Summary of Safety and Clinical Performance (SSCP)

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 Merit Careflow Central Venous Catheter (CVC) and Catheterization Kits.

The SSCP is not intended to replace the Instructions for Use (IFU) as the main document to ensure the safe use of the Careflow Central Venous Catheter and Catheterization Kits, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals. Since the Careflow Central Venous Catheter is not intended for use as a long-term implant, a more general information summary with content specifically intended for patients and lay persons is not required.

1.0 Device identification and general information

1.1 Device trade name(s):

The device(s) and model numbers covered by this Summary of Safety and Clinical Performance (SSCP) are presented in Table 1.

Table 1. Devices Included in this SSCP

Product	Product Code	Product Description
Careflow CVC without extension tubing	681614/C	Catheters.Careflow™.2.5F.100 mm.0.5 mm x 350 mm
	681623/C	Catheters.Careflow™.2.5F.100 mm.0.5 mm x 350 mm
	681639/C	Catheters.Careflow™.3F.150 mm.0.5 mm x 350 mm
	681640/C	Catheters.Careflow™.3F.150 mm.0.5 mm x 450 mm
	681643/C	Catheters.Careflow™.3F.200 mm.0.5 mm x 450 mm
	681644/C	Catheters.Careflow™.3F.200 mm.0.5 mm x 450 mm
	681649/C	Catheters.Careflow™.4F.200 mm.0.6 mm x 450 mm
	681650/C	Catheters.Careflow™.4F.200 mm.0.6 mm x 450 mm
	681669/C	Catheters.Careflow™.5F.150 mm.0.9 mm x 450 mm
	681669/D	Catheters.Careflow™.5F.150 mm.0.9 mm x 500 mm
	681670/C	Catheters.Careflow™.5F.150 mm.0.9 mm x 450 mm

Product	Product Code	Product Description
	681670/D	Catheters.Careflow™.5F.150 mm.0.9 mm x 500 mm
	681672/C	Catheters.Careflow™.5F.200 mm.0.9 mm x 450 mm
	681672/D	Catheters.Careflow™.5F.200 mm.0.9 mm x 500 mm
	681673/C	Catheters.Careflow™.5F.200 mm.0.9 mm x 450 mm
	681673/D	Catheters.Careflow™.5F.200 mm.0.9 mm x 500 mm
	681706/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 450 mm
	681706/D	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681707/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 450 mm
	681707/D	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681709/C	Catheters.Careflow™.7F.200 mm.0.9 mm x 450 mm
	681709/D	Catheters.Careflow™.7F.200 mm.0.9 mm x 500 mm
	681710/C	Catheters.Careflow™.7F.200 mm.0.9 mm x 450 mm
	681710/D	Catheters.Careflow™.7F.200 mm.0.9 mm x 500 mm
Careflow CVC with extension tubing	681612/C	Catheters.Careflow™.2.5F.60 mm.0.5 mm x 350 mm
	681622/C	Catheters.Careflow™.2.5F.100 mm.0.5 mm x 350 mm
	681634/C	Catheters.Careflow™.2.5F.200 mm.0.5 mm x 650 mm
	681662/C	Catheters.Careflow™.5F.150 mm.0.9 mm x 450 mm
	681662/D	Catheters.Careflow™.5F.150 mm.0.9 mm x 500 mm
	681763/C	Catheters.Careflow™.150 mm.0.9 mm x 700 mm
	681763/D	Catheters.Careflow™.150 mm.0.9 mm x 800 mm
	681788/C	Catheters.Careflow™.5F.150 mm.0.9 mm x 450 mm
	681666/D	Catheters.Careflow™.5F.200 mm.0.9 mm x 800 mm
	681762/D	Catheters.Careflow™.200 mm.0.9 mm x 800 mm
	681679/C	Catheters.Careflow™.5F.300 mm.0.9 mm x 700 mm
	681679/D	Catheters.Careflow™.5F.300 mm.0.9 mm x 800 mm
	681698/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 450 mm
	681698/D	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681761/D	Catheters.Careflow™.200 mm.0.9 mm x 800 mm

Product	Product Code	Product Description
	681699/C	Catheters.Careflow™.7F.200 mm.0.9 mm x 700 mm
	681699/D	Catheters.Careflow™.7F.200 mm.0.9 mm x 800 mm
	681701/C	Catheters.Careflow™.7F.300 mm.0.9 mm x 700 mm
	681701/D	Catheters.Careflow™.7F.300 mm.0.9 mm x 800 mm
	681617/C	Catheters.Careflow™.4F.60 mm.0.5 mm x 350 mm
	681627/C	Catheters.Careflow™.4F.100 mm.0.5 mm x 350 mm
	681652/C	Catheters.Careflow™.4F.150 mm.0.5 mm x 450 mm
	681619/C	Catheters.Careflow™.5F.60 mm.0.6 mm x 450 mm
	681684/C	Catheters.Careflow™.5F.150 mm.0.5 mm x 450 mm
	681682/C	Catheters.Careflow™.5F.150 mm.0.6 mm x 450 mm
	681683/C	Catheters.Careflow™.5F.150 mm.0.6 mm x 450 mm
	681688/C	Catheters.Careflow™.5F.200 mm.0.6 mm x 650 mm
	681687/C	Catheters.Careflow™.5F.200 mm.0.6 mm x 650 mm
	681783/C	Catheters.Careflow™.5F.200 mm.0.6 mm x 650 mm
	681702/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 450 mm
	681702/D	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681703/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 450 mm
	681703/D	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681767/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681771/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681715/C	Catheters.Careflow™.7F.200 mm.0.9 mm x 700 mm
	681713/C	Catheters.Careflow™.7F.200 mm.0.9 mm x 700 mm
	681713/D	Catheters.Careflow™.7F.200 mm.0.9 mm x 800 mm
	681714/C	Catheters.Careflow™.7F.200 mm.0.9 mm x 700 mm
	681714/D	Catheters.Careflow™.7F.200 mm.0.9 mm x 800 mm
	681772/C	Catheters.Careflow™.7F.200 mm.0.9 mm x 600 mm
	681717/C	Catheters.Careflow™.7F.300 mm.0.9 mm x 700 mm
	681718/C	Catheters.Careflow™.7F.300 mm.0.9 mm x 700 mm

Product	Product Code	Product Description
	681717/D	Catheters.Careflow™.7F.300 mm.0.9 mm x 800 mm
	681718/D	Catheters.Careflow™.7F.300 mm.0.9 mm x 800 mm
	681620/C	Catheters.Careflow™.5F.60 mm.0.6 mm x 450 mm
	681618/C	Catheters.Careflow™.5F.100 mm.0.6 mm x 450 mm
	681690/C	Catheters.Careflow™.5F.150 mm.0.6 mm x 450 mm
	681691/C	Catheters.Careflow™.5F.150 mm.0.6 mm x 450 mm
	681786/C	Catheters.Careflow™.5F.150 mm.0.6 mm x 450 mm
	681696/C	Catheters.Careflow™.5F.200 mm.0.6 mm x 650 mm
	681694/C	Catheters.Careflow™.5F.200 mm.0.6 mm x 650 mm
	681695/C	Catheters.Careflow™.5F.200 mm.0.6 mm x 650 mm
	681774/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681720/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 450 mm
	681720/D	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681721/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 450 mm
	681721/D	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681722/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 450 mm
	681722/D	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681768/C	Catheters.Careflow™.7F.150 mm.0.9 mm x 500 mm
	681775/C	Catheters.Careflow™.7F.200 mm.0.9 mm x 600 mm
	681724/C	Catheters.Careflow™.7F.200 mm.0.9 mm x 700 mm
	681724/D	Catheters.Careflow™.7F.200 mm.0.9 mm x 800 mm
	681725/C	Catheters.Careflow™.7F.200 mm.0.9 mm x 700 mm
	681725/D	Catheters.Careflow™.7F.200 mm.0.9 mm x 800 mm
	681726/C	Catheters.Careflow™.7F.200 mm.0.9 mm x 700 mm
	681726/D	Catheters.Careflow™.7F.200 mm.0.9 mm x 800 mm
	681776/C	Catheters.Careflow™.7F.300 mm.0.9 mm x 700 mm
	681776/D	Catheters.Careflow™.7F.300 mm.0.9 mm x 800 mm
	681728/C	Catheters.Careflow™.7F.300 mm.0.9 mm x 700 mm

Product	Product Code	Product Description
	681728/D	Catheters.Careflow™.7F.300 mm.0.9 mm x 800 mm
	681729/C	Catheters.Careflow™.7F.300 mm.0.9 mm x 700 mm
	681729/D	Catheters.Careflow™.7F.300 mm.0.9 mm x 800 mm
	681731/C	Catheters.Careflow™.8.5F.150 mm.0.9 mm x 450 mm
	681731/D	Catheters.Careflow™.8.5F.150 mm.0.9 mm x 500 mm
	681732/C	Catheters.Careflow™.8.5F.150 mm.0.9 mm x 450 mm
	681732/D	Catheters.Careflow™.8.5F.150 mm.0.9 mm x 500 mm
	681769/C	Catheters.Careflow™.8.5F.150 mm.0.9 mm x 500 mm
	681777/C	Catheters.Careflow™.8.5F.150 mm.0.9 mm x 500 mm
	681733/C	Catheters.Careflow™.8.5F.200 mm.0.9 mm x 700 mm
	681733/D	Catheters.Careflow™.8.5F.200 mm.0.9 mm x 800 mm
	681734/C	Catheters.Careflow™.8.5F.200 mm.0.9 mm x 700 mm
	681734/D	Catheters.Careflow™.8.5F.200 mm.0.9 mm x 800 mm
	681778/C	Catheters.Careflow™.8.5F.200 mm.0.9 mm x 600 mm
	681735/C	Catheters.Careflow™.9.5F.150 mm.0.9 mm x 450 mm
	681735/D	Catheters.Careflow™.9.5F.150 mm.0.9 mm x 500 mm
	681736/C	Catheters.Careflow™.9.5F.150 mm.0.9 mm x 450 mm
	681736/D	Catheters.Careflow™.9.5F.150 mm.0.9 mm x 500 mm
	681779/C	Catheters.Careflow™.9.5F.150 mm.0.9 mm x 500 mm
	681737/C	Catheters.Careflow™.9.5F.200 mm.0.9 mm x 700 mm
	681737/D	Catheters.Careflow™.9.5F.200 mm.0.9 mm x 800 mm
	681738/C	Catheters.Careflow™.9.5F.200 mm.0.9 mm x 700 mm
	681738/D	Catheters.Careflow™.9.5F.200 mm.0.9 mm x 800 mm
	681780/C	Catheters.Careflow™.9.5F.200 mm.0.9 mm x 600 mm
Careflow CVC with Integral Floswitch	681660/C	Catheters.Careflow™.5F.150 mm.0.9 mm x 450 mm
	681660/D	Catheters.Careflow™.5F.150 mm.0.9 mm x 500 mm
	681664/C	Catheters.Careflow™.5F.200 mm.0.9 mm x 700 mm
	681664/D	Catheters.Careflow™.5F.200 mm.0.9 mm x 800 mm

Product	Product Code	Product Description
	681678/D	Catheters.Careflow™.5F.300 mm.0.9 mm x 800 mm
CVC Accessories	Needle Introducer, Over-needle Introducer, Floswitch Introducer, Guidewire (SS, NiTi), Venaguide, Dilator, Guiding Syringe, Syringe, Rotating Luer Lock Floswitch, Pinch Clamp / Slide Clamp, Deadender, Secondary Fixation Device, Drape, and Scalpel	

1.2 Manufacturer Information

The name and address of the manufacturer of the Careflow Central Venous Catheter and Catheterization Kits is provided in Table 2.

Table 2. Manufacturer Information

Manufacturer Name	Address of Manufacturer
Merit Medical Singapore Pte. Ltd.	198 Yishun Avenue 7, Singapore 768926

1.3 Manufacturer Single Registration Number (SRN)

The Single Registration Number (SRN) for the manufacturer is included in Table 3.

1.4 Basic UDI-DI

The basic Unique Device Identifier (UDI) with Device Identification (DI) key is provided in Table 3.

1.5 Medical Device Nomenclature Description / Text

The European Medical Device Nomenclature (EMDN) and codes and descriptors for the subject device(s) are listed in Table 3.

1.6 Risk Class of Device

The EU device risk classification(s) for the Careflow Central Venous Catheter and Catheterization Kits is listed in Table 3.

Table 3. Device Identification Information

Device Name	EU Device Class	Product Number	Basic UDI-DI	Single Registration Number (SRN)	EMDN Code	EMDN Terms
Careflow CVC	III	Per Table 1	088445048762E6	SG-MF-000002111	C01020201	Central Venous Mono-lumen Catheters, Not Tunnellized
					C01020202	Central Venous Bi-lumen Catheters, Not Tunnellized
					C01020203	Central Venous Multi-lumen (>2) Catheters, Not Tunnellized
Accessory Guidewire	III				C04	Cardiovascular guidewires
CVC Accessories	IIa				C010280	Central Venous Catheters - Accessories
					C9002	Vascular and Fascial Dilators
					V010102	Scalpels without safety systems, single-use

1.7 Year of EU Market Introduction

The year that the Careflow Central Venous Catheter and Catheterization Kits were first placed on the EU market is presented in Table 4.

1.8 Authorised Representative (if applicable)

The name of the authorized representative(s) and, if applicable, the SRN are provided in Table 4.

1.9 Notified Body

The Notified Body (NB) involved in the conformity assessment of the Careflow Central Venous Catheter and Catheterization Kits in accordance with Annex IX of the MDR and responsible for validating the SSCP is listed in Table 4.

