Clinical Evaluation Report (CER)

Prepared by: Clinical Evaluation Team

Approval by: General Manager

Update history

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2014.03.16	01	
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1. Summary:

1.1 Clinical evaluation is regarded as an ongoing process conducted throughout the life cycle of a medical device. It is first performed during the conformity assessment process leading to the marketing of a medical device and then repeated periodically as new clinical safety and performance information about the device is obtained during its use in the post market phase.

1.2 Clinical evaluation is the assessment and analysis of clinical data pertaining to a medical device in order to verify the clinical safety and performance of the device.

1.3 The data summarized in this document is reported in more detail in underlying reports to which references are made in this document

1.4 This document concerns the overall clinical evaluation of Blood lines product group.

1.5 This clinical evaluation is part of the overall risk evaluation process of Blood lines product group.

1.6 The clinical evaluation is based on a comprehensive analysis of available pre-and post-market clinical data relevant to the intended purpose of the device in question, including clinical performance data and clinical safety data.

There are discrete stages in performing a clinical evaluation:

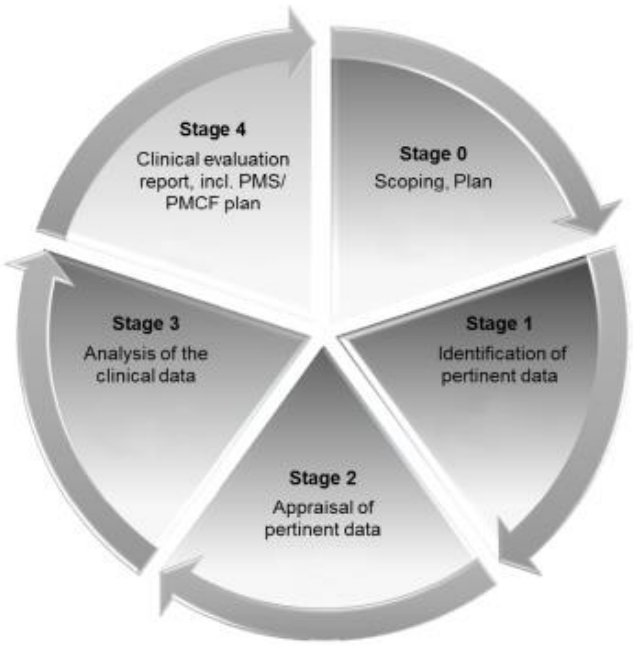


Figure: Stages of a clinical evaluation

2. Scope of Clinical evaluation:

This Clinical evaluation report provides the overall results of literature review, in performance testing, Equivalence device test comparison and Post Market Surveillance data to provide evidence for the safety and clinical performance of Blood lines product group as claimed by manufacturer.

2.1 Name of the Device

During the design and development process the following nameshave been used for the Blood lines product group:

Blood lines (Hemodialysis Blood Tubing Sets)and Related Accessories.

2.2 Manufacturer

Perfect Medical Industry (VN) Co., Ltd

Block D7/I, No.1B Road, VinhLoc Industrial Zone, Binh Hung Hoa B Ward, Binh Tan District, Ho Chi Minh City, Vietnam

2.3 Intended purpose of the device

The Blood lines are designed to transfer blood or other fluids from a patient's vascular access device to the dialyser/haemodialyser unit for the circulation. Blood lines used together with the A.V. Fistula Needle, Dialyzer and Hemodialysis machine duringhemodialysis therapy for patients with renal failure. The Blood lines isintended for single patient use only and is to be discarded at the end of each usage.

2.4 **Commercial Marketing History**

The Hemodialysis Blood Tubing Sets have been distributed to countries such as Malaysia, India, Thailand, Peru, Pakistan, Turkey, Bangladesh, Indonesia, China, Vietnam, Taiwan, EU, etc.

