patients were enrolled and 357 patients were evaluated for safety and effectiveness. The patient´s mean age was 4.26 years (range 0.5 to 21.9 years); the mean weight was 18.1 kg (range 4.7 to 109.0 kg), a total of 68.1% of the enrolled patients were female. Of the 357 evaluable patients, 347 had successful implantation of the device (technical success).

Principal safety and effectiveness results are presented in Table 4 below:

	OPC Rates	Nit-Occlud Patients	Percent	95% Lower Bound	95% Upper Bound
Technical Success at Implantation	95%[2]	347/357	97.2%	95.6%	
Clinical Closure at 12 Month Follow-up	95%[1]	308/314	98.1%	96.7%	
Echocardiographic Closure at 12 Month Follow-Up	85%[1]	299/309	96.8%	95.0%	
Mortality at 12 Months	0%[1]	0	0.0%		0.95%
Serious Adverse Events at 12 Months	1%[1]	0	0%		0.95%
Total Device and Procedure Related Adverse Events at 12 Months	6%	15/316*	4.7%		7.21%
		14/316**	4.4%		6.84%
Composite Success at 12 Months	80%[3]	294/309	95.1%	93.0%	

[1] Objective Performance Criteria (OPC) specified by the Multiorganization Advisory Panel to (FDA) Appendix (XII)
[2] Inferred from technical success rate of Gianturco coil technical success cited in Multiorganization Advisory Panel to FDA report (Appendix XII)
[3] Defined in IDE protocol but not defined by the Multiorganization Advisory Panel report
* Numerator is number of events; denominator is number with 12 mos fu + 2 with AE before 12 months
** Numerator is number of person; denominator is number with 12 mos fu + 2 with AE before 12 months

Table 4: Principal Safety and Effectiveness Results

Refer to Table 5 below for procedural and fluoroscopy times by device size and type.

Catalog #	Device Size Distal x Proximal Diameter	Device Type	Number of Implants	Mean Procedure Duration [min.]	Median Procedure Duration [min.]	Mean Fluoroscopy Time [min.]	Median Fluoroscopy Time [min.]
145044	4 x 4 mm	Flex	38	68.6	66.0	17.2	14.0
145054	5 x 4 mm	Flex	27	77.8	72.0	19.6	17.0
145065	6 x 5 mm	Flex	57	91.5	82.0	19.8	18.5
145076	7 x 6 mm	Medium	110	83.3	73.5	17.0	15.0
145096	9 x 6 mm	Medium	97	92.0	79.0	18.8	16.0
145116	11 x 6 mm	Medium	26	93.0	85.0	25.5	23.5

Table 5: Procedure and Fluoroscopy Times by Nit-Occlud Device

Differing Technical Failure Rates were observed based on Angiographic Classification of the PDA on the lateral aortogram and are summarized in the Table 6 below.

Classification	N(% of Total)	Technical Failure Rate	n/N (%)
Conical (A)	267 (74.8%)	4/267	(1.5%)
Short (B)	17 (4.8%)	3/17	(17.6%)
Tubular (C	5 (1.4%)	1/5	(20%)
Complex (D)	18 (5.0%)	1/18	(11.1%)
Elongated (E)	50 (14.0%)	1/50	(2%)
TOTAL	357 (100%)	10/357	(2.8%)

Table 6: Technical Failure rate by Angiographic Classification (See Figure above)

Study Adverse events were defined as follows:

Serious Adverse Events:
- Procedural or device related events which were life-threatening, required surgery to correct, resulted in hospitalization or prolonged hospital stay, caused long-term disability, or resulted in genetic damage or birth defect.

Major Adverse Events:
- Procedural or device related events which were not life-threatening, required interventional (catheter based) and /or medical treatment to correct up to one year follow-up evaluation but were resolved without surgical intervention.

Minor Adverse Events:
- Procedural or device related events which were not life-threatening, and were resolved without intervention or with a brief specific non-surgical intervention up to one year follow-up evaluation.

The combined studies safety results were the following:
- Mortality at 12 months: 0.0% (0/314)
- Serious Adverse Events at 12 months (device related): 0.0% (0/314)
- Serious Adverse Events at 12 months (procedure related): 0.0% (0/314)
- Total AEs (Serious, Major, and Minor) at 12 months or last follow up (related to the procedure or the device): 4.7% (15/316*)

The 15 Adverse Events are further described in Table 8 below:

DSMB Adjudication	Category	No. of Events
Major Device Related	Device embolization	2
	Device Retrieval/Removal	2
	Obstruction of descending aorta	1
Minor Device Related	Possible Thrombus	1
Major Procedure Related	Decreased Pulse in Right Foot	1
	Reaction to anesthesia	2
Minor Procedure Related	Reaction to anesthesia	1
	Vascular access site complication	1
	Other Adverse Event	2
	Nausea	1
	Fever	1

Table 7: Adverse Events
Procedural success, effectiveness and safety results were comparable to or better than predefined objective performance criteria.*

Disposal after Use

After use, medical products and accessories pose a potential biological hazard. For this reason, the products and their accessories should be handled and disposed of in accordance with recognised medical procedure, and in compliance with the relevant legal regulations and local ordinances.

Warranty

pfm medical warrants that this medical device is free from defects in both materials and workmanship. The above warranties are in lieu of all other warranties, either expressed or implied, including any warranty of merchantability or fitness for a particular purpose. Suitability for use of the medical device for any surgical procedure shall be determined by the user. pfm medical shall not be liable for incidental or consequential damages of any kind.

* Patients with 12 month follow up and those with an adverse event at any time
* Multiorganization Advisory Panel to FDA for Pediatric Cardiovascular Devices.
Proposed Standards for Clinical Evaluation of Patent Ductus Arteriosus Occlusion Devices.
Catheter Cardiovasc Interv 2000; 51:293-296.t.

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