1.10 NB Single Identification Number

The NB Single Identification Number is listed in Table 4.

Table 4. Authorized Representative and Notified Body Information

Device Name	Year Placed on EU Market	Authorized Representative		Notified Body (NB)	
		Name	SRN	Name	ID Number
Careflow CVC and Catheterization Kits	1998	Merit Medical Ireland Ltd.	IE-AR-000001011	BSI	2797

2.0 Intended Use of the Device

2.1 Intended Purpose

The Merit Careflow Central Venous Catheter and Catheterization Kits are intended to be used to infuse or withdraw fluids from the central venous system of patients, and to provide direct fluid path connection to the central venous circulation for the purpose of venous pressure monitoring for short term use (less than 30 days).

2.2 Indication(s) and Intended Patient Groups

The Merit Careflow Central Venous Catheter and Catheterization Kits are indicated for use in patients requiring large volume infusions of therapeutic agents, parenteral nutrition, or other fluids as well as central venous pressure monitoring and blood sampling.

The Careflow CVC is indicated for both adult and pediatric critical care patients who require infusion of drugs, total parenteral nutrition (TPN) fluids, large volume infusions, repeated blood sampling and monitoring of the central venous pressure. Per suggestions from the Global Emergency Medicine Wikipedia – WikEM.org (https://wikem.org/wiki/Pediatric_central_line), the following catheter sizes are suggested for the pediatric patient populations: ≤3FR for patients of < 6 months; 3-4FR for patients from 6 months to 6 years; 4-5FR for patients from 7 to 12 years. **Note: The above guidelines are only suggestions from the Global Emergency Medicine Wikipedia website. Selection of an appropriate catheter should be made by fully trained physicians after thorough evaluation and consideration of patient's physical conditions and medical needs. The manufacturer supplies various configuration options only to better support different patient's needs and physician's choices*.

The Careflow Central Venous Catheter is designated for use on critical care patients.

2.3 Contraindications

Percutaneous puncture of a central vein may be contraindicated in patients with pulmonary hypertension.

3.0 Device Description

3.1 Materials/Substances in Contact with Patient Tissues

The Careflow CVC and Catheterization Kits are part of the Merit central venous catheter product family. The Careflow CVC is an intravascular catheter designed in single-lumen or multi-lumens with a radiopaque polyurethane catheter tubing available in gauge sizes from 2.5 to 9.5 Fr and in lengths from 60 mm to 300mm. The catheter tubing for the Careflow CVC is uncoated.

The Careflow CVC is supplied sterile in a Catheterization Kit containing CVC Accessories to facilitate catheter placement. The Careflow CVC and Catheterization Kits are individually packed into a rigid thermoformed tray or Tyvek pouch in which the components are securely held.

The Careflow CVC devices is available in various configurations: single, double, and multi-lumen catheter configurations with and without extension arms. The device configurations are shown in figures 1-6. The Careflow CVC is packaged with the CVC Accessories in Figure *7*.

Figure 1: Typical Drawing of a Careflow CVC (1 lumen without extension arm)

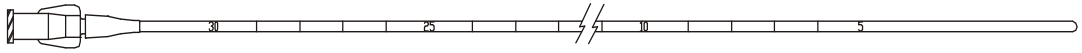


Figure 2: Typical Drawing of a Careflow CVC (1 Lumen with extension arm)

Figure 3: Typical Drawing of a Careflow CVC (2 Lumens)

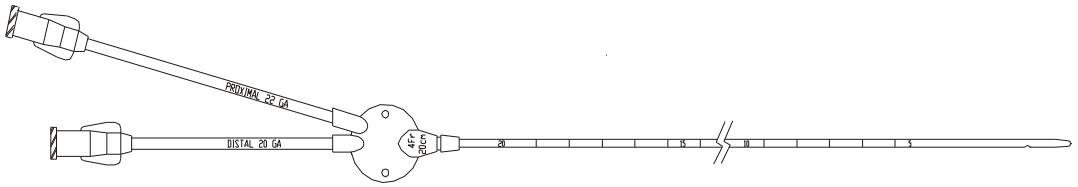


Figure 4: Typical Drawing of a Careflow CVC (3 Lumens)

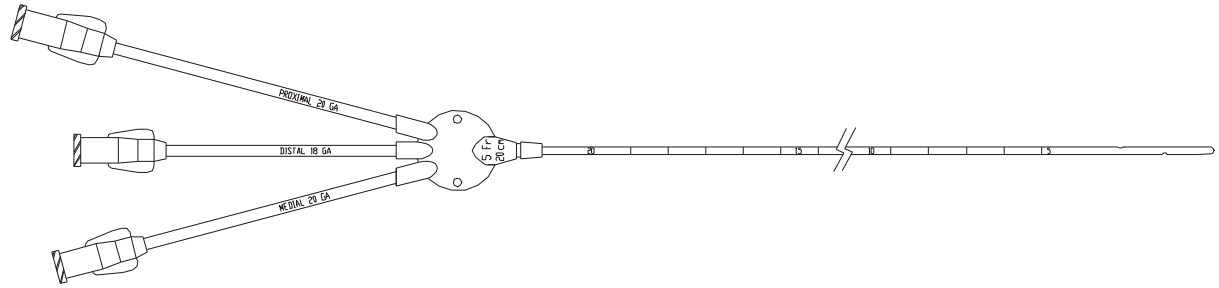


Figure 5: Typical Drawing of a Careflow CVC (4 Lumens)

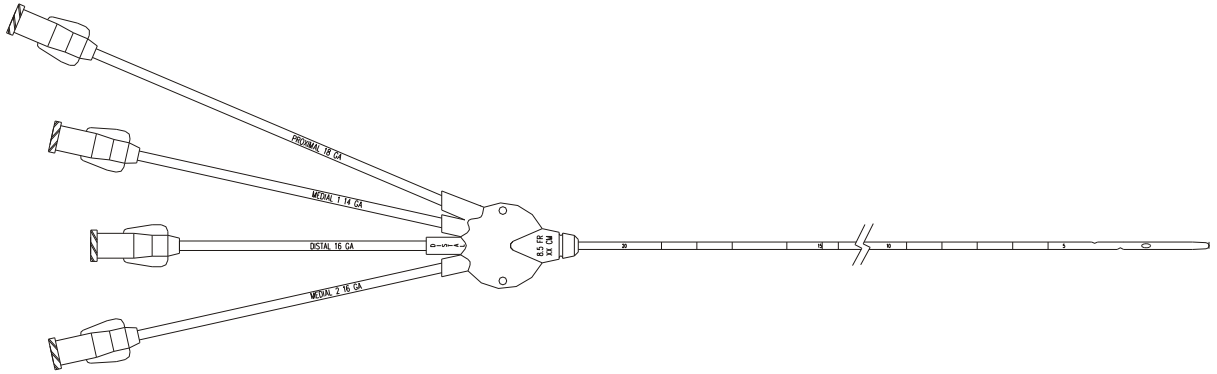


Figure 6: Typical Drawing of a Careflow CVC (5 Lumens)

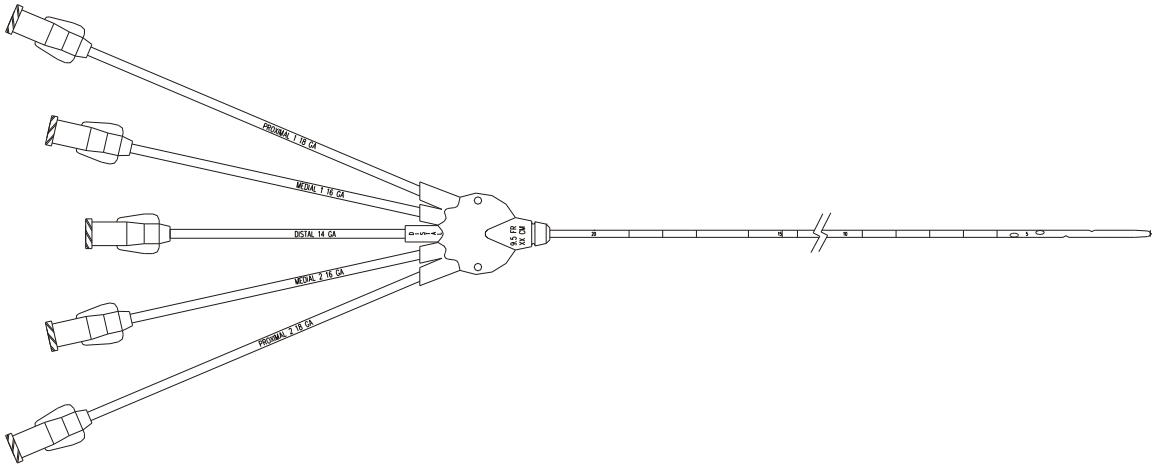
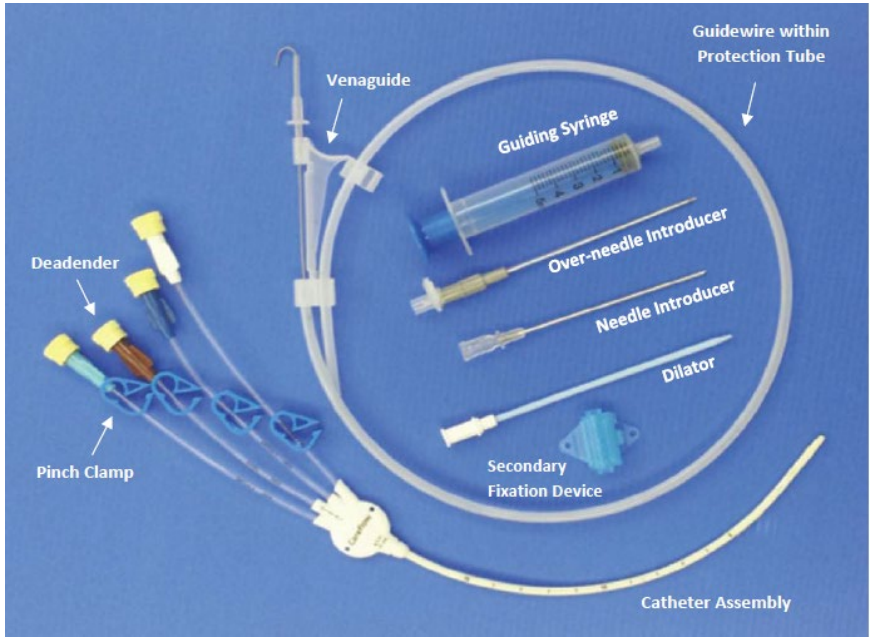


Figure 7: Typical 4-lumen Careflow CVC and Catheterization Kit



The materials of construction for the Careflow CVC components are summarized in Table 5 and Table 6. The Careflow CVC does not contain any medicinal substances.

Table 5. Material Specifications for Merit Careflow Central Venous Catheter

Component	Material
Hub	Thermoplastic polyurethane
Catheter tubing	Polyurethane
Extension tubing	Polyurethane
Junction boot	Polyurethane
Identification Marking	Black Ink

Table 6. Material Specifications for Kit Components (not elsewhere addressed)

Component	Component Part	Material
Needle Introducer	Protection Tube	LDPE
	Needle	Stainless Steel
	Hub	TPX Polymethylpentene
Over-Needle Introducer	Needle	Stainless Steel
	Protection Tube	LDPE
	Catheter Bush	PC
	Tubing	FEP with Barium Sulfate
	Needle Grip	Polypropylene
	Guide Bush	Polypropylene
	Hub	HDPE
Floswitch Introducer	Needle	Stainless Steel
	Protection Tube	LDPE
	Silicone Tubing	Silicone rubber
	Guide bush	PC
	Needle Grip	Polypropylene
	Catheter Bush	PC

Component	Component Part	Material
	Housing	Polypropylene
	Floswitch Button	ABS
	Tubing	PTFE or FEP with Barium Sulfate
Guidewire (SS)	Fixed Core Wire	Stainless Steel
	Spring Wire	Stainless Steel
	Safety Wire	Stainless Steel
	Protection Tube	HDPE
Guidewire (Niti)	Fixed Core Wire	Nickel Titanium
	Spring Wire	Stainless Steel
	Protection Tube	HDPE
Venaguide	Venaguide With Hump	PP
Dilator	Hub	HDPE
	Tubing	HDPE
Guiding Syringe	Barrel	PP
	Plunger	PP
	Stopper	Rubber
	Internal Tubing	ABS
	Gasket and Airtight Valve	Rubber
	Partition	PP
	Back Cap	PP
Syringe	Barrel	PP
	Plunger	PP
	Stopper	Synthetic Rubber
Pinch Clamp	Body	POM
Slide Clamp	Body	PC
Floswitch	Luer Lock Nut	PP
	Housing	PP
	Guide bush	PC

Component	Component Part	Material
	Floswitch Button	ABS
	Steel Ball	Stainless Steel
	Silicon Tubing	Silicone rubber
Deadender	Body	PP
Secondary Fixation Device	Body	PP
Drape	Body	Non-woven tissue
Scalpel	Blade	Stainless Steel
	Spring (for Futura scalpel)	Stainless Steel
	Blade Holder	Polystyrene
	Protection Tube	LDPE

Abbreviations: ABS = acrylonitrile butadiene styrene, FEP = fluorinated ethylene propylene, HDPE = high-density polyethylene, HDPP = high-density polypropylene, LDPE = low-density polyethylene, PC = polycarbonate, PE = polyethylene, POM = polyoxymethylene, PP = polypropylene, PTFE = polytetrafluoroethylene

3.2 Operating Principles

The Careflow CVC is an intravenous catheter that is intended for short term use (less than 30 days) to access the human circulatory system via insertion through either the Internal Jugular or Subclavian vein using Seldinger technique, where the catheter tip resides in the superior vena cava.