Year / Country	2014	2015	2016	2017	2018
Bangladesh	42,008	25,008	12,000	-	12,360
Indonesia	244,416	360,504	541,296	691,656	851,880
India	5,448	109,584	170,232		59,904
Korea	13,152	130,104	184,776	240,744	233,208
Malaysia	440,232	431,448	171,262	122,400	149,688
Philippines	200,544	214,296	507,432	245,520	158,232
Thailand	116,424	102,552	13,008	340,104	457,920
China	419,712	269,760	56,680	149,996	127,328
Pakistan	214,448	178,344	176,928	361,800	111,720
Peru	114,072	-	-	-	-
Taiwan	448,080	586,392	631,176	1,238,080	1,323,492
Vietnam	354,960	586,723	646,848	722,832	771,048
South Africa	-	-	-	18,280	60,144
EU(Germany)	-	-	-	30,000	70,008

2.5 Regulatory Approval

The product has obtained its regulatory approval from the European Union since September 2004. The EC Certificate issued by DNV GL NEMKO PRESAFE as service contract on 8 October 2014 and EC Declaration of Conformity can be referred in Annex 1 and Annex 4, respectively. The EC Certificate awarded is based on Article 11.3.a and Annex II, excluding Section 4 (Module H), of Council Directive 93/42/EEC(as amended by directive 2007/47/EC) on Medical Devices conformity assessment.

2.6 General description of medical device.

2.6.1 Production technology: Blood Lines are products manufactured by the company with over 20 years of experience, so far there is no new production technology has been applied.

2.6.2 The technical specifications and mechanical characteristic:

The Hemodialysis Blood Tubing Set consists of arterial and venous lines are used in dialysis where it is attaching to the A.V.fistula needle and dialyser.

The arterial blood tubing is the portion of the tubing set that transports blood from the patient to the hemodialyzer inlet port.

The venous blood tubing is the portion of the tubing set that transports blood from the hemodialyzer outlet port back to the patient.

It has the guarded access ports to reduce risk of infection. Various diameter and type ofguarded access ports are available for different machines. The device also consists of Pump Segment for conventional and high flow rates. It is easy to handle and kink-resistant tubing, special design on clamp preventing leakage while locking.

This device is Non-DEHP, Non-pyrogenic and Non-toxic.

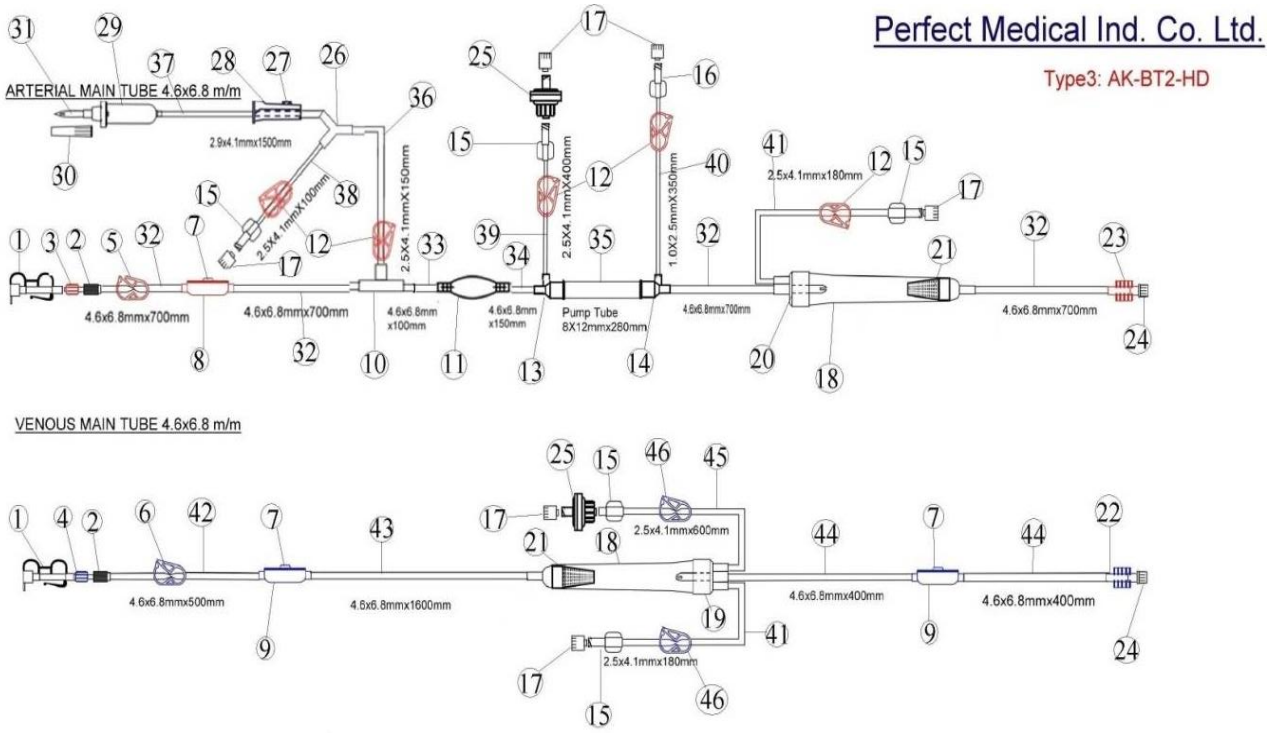
The material used for construction is the Medical Grade polyvinyl chloride (PVC), Propylene/Ethylene- copolymer Pellets (PP/PE) and (Acrylonitrile- Butadiene-Styrene Copolymer (ABS).