Before insertion of the catheter, the patient is first assessed for CVC placement to minimize risks and complications of the procedure. Next, the area of skin over the planned insertion site is cleaned. A local anesthetic is applied if necessary. The location of the vein is identified by landmarks or with the use of ultrasound devices.

The catheter is then inserted using the Seldinger technique. An introducer is advanced through the skin until blood is aspirated. A guidewire is passed through the introducer and the introducer is removed subsequently. A dilator may be passed over the guidewire to expand the tract. Finally, the central line itself, which is the catheter, will then be passed over the guidewire, after which the guidewire will be removed. The catheter may now be secured, and the puncture site dressed as required. Administration of drugs, Total Parenteral Nutrition (TPN) fluids, large volume infusions, repeated blood sampling and monitoring of the central venous pressure may be performed using the central venous catheter.

3.3 Previous Generations or Variants

The Careflow CVC devices are marketed globally. The initial CE-marking in 1998 was by Ohmeda at Swindon, UK. These devices were subsequently transferred to Becton Dickinson Critical Care Systems, Singapore and was subsequently acquired by Argon Critical Care Systems, Singapore in 2010

and by Merit Medical, Singapore in February 2017. The design authority is now owned by Merit Medical Singapore and the devices continue to be manufactured at the same facility. There are no previous device generations or variants within the scope of this evaluation.

3.4 Accessories

The Careflow CVC is supplied sterile in a Catheterization Kit containing below listed CVC Accessories to facilitate catheter placement as shown in Figure 8. These components are packed into the catheterization tray in various configurations:

- Needle Introducer
- Over-Needle Introducer
- Floswitch Introducer
- Guidewire (SS, Niti)
- Venaguide
- Dilator
- Guiding Syringe
- Syringe
- Pinch Clamp / Slide Clamp
- Rotating Luer Lock Floswitch
- Deadender
- Secondary Fixation Device
- Drape
- Scalpel

Figure 8: Typical CVC and Accessory kit in Catheterization Tray

3.5 Devices Used in Combination (if applicable)

There are no other devices and products intended to be used in combination with the Careflow CVC and Catheterization Kits, other than generic surgical equipment.

4.0 Risks and Warnings

4.1 Residual Risks and Undesirable Effects

The Merit Risk Management process is conducted in accordance with ISO 14971:2019. Risk assessment processes are utilized to analyse risks associated with the use of Merit devices, including possible misuses of a device. This ensures that all foreseeable potential failure modes and associated risks have been considered and addressed in the device design and/or production quality system. The process involves the following key aspects:

- Identifying potential failure modes, and their likely causes and effects
- Evaluating the probability of occurrence, degree of severity and relative detectability of each failure
- Identifying controls and preventive measures

All possible risk control measures have been implemented and verified and the Careflow CVC and Catheterization Kits have met all applicable regulations and standards. Through the clinical evaluation process, information relative to the clinical state-of-the-art and potential adverse events are identified based on a review of the pertinent clinical evidence.

Intended clinical benefits:

The Merit Careflow Central Venous Catheter and Catheterization Kits provide an indirect clinical benefit to patients by:

- Facilitating blood pressure monitoring.
- Facilitating repeated blood sampling
- Facilitating infusion of drugs, TPN fluids, and large volume infusions

Merit does not claim any direct benefits of the Careflow Central Venous Catheter and Catheterization Kits.

Articles published between January 1, 1998 and June 30, 2022 were reviewed in the clinical evaluation for Careflow CVC. Based on the literature, Careflow CVC has been successfully used to facilitate blood pressure monitoring, repeated blood sampling, infusion of drugs, administration of TPN, and large volume infusions. For the clinical evaluation, the performance outcomes were defined as follows:

> Careflow CVC Composite Technical Success: Successful placement of the catheter at its intended location and facilitation of successful hemodynamic pressure monitoring, blood sampling and/or fluid infusions.

Composite Technical Success rates from the clinical literature are very high. Overall, technical success rate was 97.5% for the Careflow CVC and 99.9% for the benchmark devices. Statistical analysis in the clinical evaluation demonstrated that the Careflow CVC Composite Technical Success rate is non-inferior to the benchmark devices, and therefore the Careflow CVC performance is consistent with the state of the art. See summary comparative performance Careflow CVC and Benchmark in Table 7.

Table 7. Comparative Performance for Careflow CVC with Benchmark Competitors

Device Type/Application	Subject Device, n/N (%)	Benchmark CVCs, n/N (%)
Composite Technical Success		
Careflow CVC	795/815 (97.5)	2249/2251 (99.9)

Potential Complications/Adverse Events

The potential complications/adverse events related to the subject device as identified in the Instructions For Use (IFU) are summarized in Table 8.

Table 8. Potential Complications

Product Configuration	Complications
Careflow CVC (IFU: 407096001MLP)	• Air embolism • Catheter embolism • Pulmonary embolism • Pleural or mediastinal damage • Atrial perforation • Vessel dissection or perforation • Hemorrhage • Septicemia • Arrhythmia • Thrombosis • Delayed tension pneumothorax • Thrombophlebitis • Cardiac tamponade • Central venous catheter (CVC) migration and tip misplacement • Misfunction • Occlusion • Infection • Inflammation • Soft tissue injury • Impaired central venous pressure (CVP) measurement • Insertion site infection/inflammation

In addition, the device/procedure-related events identified in the literature, and the corresponding risk assessment harms (where applicable) are presented in Table 9 and Table 10, respectively.

Table 9. Adverse Events Reported in Clinical Literature

Adverse Events (AEs)	Careflow CVC AE Rate n/N (%)	Device-Related	Procedure-Related	Time of Occurrence	Risk Assessment Harms
Accidental dislodgement	2/270 (0.7)[1]	-	X	< 30 days	N/A
Arterial puncture	5/270 (1.9)[1]	-	X	Procedural	N/A
Catheter malposition	31/270 (11.5)[2,3]	-	X	< 30 days	N/A
Migration	5/270 (1.9)[1]	X	X	< 30 days	Procedure, Additional (3) Procedure, Delay (2)
Occlusion	11/270 (4.1)[1]	X	X	< 30 days	Procedure, Additional (3) Procedure, Delay (2)
Pneumothorax	4/270 (1.5)[3]	-	X	Procedural	N/A
Thrombosis	2/270 (0.7)[3]	-	X	< 30 days	Foreign Body, Vascular (3)
TOTAL	**60/270 (22.2)**				

*Harms Level: 1 = Negligible (inconvenience or temporary discomfort), 2 = Minor (results in temporary injury or impairment not requiring professional medical intervention), 3 = Serious/Major (results in injury or impairment requiring professional medical intervention), 4 = Critical (results in permanent impairment or life-threatening injury)

Table 10. Adverse Events from Identified Case Reports

Author (Year)	Device	Narrative	Adverse Event	Device-related	Procedure-related
Careflow CVC					
Lee (2008)[4]	Careflow CVC, 5Fr	On postoperative day 4, patient complained of chest pain and dyspnea. Chest x-ray showed bilateral pneumothorax. Pneumothorax treated with bilateral thoracotomy tubes (20Fr) for 4 days.	Pneumothorax	-	X
McGrath (2006)[5]	Careflow quad lumen CVC, 8.5 Fr	During transport to CT, the intensive care team noted arterial pressure waveforms in the central line. Fluid infusion was stopped immediately, and the patient was scheduled for surgical removal of the CVC. The CVC was found inserted into the artery underneath the clavicle. Catheter mobilization resulted in significant hemorrhage necessitating partial clavicle resection and arterial suture and muscle patch repair.	Arterial puncture and catheter misplacement	-	X
Moller (2012)[6]	Careflow CVC	Carotid artery punctured with a 17G needle during attempted CVC insertion. Arterial injury was immediately recognized and compression applied. A large hematoma formed, and the patient went into respiratory failure. He was intubated and admitted to ICU. On day 4, a pseudoaneurysm of the right carotid and large hematoma were noted on CT. Patient developed ventricular fibrillation upon return to ICU. Decision made to attempt bedside percutaneous thrombin injection without neuroprotection. Under ultrasound guidance, thrombin injected using 21G needle inserted into pseudoaneurysm. Flow was maintained in the parent carotid artery. There was no further cardiac arrhythmia nor symptoms of focal neurological deficit.	Arterial puncture	-	X
Pal (2014)[7]	Careflow triple-lumen CVC	While introducing the guidewire, mild resistance felt. After approximately half of the guidewire length was introduced, resistance was felt that prevented further guidewire introduction. Guidewire extraction was attempted, but 12 cm of the wire remained within the patient. Chest x-ray showed the guidewire coiled about 3-cm distal to the puncture site. Surgical extraction was performed in a 30-minute procedure and recovery was uneventful.	Guidewire coiling and entrapment	X	X

Based on the clinical literature data, the reported Device-related Adverse Event (AE) rate for the Careflow CVC is 5.9% (16/270). Safety data for the Careflow CVC and for comparable benchmark devices from the clinical literature are summarized in Table 11. The Device-related AE rate for the

comparable benchmark devices is 0.0% (0/2209). Statistical analysis in the clinical evaluation process indicated that the Device-related AE rate for the Careflow CVC was non-inferior to the benchmark competitors. See summary comparison of Careflow CVC and benchmark adverse events in Table 11.

Table 11. Comparative Safety for Careflow CVC with Benchmark Competitors

Device Type/Application	Subject Device, n/N (%)	Benchmark Competitors, n/N (%)
Device-related AE Rate		
Careflow CVC	16/270 (5.9)	0/2209 (0.0)

In summary, the safety of the subject device has been substantiated via objective evidence from clinical literature data. The results of the clinical risk/safety analysis demonstrate that the subject device meets the established acceptance criteria with respect to safety and exhibit an acceptable overall safety profile. No new safety concerns specific to the subject device were identified in this evaluation, and the rates reported in the literature are consistent with available data for state-of-the-art alternative treatments.

4.2 Warnings and Precautions

The labeled warnings and precautions for the Careflow CVC device configurations are summarized in Table 12.

Table 12. Careflow CVC: Warnings & Precautions

Product Configuration	Labeling
Careflow CVC	**General Warnings**
	1. Use only as directed by a physician. 2. Sterile, Single use: Do not reuse, reprocess, or resterilise. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient. 3. Read all warnings, precautions, and instructions prior to use. Failure to do so may result in severe patient injury. 4. Physicians must be familiar with the complications associated with central venous catheterisation, i.e., infection, inflammation, vessel perforation, soft tissue injury, air embolism, catheter embolism, pleural and mediastinal damage, septicaemia, thrombosis

Product Configuration	Labeling
	and cardiac tamponade secondary to vessel wall or atrial perforation which may require additional procedure. 5. Complications are associated with right atrial and inadvertent right ventricular catheterisation. Physicians must be aware of these complications before advancing the catheter beyond the depth required for normal vena cava placement. Do not advance the catheter past this depth unless procedure requires right atrial placement. If catheter is advanced beyond normal vena cava placement depth, monitor electrocardiogram during insertion and confirm final position by chest X-Ray. 6. It is recommended that patients be placed in a slight Trendelenburg position during insertion procedure to reduce the risk of air embolism. Avoid using femoral vein for central venous access which might be generally associated with higher rate of infectious and thrombotic complications. 7. The lumens of Careflow™ Central Venous Catheter are to be flushed with sterile saline solution prior to catheter insertion. 8. All catheter placements must be inspected for flow rates, security of dressing and security of luer connections. Use only securely tightened ISO 80369-7 compliant Luer-Lock connections with central venous access device to guard against inadvertent disconnection. 9. To reduce or eliminate the potential for catheter migrations, the catheter should be secured by suturing at the eyelets of the junction boot housing/hub and that, where the use of the secondary fixation device is necessary, it should be used as additional support and not the only means of fixation. Additionally, the security of catheter fixation and position of the catheter tip should be checked throughout use. 10. When removing dressings at or close to catheter sites, care must be taken to avoid severing the catheter. 11. Acetone must not come into contact with the catheter as the material may weaken and this may result in leakage or air embolism. If necessary, minimize contamination risk by cleaning the device with an appropriate antiseptic (70% Alcohol or per hospital protocol). 12. Exposure of product componentry to topicals containing alcohol is not recommended. 13. Do not attempt to re-insert a partially or completely withdrawn introducer cannula. 14. Use of a syringe smaller than 5 mL to irrigate or de-clot an occluded catheter may cause intraluminal or catheter rupture. 15. Syringes are supplied for blood aspiration only. 16. Luer connections: as standard practice the security of luer connections must be checked routinely. Do not overtighten connections as this may crack the connection leading to leaks, air embolism. 17. Patients with suspected hypersensitivity to nickel should undergo skin test to assess hypersensitivity prior to use of Merit Guidewires in the placement of central venous catheter. 18. The Guidewire / Needle Introducer / Over-needle Introducer / Floswitch Introducer / Scalpel in this device contains Cobalt (CAS number: 7440-48-4) defined as CMR 1B in a concentration above 0.1% weight by weight. The risk associated with any potential CMR

Product Configuration	Labeling
	activity is mitigated substantially by the exceptionally low rate of Cobalt elution from the stainless steel components into the patient. Current scientific evidence supports that medical devices manufactured from cobalt alloys or stainless steel alloys containing cobalt do not cause an increased risk of cancer or adverse reproductive effects.
	Warnings – Seldinger Technique
	1. Do not withdraw the guidewire against needle bevel, as this increases the risk of severing the guidewire. 2. During insertion do not reinsert a partially or completely withdrawn needle into the cannula. 3. Ensure the flexible end of the guidewire is advanced into the vein. 4. Ensure the guidewire moves freely in the needle introducer. 5. A firm grip must be maintained on the guidewire at all times. 6. When using the 'J' wire straightener maintain a firm grip on the plastic sleeve. 7. Ensure the dilator is removed prior to catheter advancement. 8. The moveable suture devices are designed as additional support and must not be used as the only means of fixation. 9. Potential for guidewire breakage. Although the incidence of guidewire breakage is extremely uncommon, physicians must be aware of the potential of guidewire breakage if undue force is applied to the wire. If resistance is met when attempting to remove the guidewire after central venous placement, the wire may be kinked within the area of the catheter tip and the vessel. Undue force may cause the wire to break. If resistance is encountered, withdraw the catheter relative to the guidewire (2-3 cm) and attempt to remove the wire. If resistance is still apparent remove the wire and the catheter simultaneously. 10. Physicians should be aware that the guidewire can pick up material from the vein. This may prevent the guidewire from being withdrawn through the catheter. 11. Do not force the guidewire. If resistance is met, carefully withdraw the guidewire and re-attempt insertion. 12. Careflow™ catheters are not indicated for high pressure injection for such applications can result in inter-lumen crossover or rupture with potential for injury.
Venaguide	**Warning**
	• If the included guidewire does not have depth markings, Electrocardiogram (ECG) monitoring or Ultrasound guidance, or a combination of both is recommended to prevent under insertion/ over insertion of the guidewire
Guiding Syringe	**Warning**
	• Do not aspirate with guidewire in place or air may enter the syringe
Floswitch Products	**Warning**
	1. The Floswitch™ should not be switched off (black marks covered) before the needle has

Product Configuration	Labeling
	been fully withdrawn. This applies to Floswitch™ introducers only. 2. The Floswitch™ must not be switched off (black marks covered) until the guidewire has been fully withdrawn. 3. When the catheter is not in use for infusion or aspiration, the Floswitch™ must be switched off and a suitable luer cap locked into the hub. 4. When using an intermittent injection bung attached to a Floswitch™, only use short needles. Ensure Floswitch™ is in 'ON' position prior to injecting or aspirating. Do not insert the needle more than 8 mm into the Floswitch™. 5. As standard practice, the security of the luer connection must be checked routinely. This is essential when lubricious substances such as Intralipids are being used. This applies to Floswitch™ luer lock attachment only.
Scalpel	**Warning**
	Used sharps are contaminated. Handle carefully. Dispose scalpel in accordance with all applicable local and national laws and regulations.
Guidewires	**Warning**
	1. If the included guidewire does not have depth markings, Electrocardiogram (ECG) monitoring or Ultrasound guidance, or a combination of both is recommended to prevent under insertion/ over insertion of the guidewire. If the included guidewire has depth markings, stop when last depth mark of the guidewire reaches the insertion site to prevent over-insertion

4.3 Other Relevant Safety Aspects

There have been no field safety corrective actions or field notifications for the Careflow CVCs for the reporting period from January 1, 2017 to June 30, 2022.

5.0 Summary of Clinical Evaluation and Postmarket Clinical Follow-up (PMCF)

5.1 Summary of Clinical Data for the Equivalent Device

The Careflow CVC has been commercialized for several years and has an established history of use. In addition, the subject device utilizes well-established technology and exhibit a low complaint/incident rate. As an EU MDD and EU MDR Class III device, demonstration of equivalence to competitor devices is not permitted without access to the manufacturer technical file per MDR, Chapter VI, Article 61, Paragraph 5. Therefore, this evaluation is based on the subject device - the Careflow CVC. No equivalent device is claimed.

5.2 Summary of Clinical Investigations of the Subject Device

The Careflow CVC has been evaluated in two clinical investigations. Due to the age of these studies and the lack of access to the study reports pre-dating the Merit acquisition, these investigations were not included as pivotal data in this clinical evaluation.

5.3 Summary of Clinical Data from Other Sources – Literature

5.3.1 Literature Data - Safety and Performance

The clinical evaluation was based on the clinical literature and PMS data on the subject device. The subject device safety and performance outcomes from literature are summarized in Table 13. Technical Success represents a composite of device placement and subsequent pressure monitoring, TPN delivery, and/or fluid infusion. Device-related and procedure-related AEs are also listed in Table 13. The Device-related AE rate represents the established safety measure for the evaluation.

Table 13. Summary Performance and Safety Data Measures

Device	Careflow CVC
Technical Success (Composite)	**779/783 (99.5)**
Device Placement	420/420 (100)
Hemodynamic Pressure Monitoring	147/150 (98.0)
Blood Sampling	62/63 (98.4)
TPN Delivery	16/32 (50.0)
Fluid Infusion	150/150 (100)
Antimicrobial Activity	N/A
Device-related AE Rate	**16/270 (5.9)**
Procedure-related AE Rate	44/270 (16.3)

The rates of device- and/or procedure-related AEs are provided in Table 14. Additionally, AEs identified in case reports are summarized in Table 10. Catheter malposition, occlusion, and vein thrombosis were the most common device-related AEs attributed to the Careflow CVCs.

Table 14. Adverse Events Reported in the Literature

Adverse Events (AEs)	Careflow CVC AE Rate n/N (%)	Device-Related	Patient Condition/ Procedure-Related	Time of Occurrence
Accidental dislodgement	2/270 (0.7)[100]	-	X	< 30 days

Adverse Events (AEs)	Careflow CVC AE Rate n/N (%)	Device-Related	Patient Condition/ Procedure-Related	Time of Occurrence
Arterial puncture	5/270 (1.9)[100]	-	X	Procedural
Catheter disconnect	0/270 (0)	-	X	< 30 days
Catheter malposition	31/270 (11.5)[99, 101]	-	X	< 30 days
Erythema	0/270 (0)	-	X	< 30 days
Migration	5/270 (1.9)[100]	X	X	< 30 days
Occlusion	11/270 (4.1)[100]	X	X	< 30 days
Pain during infusion	0/270 (0)	-	X	< 30 days
Pneumothorax	4/270 (1.5)[101]	-	X	Procedural
Pulmonary embolism	0/270 (0)	X	X	< 30 days
Thrombophlebitis	0/270 (0)	X	X	< 30 days
Tissue overgrowth	0/270 (0)	X	X	< 30 days
Thrombosis	2/270 (0.7)[101]	X	X	< 30 days
TOTAL	**60/270 (22.2)**			

Based on the clinical literature data, the subject devices exhibit acceptable safety and performance in patients requiring central venous catheterization. Clinical safety (lack of Device/Procedure-related AEs) and performance (Technical Success) are all high and comparable to the identified benchmark devices. All adverse events identified in the literature are appropriately captured in the risk documentation.

5.3.2 Patient Population Data Mapping

The Careflow CVCs are intended for both pediatric and adult patients, which include all age groups. The published clinical data have been stratified to support the use the Careflow in patients of all age groups. See table below:

Table 15. Patient Population, Indications and Careflow Configurations

Patient Populations		Author (Year) LOE Study Type	Indications	Access Sites	Patient #, age	Careflow Configurations, #	Performance Outcomes (Technical success)	Safety Outcomes (Total Device AE %)
Pediatric	**Neonate - Infant**	Ragavan (2010)[11]	Parenteral Nutrition (PN)	Internal jugular	32/92	2.5 Fr 100-mm single lumen (32)	100% (with 2 attempts)	Occlusion (11) [Migration (5) these AEs were either device related or

Patient Populations		Author (Year) LOE Study Type	Indications	Access Sites	Patient #, age	Careflow Configurations, #	Performance Outcomes (Technical success)	Safety Outcomes (Total Device AE %)
0-21	**0-6 months**	LOE: B2		vein	4.82 d			procedural related or both
				Cubital vein	60/92 4.76 d	2.5 Fr 100-mm single lumen (60)	100% (with 1.1. attempts)	Occlusion (5), Migration (4) these AEs were either device related or procedural related or both
	Infant-children 6 months – 12 yr	• No published data available • Merit will plan to collect relevant data from the continued PMCF activities						
	Adolescent 12-21 yr	Jung (2007)[5] LOE: B2	Evaluation of a novel approach for CVC subclavian placement	Right subclavian vein	105/105 53 ± 14 yrs (18-82)	double-lumen (105)	100%	No device or other AEs reported N=2 procedural AEs
Adults (≥22 yrs)	**Adults (22-79)**	Hansen (2013)[3] LOE: C	Blood sampling	IJV	16/16 27.5 (21-35)	5Fr 200-mm (16)	100%	0 SAE or procedural AEs; Minor discomfort including neck/body-tightness and pressure, headache and warm feeling, resolved within 30 mins of drug administration
		Pal 2014[8] LOE D	Infusion Blood monitoring	LIJV	35-year (1)	3-lumen, other details not reported	100% (surgery placement)	Guide-wire complications (solved by surgery) Patient (70% burn injury) recovered
		McGrath 2006[10] LOE D	Infusion Blood sampling PM	SCV	28 yrs (1)	Quadruple-lumen CVC 8.5 Fr, 2.9mm outer diameter, Careflow, BD	100% Clinically successful for treatment procedure and remained in patient for 3 days for further monitor and infusion	Removed in 3 days for dislodgement
		Gopal (2014)[2]	Infusion	IJV or	22/22	4 and 5 lumen (22)	100%	0

Patient Populations		Author (Year) LOE Study Type	Indications	Access Sites	Patient #, age	Careflow Configurations, #	Performance Outcomes (Technical success)	Safety Outcomes (Total Device AE %)
	Adults (22-79)	LOE: C	Blood Sampling Blood Pressure monitoring	subclavian vein (SCV)	66.5 (19-80) yrs	(Fr size unspecified, based on size of veins)		
		Hong (2017)[4] LOE: B2	Blood pressure monitoring Infusion	SCV	109/109 59.0 ± 19.3 yrs	7Fr 150-mm (109)	100%	Not reported
		Vezzani (2010)[6] LOE: B1	Not Specified	Subclavian vein (85) Internal jugular vein (26)	111/111 60 ± 18 yrs	Careflow, 7Fr 20-cm dual-lumen (BD) (111)	100%	No device AE reported
	Elderly (≥80)	Blixt (2013)[1] LOE: C	Blood Sampling	Right jugular vein (RJV)	6/10 59.7(27-81) yrs	5Fr, 15-cm double-lumen (6)	100%	0
		Zhang (2016)[7] LOE: C	BPM BS Infusion	NR	19/19 74.6 ± 12.3 yrs	Not specified (configuration choice based on patient needs)	100%	Not reported

As shown in the table, published clinical data support the Careflow CVC application, clinical safety and performance in neonatal (pediatric) and adult patients:

- Sufficient data support the application of the majority of configurations in adult patient populations of all ages (≥ 22 years) for all IFU indications, including infusions of therapeutic agents, parenteral nutrition (PN), or other fluids as well as central venous pressure monitoring and blood sampling.
- For pediatric patients, only the small sized Careflow CVCs (2.5Fr) were used in neonatal patients for PN. There is no published data support the performance of Careflow CVCs in pediatric patient groups ages 6 months – 21 years. To obtain clinical data in pediatric patients from 6 months to 21 years old for all IFU indications (infusion, pressure monitoring and blood sampling, Merit will continue to

collect all data relevant to the Careflow CVCs in all patient age groups to close the data gap.

5.4 Overall Summary of Clinical Performance and Safety

5.4.1 Overall Performance Data

The Performance data from the clinical literature for the subject device and the benchmark devices are summarized in Table 16. The subject device Composite Technical Success rate is determined to be non-inferior to the benchmark devices. As presented and analyzed in Table 16, the performance acceptance criteria are satisfied. Furthermore, the results of the performance analysis demonstrate that the subject device performs as intended and is state of the art.

Table 16. Performance Objective and Criteria for Careflow CVC

Device Type/Application	Subject Device, n/N (%)	Benchmark CVCs, n/N (%)	Estimated Difference [95% LBL]	LBL > (-10%)
Composite Technical Success				
Careflow CVC	795/815 (97.5)	2249/2251 (99.9)	-2.4% (-3.3%)	**PASS**

Abbreviations: LBL = lower bound limit

Cumulative data support overall performance of the Careflow CVCs. The available data has also been stratified to support Careflow configurations as shown in Table 17. The stratification was based on lumen numbers and French size of the catheters that are available in the EU market. As presented in the table, specific data were obtained to support most of the configurations of the Careflow CVCs. For the configurations only supported by nonspecific clinical studies, Merit will continue to collect relevant data through proactive PMCF activities, as shown in the following table.