The Hemodialysis Blood Tubing Sets consist of different configurations where it can come with or without the transducer protector and/or pillow. Transducer protector is a part of hemodialysis set. It is a component of a hemodialy

sis blood tubing set with a hydrophobic membrane, designed to prevent blood contamination of the pressure transducers of a hemodialysis delivery system. Anti-bacterial hydrophobic air filter iswith female Luer lock and male luer lock which gives effective Filtration Area of 4.9 cm^2. Pore membrane is of 0.2μm. The materials

No	NameofComponents	Quantity(pcs)	Contact/non contact with body fluid	Material

used for construction of this part including the PTFE 0.2μm and PVC.This part of the device is also non-pyrogenic and non-toxic. The pillow is used to detect pressure variation into the dialysis blood line and discontinuing the treatment in case of emergency. In addition, the blood tubing set can also be attaching to an IV set primarily use for priming of the blood line. Priming tube is specifically designed to



use with hemodialysis bloodline tubing set. Before the dialysis, it can help to prevent air bubbles from entering the blood line, and it also rinses out blood line with normal saline. After the dialysis, IV Set is the channel to push the blood in the blood line back into patient's body.

The drawing for blood line product as the following:

1	RotatingMaleluerlockconnector	2	Contact	PP K1023
2	Maleluerlockconnector	2	Contact	PVC 3P- DIN P
3	RedConnectorForMaleLuerLock	1	Contact	PVC 3P- Non P
4	BlueConnectorFormaleLuerLock	1	Contact	PVC 3P- DIN P
5	PinchClamp-L(Red)	1	Non contact	PP K1023
6	PinchClamp-L(Blue)	1	Non contact	PP K1023
7	Rubber pad	3	Contact	Silicone resin
8	WingedBloodlineInjectPortBody(Red)	1	Contact	PVC 3P- DIN P
9	WingedBloodlineInjectPortBody(Blue)	2	Contact	PVC 3P- DIN P
10	Tconnectorforbloodline	1	Contact	PVC 41P–DINP
11	PILLOW	1	Contact	PVC 58P–DINP
12	PinchClamp-S Red	5	Non contact	PP K1023
13	Pump-Tconnector4mm	1	Contact	PVC 41P–DINP
14	Pump-Tconnector2.5mm	1	Contact	PVC 41P–DINP
15	Femaleluerlock 3.8connector3.8mm	5	Contact	PVC 3P– DIN P
16	Female luer lock connector 2.5mm	1	Contact	PVC 3P- DIN P
17	Female luer lock cap	6	Non Contact	PE 606
18	Chamber for blood lines	2	Contact	PVC 41P–DINP
19	Cover for chamber 3 way	1	Contact	PVC 3P/PVC 30P–DINP
20	Cover for chamber 2 way	1	Contact	PVC 3P/PVC 30P–DINP
21	Filter	2	Contact	PP K1023
22	Dialyzer adaptor (Blue)	1	Contact	PVC 41P–DINP
23	Dialyzer adaptor (Red)	1	Contact	PVC 41P–DINP
24	Dialyzer adaptor cap	2	Non Contact	PE 606
25	Transducer protector in bulk	1	Non Contact	PVC 5P
26	Y type connector	1	Contact	PVC 41P–DINP
27	Roller	1	Non Contact	ABS 707
28	Roller clamp	1	Non Contact	ABS 707
29	Drip chamber	1	Contact	PVC 50P–DINP
30	Spike cap (Blue)	1	Non Contact	PP K1023
31	Spike	1	Contact	ABS 707
32	Tubing	2	Contact	PVC 70P–DINP
33		1		
34		1		
35	Tubing segment	1		PVC 90P–DINP
36	Tubing	1		PVC 70P–DINP
37		1		
38		1		