Table 17. Performance Analysis of Careflow Configurations

Careflow Configurations		Literature	Performance Technical Success (%)	Criteria: ≥ 99.9%) Met or Not (Justifications)
Lumens	OD (Fr)			
Configurations not specified;		Zhang (2016)	100% (19/19)	**Yes** Data may support any configurations
1 Lumen	2.5 Fr	Ragavan (2010)	100% (91/92, with 1-2 attempts)	**Yes**
	3 Fr	• Devices may be supported by clinical studies but not being specified (Zhang 2016) • Merit will plan to collect relevant data through PMCF activities		

Careflow Configurations		Literature	Performance Technical Success (%)	Criteria: ≥ 99.9%) Met or Not (Justifications)
Lumens	OD (Fr)			
	4 Fr			
	5 Fr	Hansen (2013)	100% (16/16)	**Yes**
	7 Fr	Hong (2017)	100% (109/109)	**Yes**
2 Lumen	unspecified	Jung (2007)	100% (105/105)	**Yes** Data may support any 2 lumen Configurations
	4 Fr	• Devices may be supported by clinical studies but not being specified (Zhang 2016, Jung 2017). • Merit will plan to collect relevant data through PMCF activities		
	5 Fr	Blixt (2013)	100% (10/10)	**Yes**
	7 Fr	Vezzani (2010)	100% (111/111)	**Yes**
3 Lumen	unspecified	Pal 2014	100% (1/1)	**Yes**
	5 Fr	• Devices may be supported by clinical studies but not being specified (Zhang 2016, Pal 2014). • Merit will continue to collect relevant data with PMCF activities		
	7 Fr			
4 Lumen	8.5 Fr	Gopal (2014)	100% (22/22)	**Yes** Study included both 4- and 5-lumen Careflow CVCs, therefore support both 8.5 and 9.8Fr configurations

5.4.2 Overall Safety and Risk Data

Safety data from the clinical literature for the subject device and the benchmark devices are summarized in Table 18. As indicated by the data, the AE rates for the subject devices are low and comparable to those reported for the benchmark devices. The subject device Device-related AE rates are determined to be non-inferior to the benchmark devices. The safety acceptance criteria are satisfied. Furthermore, the results of the safety analysis demonstrate that the subject device achieves a high level of patient safety and is state of the art.

Table 18. Safety Objective and Criteria for Careflow

Device Type/Application	Subject Device, n/N (%)	Benchmark Competitors, n/N (%)	Estimated Difference [95% UBL]	UBL < 10%
Device-related AE Rate				
Careflow CVC	16/270 (5.9)	0/2209 (0.0)	5.9% [8.3%]	PASS

Abbreviations: UBL = upper bound limit

The safety analysis for the Careflow configurations were based on the PMS and literature data. As for the PMS data, none of the complaints against the Careflow CVCs resulted in vigilance reporting or CAPA or field actions relating to a patient safety issue. Collective literature safety data on all configurations have met the predefined criteria in above section. For the configurations lack of literature data, the low complaint rates vs sales data fully support the safety of those device configurations. See the table below for details.

Table 19. Risks and Safety of Careflow Configurations

Careflow Configurations		PMS		Literature Safety		Criteria Met or Not (Justification)
Lumens	OD (Fr)	Global Sales	Complaints	Source	Total Device-Related AE%	
Configurations not specified; choices based on patient needs		—	—	Zhang (2016)	0% (0/19)	**Yes** May support safety for all configurations
1 Lumen	2.5 Fr	14528	1 (0.007%)	*Ragavan (2010)	27% (25/92)	**Yes** with Justifications (see below*)
	3 Fr	21265	1 (0.005%)	—	—	**Yes**
	4 Fr	9969	2 (0.02%)	—	—	**Yes**
	5 Fr	27886	27 (0.097%)	Hansen (2013)	0% (0/16)	**Yes**
	7 Fr	8530	2 (0.023%)	Hong (2017)	0/109	**Yes**
2 Lumen	Unspecified	—	—	Jung (2007)	0/105	**Yes** May support safety of all 2 lumen configurations
	4 Fr	13311	1 (0.008%)	—	—	**Yes**
	5 Fr	4733	1 (0.021%)	Blixt (2013)	0/10	**Yes**

Careflow Configurations		PMS		Literature Safety		Criteria Met or Not (Justification)
Lumens	OD (Fr)	Global Sales	Complaints	Source	Total Device-Related AE%	
	7 Fr	75619	6 (0.008%)	Vezzani (2010)	0/111	**Yes**
3 Lumen	Unspecified	—	—	Pal 2014	0/1	**Yes**
	5 Fr	8585	1 (0.012%)	—	—	**Yes**
	7 Fr	158329	19 (0.012%)	—	—	**Yes**
4 Lumen	8.5 Fr	27500	4 (0.015%)	Gopal (2014)	0/22	**Yes**
5 Lumen	9.5 FR	76965	4 (0.005%)			**Yes**

*Most of the patients had complications that were not related to the CVC but caused by critical medical conditions and CVC-related or unrelated medical procedures. The main CVC-related complications were arterial punctures, occlusion, dislodgement and migration, which were mostly minor to moderate events that required no further interventions. The majority of the patients were able to complete the CVC therapies. No death was reported in this study. According to the authors, the event rates were comparative with the literature review and the application of the 2.5Fr Careflow CVCs in newborns was considered safe, effective and reliable.

5.4.3 Summary of Risk vs Benefits

The clinical data demonstrates that the risks associated with the devices in the Careflow CVCs and Kits are acceptable when weighed against the clinical benefits to the patient. All CVC catheterization modalities have a risk of complications and/or failure, and the risks for an individual are an unpredictable combination of patient, the primary surgical/interventional procedure, and device-related interactions. The subject devices are intended to facilitate invasive blood pressure monitoring, blood sampling, and fluid infusion in patients who require or elect the supported procedures as their treatment modality.

The subject devices were deemed consistent with the state-of-the-art benchmark devices for safety and performance in this patient population. The devices in the Careflow CVCs and Kits are well established, having demonstrated acceptable safety and performance profile since the implantation tools/accessories and catheters were first commercialized in 1998. Based on design verification/validation testing results, safety and performance outcomes in the literature, and Post-market surveillance data, there are no known uncertainties regarding safety and performance of the subject device or the intended use. The known risks are well-documented, and the risk of occurrence is low and not associated with any safety or performance signals.

The clinical indications identified in the IFUs for the Careflow CVC and Kits product configurations are supported by the clinical evidence presented in the clinical evaluation report. Furthermore, the IFUs contain correct and sufficient information to reduce the risk of user error as well as information on residual risks and their management as supported by clinical evidence (e.g., handling and use instructions, description of risks, warnings, precautions, cautions, indications and contraindications, and instructions for managing foreseeable unwanted situations). The overall

clinical benefits to the patient of the Careflow CVC and Kits substantially outweigh any residual risks associated with their clinical use. The risk/benefit assessment for the Careflow CVC is summarized in Table 20. The devices in the Careflow CVC and Kits are indicated for use in patients undergoing procedures requiring devices which facilitate invasive blood pressure monitoring, blood sampling, and fluid infusion. High Technical Success rates and acceptable device-related AE rates have been demonstrated for the Careflow CVC and Kits. Therefore, the risks associated with the use of subject devices are low and outweighed by the clinical benefits, when used in accordance with the IFU.

Table 20. Summary of Benefit/Risk Assessment[8,9]

Factor	Notes	Assessment
Uncertainty		
Quality of the study design	• How robust were the data?	8 articles; Careflow CVC (n=8)
Quality of the study conduct	• How was/were the study/studies designed, conducted and analyzed?	RCTs, prospective observational, retrospective series
	• Are there missing data?	No
Robustness of the study results analysis	• Are the results from the study/studies repeatable?	RCTs - yes
	• Is/Are this/these study/studies first-of-a-kind?	No
	• Are there other studies that achieved similar results?	Yes
Generalizability of the results	• Can the results of the study/studies be applied to the population generally, or are they more intended for discrete, specific groups?	Yes
Characterization of the disease/condition	• How does the disease/condition affect the patients that have it?	Patients requiring parenteral nutrition, or procedures requiring invasive blood pressure monitoring or blood sampling may have conditions that would otherwise be terminal
	• Is the condition treatable?	Yes, in many cases
	• How does the condition progress?	Conditions are often terminal and may results in substantial morbidity or death
Patient tolerance for risk, and perspective on benefit:	• Is there data regarding how patients tolerate the risks posed by the device?	No, patient feedback in terms of procedure tolerance or quality of life is not available.
	• Are the risks identifiable and definable?	Yes; see Table 8, Table 9, and Table 10

Factor	Notes	Assessment
Disease severity	• Is the disease so severe that patients will tolerate a higher amount of risk for a smaller benefit?	Yes, patients requiring parenteral nutrition, or procedures requiring invasive blood pressure monitoring or blood sampling may have conditions that would otherwise be terminal
Disease chronicity	• Is the disease/condition chronic? • How long do patients with the disease/condition live? • If chronic, is the illness easily managed with less invasive or difficult therapies?	Yes, in many cases the disease is chronic It depends on the specific condition of the patient No
Patient-centric assessment	• How much do patients value this treatment?	NA – subject device does not provide treatment; strictly for purposes of facilitating diagnostic tissue sample assessment
	• Are patients willing to accept the risk of this treatment to achieve the benefit?	N/A
	• Does the treatment improve overall quality of life?	N/A
	• How well are patients able to understand the benefits and risks of the treatment?	N/A
Availability of alternative treatments or diagnostics	• What other therapies are available for this condition?	CVC catheterization is not a therapy. There are typically no alternatives to the use of CVC catheterization.
	• How effective are the alternative treatments?	N/A
	• How does their effectiveness vary by subpopulation?	N/A
	• How well-tolerated are the alternative therapies?	N/A
	• How does their tolerance vary by subpopulation?	N/A
	• What risks are presented by any available alternative treatments?	N/A
Risk mitigation	• Could you identify ways to mitigate the risks (such as using product labeling, establishing education programs, providing add-on therapy, etc.)? • What is the type of intervention proposed?	No N/A

Factor	Notes	Assessment
Postmarket data	• Are there other devices with similar indications on the market? Are the probabilities for effectiveness and rates of harmful events from those devices similar to what is expected for the device under review?	Yes; see Table 7 and Table 11
	• Is postmarket data available that change the risk/benefit evaluation from what was available when the previous devices were evaluated?	No
	• Is there reason to consider evaluation of any of the following elements further in the postmarket setting, due to the risk/benefit evaluation as described above? ○ Longer-term device performance. ○ Effectiveness of training programs or provider preferences in use of device. ○ Subgroups (e.g., pediatrics, women). ○ Rare adverse events.	See Section 5.5
	• Is there reason to expect a significant difference between real-world performance of the device and the performance found in pre-market experience with the device?	No; data presented are derived from real-world randomized studies, case series, and case reports
	• Is there data that otherwise would be provided to support approval, which could be deferred to the postmarket setting?	No
	• Is there off-label use, or on-label use that is different than originally expected?	No
Novel technology addressing unmet medical need	• How well is the medical need this device addresses being met by currently available therapies?	Comparable state-of-the-art CVC devices are commercially available
	• How desirable is this device to patients?	Use of the device to facilitate invasive blood pressure monitoring, blood sampling, and fluid infusions is medically necessary, safe, effective, and desirable

<table>
<tr><th>Factor</th><th>Notes</th><th>Assessment</th></tr>
<tr><th>Summary of the Benefit(s)</th><th>Summary of the Risk(s)</th><th>Summary of Other Factors</th></tr>
<tr><td>
<table>
<tr><th>Device/System</th><th>Technical Success n/N (%)</th></tr>
<tr><td>Careflow CVC</td><td>795/815 (97.5)</td></tr>
<tr><td>Benchmark Competitor Devices</td><td>2249/2251 (99.9)</td></tr>
</table>
</td><td>
<table>
<tr><th>Device/System</th><th>Device-Related AE Rate n/N (%)</th></tr>
<tr><td>Careflow CVC</td><td>16/270 (5.9)</td></tr>
<tr><td>Benchmark Competitor Devices</td><td>0/2209 (0.0)</td></tr>
</table>
</td><td>CVCs provide a safe and effective means to facilitate invasive blood pressure monitoring, blood sampling, and fluid infusions.</td></tr>
</table>

5.5 Postmarket Clinical Follow-up (PMCF)

Consideration has been made regarding Postmarket Clinical Follow-Up (PMCF). Known and foreseeable hazards and associated risks have been identified and reduced as low as possible. The Merit Tech Team group actively monitors all after-market field data. In an effort to establish additional clinical data for the Careflow CVCs and Kits, additional PMCF studies are planned as detailed in the PMCF Plan. Briefly, the plan summarizes:

Specific PMCF activities: A patient-level survey will be conducted. Questionnaires will be distributed to healthcare providers who conducted procedures with the Merit Careflow CVCs. The questionnaires contain questions relevant to patient population, indications for use, CVC insertion sites, and other safety and performance results: device related adverse events, purposes of insertions and insertion success and dwell time. The survey data will be collected and analyzed according to the plan and reported in the PMCF report.

Other general PMCF activities may include literature review, database searches for publicly available safety and performance information on the subject devices and similar devices. Currently, no PMCF data is available for the CVCs. The future clinical data and results from the PMCF activities will be collected, analyzed and reported in the PMCF Report, CER and SSCP, per applicable EU MDR requirement and MDCG guidance.

6.0 Diagnostic or Therapeutic Alternatives

6.1 Review of Medical Condition

Central venous catheterization is integral to the clinical management of critically ill patients, irrespective of age.[10-12] Medical conditions that often warrant central venous catheterization may include cancer, kidney failure, cardiac arrest, neurologic bleeding, acute respiratory failure, sepsis, and trauma. Placement of central venous catheters typically occurs in the intensive care unit,[13,14] although insertion in the emergency room may be warranted.[15] The main sites for catheter insertion include the internal jugular vein, common femoral vein, and subclavian vein.[16] Central access is used for intravenous administration of medications (e.g., chemotherapy, hemodialysis), total parenteral nutrition, and to conduct repeated blood sampling and monitoring of central venous pressure.[13,17,18]

6.1.1 Treatment Options and Interventions

Since the first description of CVC placement in 1929, central access has remained a mainstay resource for the clinical management of acute and chronic conditions.[19] However, placement of CVCs is not without risk. Some of the complications related to catheterization include infection, thrombosis, device misplacement, and dislodgement.[20-22] The risks associated with central access varies based on the patient population and duration of catheter placement. Nevertheless, the diagnostic and therapeutic benefits of CVCs outweigh their potential risks, and they continue to be widely used in clinical practice.[12] Below, are common factors to consider as means to mitigate complications related to the use of CVCs in diverse patient populations.

Short-term vs Long-term CVCs

The duration of central venous access is determined based on the therapeutic needs of the patient.[23] Although cutoffs for what is considered short- versus long-term vary slightly, historically, catheters in place for over six weeks have been referred to as long-term access devices[24], although others define long-term access as greater than 30 days.[25] Short-term CVCs are critical for patients with limited peripheral access that require administration of intravenous therapies as well as patients that require frequent blood sampling.[26,27] Circumstances warranting long-term CVCs include delivery of chemotherapy, hemodialysis, and home total parenteral nutrition.[24] Despite the medical necessity of long-term access, there is an increase in risk of complications, such as catheter-related bloodstream infections and catheter-related thrombosis, that are associated with its use.[23,28] As a result, clinical guidelines specifically indicate prompt removal of catheters when they are no longer considered to be clinically necessary.[29]

Coated vs Non-coated CVCs

Bacterial colonization effectively begins once a CVC is placed; the resulting biofilm may be antibiotic resistant.[26] Catheter-related bloodstream infections associated with the use of CVCs represent one of the most common, potentially fatal, and costly complications of CVC use.[30] To reduce the risk of catheter-related blood stream infections, CVCs may be coated with a variety of anti-adhesive and anti-infective materials.[31,32] Common materials used to coat CVCs include benzalkonium, carbon, chlorhexidine, heparin, minocycline, platinum, rifampicin, and silver; these materials may be used alone or in various combinations.[33] However, some of the materials used to coat CVCs may induce allergic reactions in patients.[33] For example, chlorhexidine can cause severe anaphylactic reactions, particularly in the perioperative setting[34]; therefore, pre-screening and testing patients prior to use of coated catheters represent a necessary precaution to avoid severe and potentially fatal complications.[35]

Studies comparing clinical outcomes of patients with coated versus uncoated CVCs have been mixed. A systematic literature review and meta-analysis of 23 studies found that relative to uncoated CVCs, catheters impregnated with chlorhexidine-silver sulfadiazine or other antibiotics resulted in substantially lower catheter-related bloodstream infections per 1000 catheter days (odds ratio [95% credibility interval]: 0.64 [0.40–0.955] and 0.53 [0.25–0.95], respectively) and a lower incidence of catheter colonization (odds ratio [95% credibility interval]: 0.44 [0.34–0.56] and 0.30 [0.20–0.46], respectively).[36] However, others have found no clear benefit associated coated versus non-coated CVCs.[37] [38] A pilot study that compared adverse events and microbial colonization among patients randomized to receive metal alloy coated CVCs or uncoated CVCs prior to major surgery found that although adverse events were lower in the coated versus uncoated CVC group (0 vs. 5 events; p=0.011), no differences in microbial colonization

were observed between the groups.[39]

In the absence of a consensus regarding the clear benefit of coated versus uncoated CVCs, some clinicians may opt to use uncoated CVCs.[33] Factors to consider when making this decision include whether patients have an allergy to coating material, duration of CVC use, duration of stay in the intensive care unit (e.g., short, long), context of CVC insertion (e.g., emergency, elective), patient immune function (e.g., compromised, normal), acute condition (e.g., single organ disease, multi-organ failure), and transplantation (e.g., solid organ recipient).[33]

6.1.2 CVC Placement Techniques

Correct positioning of a CVC tip is critical to avoid complications.[40] Adverse events that can result from ill-placed CVCs include catheter displacement, kinking, loss of fixation, insertion site hyperemia, purulent discharge at the insertion site, pneumothorax, and possible device loss.[41] [20,21,42,43] Historically, CVCs were inserted and positioned based on the operator's knowledge of anatomical landmarks. A chest radiograph after CVC placement using the anatomical landmark technique was obtained to confirm positioning; however, this delayed CVC use, and chest radiographs do not have sufficient sensitivity to detect critical complications, such as pneumothorax, and expose patients to radiation.[44] Compared to radiographs, electrocardiography and ultrasonography are increasingly used to assist with CVC placement in real-time thus reducing procedure time and the need for corrections post-placement.

Electrocardiogram guided CVC placement allows the operator to confirm correct positioning of the CVC tip in real-time by monitoring changes in P-wave morphology.[40,45] Real-time monitoring of electrocardiographic changes during CVC placement have been reported to have procedural success rates as high as 100% (compared to 82% when anatomical landmarks are used for CVC placement).[45]

Similar to electrocardiogram-guided CVC placement, the benefits associated with the use of real-time ultrasonography to guide CVC placement are that it permits the operator to confirm correct positioning of the CVC and reduces complications. However, with real-time ultrasonography operators can visualize the intended vein and its anatomical relationship to adjacent structures in addition to the needle for catheterization.[46,47] Moreover, relative to electrocardiography real-time ultrasound guidance allows for more consistent visualization of the catheter.[44] Several studies have documented the substantial benefits associated with real-time ultrasound guided CVC placement.[14,46,48-53] For example, a prospective study that compared procedural success and complications of CVC placement using standard anatomical landmarks versus ultrasound guidance reported that compared to use of anatomical landmarks, real-time ultrasound guidance was more successful (98% vs. 90.5%) with significantly lower complication rates (4% vs. 14.5%).[46]

Any technique that will allow operators to safely and reliably position CVCs is desired for patient safety and procedural success.[42,54] Based on the information retrieved from the literature, placement of CVCs using electrocardiography and ultrasound guidance are common practices that have helped achieve both of these goals.

6.2 Alternative Interventions

While CVCs are likely to remain essential for the clinical management of critically ill patients, lower risk options that do not require surgery and urgency in removal to avoid complications such as infection and thrombosis may be preferred. In certain settings, CVCs have become replaced by port catheters which have the advantage no visible external line thus eliminating the risk of pulling and impairing patients' quality of life.[55] Another increasingly recognized alternative to CVCs is the peripherally inserted central catheter.[56] Peripheral catheters are safer to insert and have been reported to have low procedural-related risks relative to CVCs.[55,57,58] For example, one study that evaluated the safety and efficacy of 137 peripherally inserted central catheters in elderly patients with multiple comorbidities that often required concomitant therapies (e.g., non-invasive ventilation and continuous veno-venous hemofiltration) found that none of the inserted catheters were associated with major complication. Moreover, the rate of catheter-related peripheral thrombosis was 1.4% (compared to the 5-18% with CVCs) and the rate of catheter-related bloodstream infection was 0.7% (occurring in one patient).[57]

Midline catheters are another alternative to CVCs (and peripheral venous catheters).[59] In select patients, midline catheters allow for a longer duration of access and are associated with lower risk of complications relative to CVCs.[60] One study that evaluated the safety and efficacy of intravenous vancomycin administered through short- and long-term midline catheters in 1,086 patients found no catheter-associated bloodstream infections nor any evidence of deep vein thromboses, in rare instances, phlebitis occurred (0.6%) and benign infiltrations (1.2%).[61]

While alternatives to CVCs are available, it is necessary to balance the urgency of access, risk posed to patients, comorbidities present, and duration of treatment required.[62]

6.3 Professional Guidelines and Recommendations

Clinical practice guidelines and consensus statements issued by professional societies were reviewed[29,62-70] to inform with respect to conventional and guided CVC placement as well as CVC management. The practice guidelines identified are listed below:

- Practice Guidelines for Central Venous Access 2020: An Updated Report by the American Society of Anesthesiologists Task Force on Central Venous Access[29].
- Indian Society of Critical Care Medicine Position Statement for Central Venous Catheterization and Management 2020[67].
- Clinical practice guidelines for the management of central venous catheter for critically ill patients 2018[65]
- CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections, 2011 with 2017 updates[66]

The published guidelines reflect the judgment of acknowledged experts in the field who, based on their experience and on a detailed examination of the available literature, provide guidance to the general medical community on central venous catheterization / central venous access. These guidelines utilize various levels of evidence and strength of recommendation grading systems. These are summarized in the following section.

Table 21. Clinical Evidence Appraisal Methods

<table>
<tr><th>Guideline</th><th>Grading System</th></tr>
<tr><td>Practice Guidelines for Central Venous Access 2020: An Updated Report by the American Society of Anesthesiologists Task Force on Central Venous Access[29]</td><td>
Strength of Recommendation
<table>
<tr><th>Rank</th><th>Description</th></tr>
<tr><td>Category A</td><td>RCTs report comparative findings between clinical interventions for specified outcomes. Statistically significant (P < 0.01) outcomes are designated as either beneficial (B) or harmful (H) for the patient; statistically nonsignificant findings are designated as equivocal (E).</td></tr>
<tr><td>Category B</td><td>Deemed appropriate by the majority of experts, but some degree of dissension exists. The desirable effects of adherence to the recommendation probably outweigh the undesirable effects.</td></tr>
</table>
Level of Category A Evidence
<table>
<tr><th>Level</th><th>Description</th></tr>
<tr><td>Level 1</td><td>The literature contains a sufficient number of randomized controlled trials (RCTs) to conduct meta-analysis and meta-analytic findings from these aggregated studies are reported as evidence.</td></tr>
<tr><td>Level 2</td><td>The literature contains multiple RCTs, but the number of RCTs is not sufficient to conduct a viable meta-analysis for the purpose of these Guidelines. Findings from these RCTs are reported separately as evidence.</td></tr>
<tr><td>Level 3</td><td>The literature contains a single RCT, and findings from this study are reported as evidence.</td></tr>
</table>
Level of Category B Evidence
<table>
<tr><th>Level</th><th>Description</th></tr>
<tr><td>Level 1</td><td>The literature contains nonrandomized comparisons (e.g., quasiexperimental, cohort [prospective or retrospective], or case-control research designs) with comparative statistics between clinical interventions for a specified clinical outcome.</td></tr>
<tr><td>Level 2</td><td>The literature contains noncomparative observational studies with associative statistics (e.g., correlation, sensitivity, and specificity).</td></tr>
<tr><td>Level 3</td><td>The literature contains noncomparative observational studies with descriptive statistics (e.g., frequencies, percentages).</td></tr>
<tr><td>Level 4</td><td>The literature contains case reports.</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Guideline</th><th>Grading System</th></tr>
<tr><td>Indian Society of Critical Care Medicine Position Statement for Central Venous Catheterization and Management 2020[67]</td><td>
Strength of Recommendation
<table>
<tr><th>Grade</th><th>Description</th></tr>
<tr><td>A</td><td>Strong recommendations to do (or not to do) where the benefits clearly outweigh the risk (or vice versa) for most, if not all patients.</td></tr>
<tr><td>B</td><td>Weak recommendations, where benefits and risk are more closely balanced or are more uncertain.</td></tr>
</table>
Level of Evidence
<table>
<tr><th>Level</th><th>Description</th></tr>
<tr><td>Level 1</td><td>Evidence from ≥1 good quality and well-conducted randomized control trial(s) or meta-analysis of RCT's.</td></tr>
<tr><td>Level 2</td><td>Evidence from at least 1 RCT of moderate quality, or well-designed clinical trial without randomization; or from cohort or case-controlled studies.</td></tr>
<tr><td>Level 3</td><td>Evidence from descriptive studies, or reports of expert committees, or opinion of respected authorities based on clinical experience.</td></tr>
<tr><td>Useful Practice Point (UPP)</td><td>Not backed by sufficient evidence; however, a consensus reached by the working group, based on clinical experience and expertise.</td></tr>
</table>
</td></tr>
<tr><td>Clinical practice guidelines for the management of central venous catheter for critically ill patients 2018[65]</td><td>
Strength of Recommendation
<table>
<tr><th>Grade</th><th>Description</th></tr>
<tr><td>Strong</td><td>Strong recommendations to do (or not to do) where the benefits clearly outweigh the risk (or vice versa) for most, if not all patients.</td></tr>
<tr><td>Week</td><td>Weak recommendations, where benefits and risk are more closely balanced or are more uncertain.</td></tr>
</table>
Level of Evidence
<table>
<tr><th>Level</th><th>Description</th></tr>
<tr><td>Level A</td><td>High level of evidence. The true effect is close to our estimate of the effect</td></tr>
<tr><td>Level B</td><td>Moderate level of evidence. The true effect is likely to be close to our estimate of the effect, but there is a possibility that it is substantially different.</td></tr>
<tr><td>Level C</td><td>Low level of evidence. The true effect may be substantially different from our estimate of the effect.</td></tr>
<tr><td>Level D</td><td>Very low level of evidence. Our estimate of the effect is just a guess, and it is very likely that the true effect is substantially different from our estimate of the effect.</td></tr>
</table>
</td></tr>
</table>

Guideline	Grading System
CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections, 2011 with 2017 updates [66]	**Strength of Recommendation** **Grade** / **Description** Category IA. — Strongly recommended for implementation and strongly supported by welldesigned experimental, clinical, or epidemiologic studies. Category IB. — Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale; or an accepted practice (e.g., aseptic technique) supported by limited evidence. Category IC. — Required by state or federal regulations, rules, or standards. Category II. — Suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.

6.4 Standard of Care Recommendations

The relevant standard of care and clinical practice guidelines for CVC placement and maintenance are summarized in Table 22.

Table 22. Standard of Care Guidelines and Recommendations for the Management of Medical Condition

Recommendation	Strength of Recommendation/	Level of Evidence
Practice Guidelines for Central Venous Access 2020: An Updated Report by the American Society of Anesthesiologists Task Force on Central Venous Access[29]		
Aim: To provide guidelines for anesthesiologists and those under the supervision of an anesthesiologist. These guidelines can also serve as a resource for other clinicians (e.g., surgeons, radiologists), nurses, or healthcare providers who manage patients with CVCs.		
Resource preparation: (1) perform central venous catheterization in an environment that permits use of aseptic techniques and to ensure that a standardized equipment set is available for central venous access; (2) use a checklist or protocol for placement and maintenance of CVCs; (3) use an assistant during placement of a CVC.	Strong	
Do not recommend routine administration of intravenous antibiotic prophylaxis.	Strong	
Aseptic Preparation of practitioner, staff, and patients should include aseptic techniques (e.g., hand washing) and maximal barrier precautions (e.g., sterile gowns, sterile gloves, caps, masks covering both mouth and nose, and full-body patient drapes) in preparation for the placement of CVCs.	Strong	
Suggest chlorhexidine containing solution for skin preparation in adults, infants, and children. For neonates, determine the use of chlorhexidine-containing solutions for skin preparation based on clinical judgment and institutional protocol. If there is a contraindication to chlorhexidine, povidone–iodine or alcohol may be used or skin preparation solutions containing alcohol unless contraindicated.	Strong	

Recommendation	Strength of Recommendation/	Level of Evidence
Recommend use of catheters coated with antibiotics or a combination of chlorhexidine and silver sulfadiazine based on infectious risk and anticipated duration of catheter use.	Strong	
Discourages use of antimicrobial agents as a substitute for additional infection precautions.	Strong	
Determine catheter insertion site selection based on clinical need that is not contaminated or potentially contaminated (e.g., burned or infected skin, inguinal area, adjacent to tracheostomy, or open surgical wound) and is present in the upper body whenever feasible to minimize risk of infection.	Strong	
Determine the use of sutures, staples, or tape for catheter fixation on a local or institutional basis.	Strong	
Use transparent bioocclusive dressings to protect the site of CVC insertion from infection containing chlorhexidine in adults, infants, and children unless contraindicated. For neonates, determine the use of transparent or sponge dressings containing chlorhexidine based on clinical judgment and institutional protocol. If a chlorhexidine-containing dressing is used, observe the site daily for signs of irritation, allergy, or necrosis.	Strong	
Determine the duration of catheterization based on clinical need; promptly remove when no longer deemed necessary.	Strong	
Select catheter size and type based on the clinical situation and skill/experience of the operator and the smallest size catheter appropriate for the clinical situation.	Strong	
Use real-time ultrasound guidance for vessel localization and venipuncture when the internal jugular vein is selected for cannulation.	Strong	
Indian Society of Critical Care Medicine Position Statement for Central Venous Catheterization and Management 2020[67]		
Aim: To provide critical care physicians and other medical professions with recommendations for the judicious use of CVC, insight regarding CVC placement and management, strategies to reduce mechanical, infectious, and thrombotic complications, and guidance to improve CVC care quality		
Indications of central venous catheterization		
Recommend central venous catheterization after understanding clear indication.	A	3
Recommend CVC when hyperosmolar and locally irritant agents are to be administered.	B	UPP
Recommend CVC use for vasoactive drugs unless the risk outweighs benefit of placing a CVC and delaying the therapy.	A	3
CVC placement in locations other than the intensive care unit		
In care areas, where CVC is utilized there should be a central venous cannulation and maintenance standard operating procedures.	A	UPP
In all units performing central venous cannulation should have a quality improvement program in place with follow-up of outcomes.	A	UPP
Recommend daily review for the necessity of CVC should be done at all care sites.	A	2
CVC site selection		
In emergency scenarios, insertion site selection should be based on patient factors, clinical need,	A	3

Recommendation	Strength of Recommendation/	Level of Evidence
practitioner judgment, experience and skills.		
Suggest subclavian insertion site should be preferred over internal jugular vein and femoral for central venous catheterization to decrease infectious and thrombotic complications.	B	2
Recommend subclavian vein to be avoided in patient with coagulopathy, distorted anatomy, and who may have high chances of mechanical complications.	A	2
In case of burns, extensive skin loss and superficial infections, CVC insertion should be done where the skin is intact.	A	UPP
Recommend internal jugular CVC lines could safely be inserted in adult neurocritical care patients.	B	2
Catheter selection		
Suggest using a CVC with the minimum number lumens needed for patient management.	B	3
No recommendation can be made for designated lumen for parenteral nutrition. Unresolved issue.	B	3
CVC—Infection control		
Evaluate risk-to-benefit ratio of infectious and mechanical complications before choosing a particular insertion site.	B	2
Avoid using femoral vein for the routine placement of central venous catheters.	A	2
Recommend mandatory hand hygiene practice, either by washing hands with conventional soap and water or with alcohol-based hand rub, before and after any interventions or contact with CVC.	A	2
Recommend maintaining aseptic technique for insertion and maintenance of CVC.	A	2
Recommend maximal sterile barrier precautions before any insertion (de novo or exchange over guidewire) of CVC.	A	1
Recommend wearing either clean or sterile gloves when handling or dressing the CVC.	A	3
Recommend preparation and cleaning of the skin site with an alcoholic chlorhexidine solution containing a concentration more than 0.5% chlorhexidine and 70% alcohol before central venous catheter insertion and during dressing changes.	A	1
Recommend use tincture of iodine, an iodophor, or 70% alcohol use as alternatives if chlorhexidine is contraindicated.	B	3
Recommend allowing the skin antiseptic to dry completely before catheter insertion.	A	2
CVC Fixation		
No recommendation can be made for preference of securing system and operator or local practice based decision should be taken.	B	3
Port utilization and maintenance		
Recommend disinfecting catheter hubs, needleless connectors, taps and injection ports before accessing the catheter using an alcoholic chlorhexidine preparation or 70% alcohol.	A	2

Recommendation	Strength of Recommendation/	Level of Evidence
Recommend wearing either clean or sterile gloves when handling the hub and catheter.	A	3
Prophylactic antibiotics and antiseptics		
No recommendation can be made for or against the use of antiseptic solutions (aqueous chlorhexidine or aqueous povidone-iodine) for routine CVC site care.	A	3
Recommend the use of chlorhexidine-soaked sponge or dressing at the catheter exit site to prevent catheter-related bloodstream infections and daily chlorhexidine bed bath (sponging) for patients in the intensive care unit to reduce catheter-related bloodstream infections.	A	1
Suggest antibiotic lock solutions to prevent catheter-related bloodstream infection only in the following selected conditions: a) Limited or difficult venous access and a history of recurrent catheter-related bloodstream infection; b) At high risk of severe sequelae from a central line-associated bloodstream infection (e.g., recently implanted intravascular devices, such as prosthetic heart valve or aortic graft); c) When catheter-related bloodstream infection rate is high despite all measures to reduce it are implemented stringently.	B	2
Recommend against systemic intravenous antibiotics in prevention of catheter-related bloodstream infection.	A	1
Removal of central line		
Recommend removing central venous catheter as soon as its indication ceases.	A	UPP
Suggest not routinely replacing or relocating the central venous lines unless clinically indicated.	B	UPP
Recommend each institute to have central venous catheter removal protocol and only staff trained in the same should remove central line.	A	UPP
Catheters impregnated with antiseptics and antibiotics		
Recommend using minocycline/rifampicin or chlorhexidine/silver sulfadiazine coated CVCs when catheter is expected to be in use for more than five days and the central line-associated bloodstream infection rate is not decreasing to the institutional target benchmark even after implementing comprehensive strategy program. Comprehensive strategy should include education and training, maximal barrier precaution and aseptic skin preparation while insertion of CVC.	A	1
Role of sonography		
Wherever available ultrasound guidance is recommended to improve success rate, patient safety and procedural quality and reduce mechanical complications during CVC placement.	A	2
Clinical practice guidelines for the management of central venous catheter for critically ill patients 2018[65]		
Aim: The guideline aims to provide evidence based state-of-the-art guidelines for the management of CVC in the intensive care unit in all critically ill patients treated in the ICU. This is a joint clinical practice guideline document developed by an expert group of intensivists, critical care nurses, personnel from infection		

Recommendation	Strength of Recommendation/	Level of Evidence
control, and emergency physicians from China, Italy, Israel, and the UK.		
(I) we commend the use of catheter impregnation to prevent catheterrelated blood stream infection	Strong	(1A)
(II) we suggest the use of real-time ultrasound guidance for subclavian or femoral vein insertion (2B), and recommend that for internal jugular vein	Weak	(1A)
(III) we suggest the use of realtime color Doppler ultrasound guidance on central venous catheterization for adult and pediatric patients	Weak	(2C);
(IV) we suggest not to use heparin for the maintenance of CVC patency	Weak	(2A)
(V) we suggest the use contrastenhanced ultrasound for the confirmation of central venous catheter placement	Weak	(2B)
(VI) we recommend the use of bedside ultrasound together with agitated or non-agitated normal saline to confirm CVC position	Strong	(1C)
(VII) we suggest to use subclavian site for CVC insertion	Weak	(2C)
(VIII) we suggest not to use heparin-bonded catheters or warfarin to prevent CVC-related deep vein thrombosis in children	Weak	(2D)
(IX) we recommend the implementation of central-line bundles to reduce the risk of CRBSI for adult, pediatric and neonatal ICUs	Strong	(1B)
(X) we suggest skin antisepsis with chlorhexidine throughout in-dwelling period for reducing CVC-related infections	Weak	(2D)
(XI) we recommend a differential time to positivity (DTP) of blood cultures from CVC and peripheral vein of 120 minutes to diagnose CRBSI	Strong	(1B)
CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections, 2011 with 2017 updates[67]		
Aim: The objective of this article is to provide a guidelines for the prevention of Intravascular catheter-related infections. The working group was led by the Society of Critical Care Medicine (SCCM), in collaboration with the Infectious Diseases Society of America (IDSA), Society for Healthcare Epidemiology of America (SHEA), Surgical Infection Society (SIS), American College of Chest Physicians (ACCP), American Thoracic Society (ATS), American Society of Critical Care Anesthesiologists (ASCCA), Association for Professionals in Infection Control and Epidemiology (APIC), Infusion Nurses Society (INS), Oncology Nursing Society (ONS), American Society for Parenteral and Enteral Nutrition (ASPEN), Society of Interventional Radiology (SIR), American Academy of Pediatrics (AAP), Pediatric Infectious Diseases Society (PIDS), and the Healthcare Infection Control Practices Advisory Committee (HICPAC) of the Centers for Disease Control and Prevention (CDC) and is intended to replace the Guideline for Prevention of Intravascular Catheter-Related Infections published in 2002.		
1. Weigh the risks and benefits of placing a central venous device at a recommended site to reduce infectious complications against the risk for mechanical complications (e.g., pneumothorax, subclavian artery puncture, subclavian vein laceration, subclavian vein stenosis, hemothorax, thrombosis, air embolism, and catheter misplacement).	Category IA	
2. Avoid using the femoral vein for central venous access in adult patients.	Category IA	
3. Use a subclavian site, rather than a jugular or a femoral site, in adult patients to minimize infection	Category IB	

Recommendation	Strength of Recommendation/	Level of Evidence
risk for nontunneled CVC placement.		
4. No recommendation can be made for a preferred site of insertion to minimize infection risk for a tunneled CVC.	Unresolved issue	
5. Avoid the subclavian site in hemodialysis patients and patients with advanced kidney disease, to avoid subclavian vein stenosis.	Category IA	
6. Use a fistula or graft in patients with chronic renal failure instead of a CVC for permanent access for dialysis.	Category IA	
7. Use ultrasound guidance to place central venous catheters (if this technology is available) to reduce the number of cannulation attempts and mechanical complications. Ultrasound guidance should only be used by those fully trained in its technique. [60–64].	Category IB	
8. Use a CVC with the minimum number of ports or lumens essential for the management of the patient.	Category IB	
9. No recommendation can be made regarding the use of a designated lumen for parenteral nutrition.	Unresolved issue	
10. Promptly remove any intravascular catheter that is no longer essential.	Category IA	
11. When adherence to aseptic technique cannot be ensured (i.e., catheters inserted during a medical emergency), replace the catheter as soon as possible, i.e., within 48 hours.	Category IB	

6.5 Additional Guidelines on CVC management and Risk Control

Other identified relevant guidelines also have statements related to the management of CVC for specific patient groups and user groups. They are summarized below:

2021 Infusion Therapy Standards of Practice, 8th Edition [68]

The comprehensive guidelines on infusion therapy are developed by the Infusion Nurses Society (INS) and updated in alignment with the American Society for Parenteral and Enteral Nutrition (ASPEN) guidance on filtration of parenteral nutrition (PN). This is general guideline document applying to is applicable to any patient population and any setting in which vascular, intraosseous (IO), subcutaneous, and intraspinal access devices are inserted and/or managed and where infusion therapies are administered. The guidelines cover all infusion access devices including central vascular access devices (all CVADs) and peripheral access devices (e.g. PICC, PIVC, artery cannula). The CVC related statements are included in the CVAD management content. The relevant recommendations on the CVAD including patient assessment, tip location, vascular access device selection, placement and management, infection prevention and control, and a summary of commonly associated complications: phlebitis, infiltration and extravasation, nerve injury, CVAD occlusion, infection, Catheter damage, air embolism, Catheter-related deep vein thrombosis (CRT and CR-DVT), CVAD malposition, Catheter-related skin injury.

2020 Expert consensus-based clinical practice guidelines management of intravascular catheters in the intensive care unit [69]

The is a joint guidelines for the management of CVC, Arterial catheters and dialysis catheters in intensive care unit by the French Society of Intensive Care Medicine (SRLF), jointly with the French-Speaking Group of Pediatric Emergency Rooms and Intensive Care Units (GFRUP) and the French-Speaking Association of Pediatric Surgical Intensivists (ADARPEF). The CVC related recommendations are:

The preferential use of subclavian central vein (GRADE 1), a one-step skin disinfection (GRADE 1) using 2% chlorhexidine (CHG)-alcohol (GRADE 1), and the implementation of a quality of care improvement program. Antiseptic- or antibiotic-impregnated CVC should likely not be used (GRADE 2, for children and adults). Catheter dressings should likely not be changed before the 7th day, except when the dressing gets detached, soiled or impregnated with blood (GRADE 2− adults). CHG dressings should likely be used (GRADE 2+). For adults and children, ultrasound guidance should be used to reduce mechanical complications in case of internal jugular access (GRADE 1), subclavian access (Grade 2) and femoral venous, arterial radial and femoral access (Expert opinion).

2020 ESPEN Guidelines on Central Venous Access for PN[70]

The European Society for Parenteral and Enteral Nutrition (ESPEN) believes that central venous access is needed in most patients who need Parenteral Nutrition (PN). This guideline will inform physicians, nurses, dieticians, pharmacists, caregivers and other home, parenteral nutrition (HPN) providers, as well as healthcare administrators and policy makers, about appropriate and safe HPN provision. This guideline will also inform patients requiring HPN. The guideline is based on previous published guidelines and provides an update of current evidence and expert opinion; it consists of 71 recommendations that address the indications for HPN, central venous access device (CVAD) and infusion pump, infusion line and CVAD site care, nutritional admixtures, program monitoring and management: Meta-analyses, systematic reviews and single clinical trials based on clinical questions were searched according to the PICO format. For the short-term PN, nontunneled CVCs, PICC and PIVCs are recommended or considered.

2017 ACR Appropriateness Criteria Radiologic Management of CVC [71]

The American College of Radiology (ACR) Appropriateness Criteria is for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision include an extensive analysis of current medical literature and the application of well-established methodologies to rate the appropriateness of imaging and treatment procedures for specific clinical scenarios.

This document is intended to provide insights on the device type of CVCs, clinical indication, duration of treatment, CVC complications and management. According to the guidelines, the therapeutic indications for CVCs include administration of chemotherapy, parenteral nutrition (PN), blood products, intravenous medications or fluids, and performance of plasmapheresis or hemodialysis. The guidelines provided recommendations concerning specific CVC types. According to the guidelines, nontunneled CVCs are the most appropriate for short-term treatment of acute sepsis with antibiotics in hospitalized patients with renal disease.

2014 SSAICM Clinical Guidelines on Central Venous Catheterization[72]

The guidelines by the Swedish Society of Anesthesiology and Intensive Care Medicine (SSAICM) aimed at providing guidelines on bleeding diathesis, vascular approach, ultrasonic guidance, catheter tip positioning, prevention and management of associated trauma and infection, and specific training and follow-up. The guidelines recommended the right internal jugular (RIJ) vein as the primary insertion site and ultrasound guidance primarily for insertions at the RIJ sites. These recommendations align with the 2018 CVC guidelines for critically ill patients [65]. Besides, the authors also recommended structured patient history, quality programs for implementation, and follow-up after CVC placement, for improved safety and reliability.

2013 ASCO Guidelines for CVC Care in Cancer Patients[73]

The American Society of Clinical Oncology (ASCO) has developed this guideline document targeting patients with cancer. The guidelines addressed the catheter type, insertion site, and placement procedure, as well as the prevention and management of both catheter-related infection and thrombosis. According to the authors, CVC should be placed by well-trained health providers, and the use of a CVC clinical care bundle is recommended. Also, the use of antimicrobial/antiseptic-impregnated or heparin-impregnated CVCs should be considered to decrease the risk of infections for short-term CVCs in high-risk patients. There was insufficient evidence to support one CVC type or insertion site over another, but femoral catheterization should be avoided.

Further, guidelines on the management of CVC complications are also identified. Although CVC offers multiple advantages, the procedure is associated with adverse events that could be hazardous for patients. Adverse events can be divided into immediate complications and delayed complications. Immediate complications arise directly after introducing a CVC and consist of mechanical complications and malposition. The most common mechanical complications include arterial puncture, hematoma, and pneumothorax [74]. Delayed complications consist of infectious and thrombotic adverse events and may be provoked by malposition of a CVC. Three relevant guidelines were found on the management of these complications.

2015 ESMO Guidelines on CVC in Oncology: CRBSI and CRT [75]

This guideline document applies to central venous access, tunneled CVC, PICC and totally implantable devices, in adult cancer patients.

The guidelines summarized the classifications of the CVCs, definitions on CVC related complications and management, indications for CVC removal. Notably, the guidelines provide detailed treatment options and recommendations on the management of infection, especially catheter-related bloodstream infection (CRBSI) and CVC related thrombosis (CRT, especially deep vein thrombosis, DVT).

2013 International guidelines on Catheter-Related Thrombosis (CRT) management in cancer patients [76]

The International guidelines on CRT aimed to establish common international Good Clinical Practices Guideline (GCPG) for the management of CRT in cancer patients. Based on available evidence, the authors stated 1): the use of anticoagulant treatment of for routine CRT management is not recommended; 2) A CVC should be primarily inserted to the right jugular vein to minimize the risks of CRT. According to the authors, the clinical evidence obtained for this document was mainly from studies on the conventional CVCs by BD.

2002/2010 NICE Guidance on Ultrasound Guided CVC placement [with 2023 review][77]

The recommendations in this guidance represent the view of UK National Institute for Health and Care Excellence (NICE), arrived at after careful consideration of the evidence available (with periodic review). As in modern clinical practice, the CVCs are inserted with image guidance, NICE has provided the following guidelines: 1. Two-dimensional (2-D) imaging ultrasound guidance is recommended as the preferred method for insertion of central venous catheters (CVCs) into the internal jugular vein (IJV) in adults and children in elective situations. 2. The use of two-dimensional (2-D) imaging ultrasound guidance should be considered in most clinical circumstances where CVC insertion is necessary either electively or in an emergency situation. 3. It is recommended that all those involved in placing CVCs using twodimensional (2-D) imaging ultrasound guidance should undertake appropriate training to achieve competence. 4. Audio-guided Doppler ultrasound guidance is not recommended for CVC insertion.

7.0 Suggested profile and training for users

The Careflow CVC are intended to be used by trained physicians / healthcare professionals. The devices may be operated by clinicians in operating rooms, intensive care units, emergency rooms and cardiac catheterization labs.

8.0 Applicable Harmonized Standards and Common Specifications

All applied common specifications (CS), international standards harmonized under the medical device directives and/or the MDR, relevant adopted monographs of the European pharmacopoeia (MDR, Article 8 (2)), and other relevant standards, as applicable, are summarized in Table 23.

Table 23. Standard Conformance Summary

Document Number	Document Title	Compliance (Full/Partial)
MDR 2017/745	Medical Device Regulation (MDR) of the European Union (Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices	Full
Directive 2010/63/EU	Protection of animals used for scientific purposes	Full
Directive 2004/10/EC	Application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances	Full
Commission Regulation (EU)	Commission Regulation (EU) No 207/2012 of 9 March 2012 on electronic instructions for use of	Full

Document Number	Document Title	Compliance (Full/Partial)
No 207/2012	medical devices	
MDCG 2019-9 Aug 2019	Summary of Safety & Clinical Performance	Full
MDCG 2019-1 Jan 2019	MDCG guiding principles for issuing entities rules on Basic UDI-DI	Full
MDCG 2018-1 Apr 2021	Guidance on BASIC UDI-DI and changes to UDI-DI	Full
MDCG 2020-6 Apr 2020	Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC	Full
MDCG 2020-7 Apr 2020	Post-market clinical follow-up (PMCF) Plan Template	Full
MDCG 2020-8 Apr 2020	Post-market clinical follow-up (PMCF) Evaluation Report Template	Full
MDCG 2021-24 Oct 2021	Guidance on classification of medical devices	Full
MEDDEV 2.7/1 Rev 4 2016	Clinical evaluation: Guide for manufacturers and notified bodies	Full
MEDDEV 2.12/2 Rev 2 2012	Post Market Clinical Follow-up studies	Full
MEDDEV 2.12/1 Rev 8 2013	Guidelines on a Medical Devices Vigilance System	Full
ISO 11737-1:2018 + ISO 11737-1:2018/Amd 1:2021	Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products	Full
ISO 11737-2:2019	Sterilization of health care products - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process	Full
ISO 13485:2016 + EN ISO 13485:2016/A11:2021	Medical devices – Quality management systems – Requirements for regulatory purposes	Full
ISO 14971:2019	Medical Devices - Application of Risk Management to Medical Devices	Full
ISO 15223-1:2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Full
ISO 20417:2021	Medical devices — Information to be supplied by the manufacturer	Full
EN 556-1 :2001 + EN 556-1:2001/ AC:2006	Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices	Full
EN ISO 11135:2014 + ISO 11135:2014/Amd 1:2018	Sterilization of health care products -- Ethylene oxide -- Requirements for development, validation and routine control of a sterilization process for medical devices	Full
AAMI TIR28:2016	Product Adoption and process equivalency for ethylene oxide sterilization	Full
EN ISO 14644-1:2015	Cleanrooms and associated controlled environments – Part 1: Classification of air cleanliness by particle concentration	Full
ISO 10993-1:2018	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management	Full

Document Number	Document Title	Compliance (Full/Partial)
	process	
ISO 10993-3:2014	Biological Evaluation of Medical Devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity	Full
ISO 10993-4:2017	Biological Evaluation of Medical Devices – Part 4: Selection of Tests for Interactions with Blood	Full
ISO 10993-5:2009	Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity	Full
ISO 10993-6:2016	Biological evaluation of medical devices – Part 6: Tests for local effects after implantation	Full
EN ISO 10993-7:2008 + ISO 10993-7:2008/Cor 1:2009 + ISO 10993-7:2008/Amd 1:2019	Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide sterilization residuals	Full
ANSI/AAMI ST72:2019	Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing	Full
ISO 10993-10:2021	Biological evaluation of medical devices - Part 10: Tests for skin sensitization	Full
ISO 10993-11:2017	Biological Evaluation of Medical Devices – Part 11: Tests for systemic toxicity	Full
ISO 10993-12:2021	Biological Evaluation of Medical Devices – Part 12: Sample preparation and reference materials	Full
ISO 10993-18:2020	Biological Evaluation of Medical Devices – Part 18: Chemical Characterization of Medical Device Materials within a Risk Management Process	Full
ISO 10993-19:2020	Biological evaluation of medical devices - Part 19: Physico-chemical, morphological and topographical characterization of materials	Full
EN ISO 10993-23:2021	Biological evaluation of medical devices – Part 23: Tests for irritation	Full
ASTM F2475-20	Standard Guide for Biocompatibility Evaluation of Medical Device Packaging Materials	Full
ISO 11607-1:2019	Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems	Full
ISO 11607-2:2019	Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes	Full
EN ISO 2233:2001	Packaging – Complete, filled transport packages and unit loads – Conditioning for testing	Full
ASTM F2096 -11	Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)	Full
ASTM F1929 -15	Standard Test Method for Detecting Seal Leaks in porous Medical Packaging by Dye Penetration	Full
ASTM F88/F88M -15	Standard Test Method for Seal Strength of Flexible Barrier Materials.	Full
ASTM D4169 -16	Standard Practice for Performance Testing of Shipping Containers and Systems	Full
ASTM F1980 -16	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices	Full

Document Number	Document Title	Compliance (Full/Partial)
ASTM F1140/F1140M-13	Standard Test Method for Internal Pressurization Failure Resistance of Unrestrained Packages	Full
Product-specific Standards		
EN ISO 10555-1:2013 & EN ISO 10555-1:2013/ A1:2017	Intravascular catheters - Sterile and single-use catheters - Part 1: General requirements	Full
EN ISO 10555-3:2013	Intravascular catheters - Sterile and single-use catheters - Part 3: Central venous catheters	Full
EN ISO 11070:2014 & EN ISO 11070:2014/ A1:2018	Sterile single-use intravascular introducers, dilators and guidewires	Full
ISO 80369-7:2021	Small-bore connectors for liquids and gases in healthcare applications - Part 7: Connectors for intravascular or hypodermic applications	Full
ISO 7886-1:2017	Sterile hypodermic syringes for single use - Part 1: Syringes for manual use	Full
IEC 62366-1:2015 & IEC 62366-1:2015/ Cor 1:2016 & IEC 62366-1:2015/ Amd 1:2020	Medical Devices – Part 1: Application of usability engineering to medical devices	Partial Compliant to IEC 62366-1 Annex C - Product released to manufacture pre 2015 and as such only IEC 62366-1:2015+AMD1:2020 Annex C applies
ASTM F640-20	Standard Test Methods for Determining Radiopacity for Medical Use	Full

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10.0 Revision History

SSCP Revision	ECN Number	Date Issued DD/MM/YYYY	Change Description	Revision Validated by the Notified Body
REV 001	ECN180198	30/10/2023	Initial Release of SSCP0016 for the Careflow Central Venous Catheter and Catheterization Kits	☒ Yes Validation language: English ☐ No