39		1		
40		1		
41		2		
42		1		
43		1		
44		2		
45		1		
46	PinchClamp-S Blue	2	Non Contact	PP K1023

2.6.2Physical and chemical description:

Physical Test and Chemical test. They are tested by QA Dept (refer ISO 8637-2:2018 and ISO 80369-7:2016):

TEST	SPECIFICATION	RESULTS		STANDARD USED
Physical Test				
Appearance	Clarity observation	Pass		ISO 8637-2
Pump Segment performance	0mmHg to -250mmHg	Pass		
Positive- Pressure Test	to apressure of 1,5 times the manufacturer's recommended pressure	Pass		
Negative- Pressure Test	-50KPa	Pass		
Anti-heat and anti-cold test	Resist 50^0c and less than 0^0c	Pass		QW-V189
Injection site	Using a hypodermic needle with an outside diameter of 0.8mm· There is no fluid leakage underpressure 1.5kgf/cm^2 and the disconnection of component	Pass		ISO 8637-2
Locked test	There is no fluid leakage underpressure 1.5kgf/cm^2 and easily flow when locking and open the clamp respectively	Pass		
Transducer protector test	No leakage underpressure 1.5kgf/cm^2	Pass		
Pull Test	Resist to 2.0 kgf(20N)	4.12~19.56 kgf	Pass	
Conical fitting	Fit with reference female gauge	Pass		ISO 80369-7
Chemical Test				
Acidity or Alkaline	≤1.0 ml NaOH M/100 (0.01M) ≤1.0 ml HCl M/100 (0.01M)	0.46ml HCl	Pass	QW-V190
Heavy metals	< 1ppm	The color of the tested solution is lighter than the comparing solution, the standard is <1ppm		
Residue on evaporation	≤5.00mg/50ml	0.8mg	Pass	
Reducing substance	≤2.00ml	0.4ml	Pass	

KMnO4				

2.6.3 Sterility

All products are sterilized by EO gas in accordance ISO 11135:2014. This device meets 10^{-6} SAL (Sterility Assurance Level).The sterilization process is validated in compliance with ISO 11135.

Judgment: After putting biological indicator in the chamber during sterilization, judged to be the death of the bacteria were cultured at 37±2℃ in the thermostat.

Sterile judgment:

a. Method: Check Packing condition & Chemical Indicator on box.

b. Specification: Chemical indication colour changing checking.

2.6.4 Safety and perform:

The device met the ISO 10993 criterion on biocompatibility. They are tested by 3rd party, SGS, for the following tests:

- Acute systemic Toxicity test with ISO 10993-11
- Cytotoxicity test with ISO 10993-5
- Sensitization test with ISO 10993-10
- IntracutaneousReactivity Test with ISO 10993-10
- Hemocompatibility (Hemolysis test) with ISO 10993-4
- ENDOTOXIN test with USP<85>

* Assess if Blood lines product group safety and perform as claimed when used as intended and applied for hemodialysis therapy for patients with renal failure and complies to the performance requirement of the MDD 93/42/EC as amended by Directive 2007/47/EC.

***** Residual risked can be referred to Risk Management Report&Long term performance and safety can be referred to PMS. In addition, according to PMS report, there are no risk-related feedbacks up to now.For all of the above rationales, there are no requirements for Clinical Investigation PMCF for this device.

***** Achieve essential information for assessing clinical benefits and foreseeable risks of Blood lines product group. In case risks are identified, an assessment is made if risk are acceptable when weighted against the clinical benefit and a verification is made if sufficient control measures have been taken including information provided in the IFU.

2.7Clinicalevaluation plan

The plan of the clinical evaluation is summarized briefly as follows:

Aspects	For CE market devices	Section
• The device description.	V	2
• Whether there are any design features of the device, or any indications or target populations,that require specific attention. The clinical evaluation should cover any design features that pose special performance or safety concerns (e.g. presence of medicinal, human or animal components), the intended purpose and application of the device (e.g. target treatment group and disease, proposed warnings, contraindications, precautions, and method of application) and the specific claims made by the manufacturer about the clinical performance and clinical safety of the device	V	2.6 4.2
• The risk management documents of the device, e.g. the hazard	V	4.6.2

	identification list, clinical risks identified from the risk analysis. The scope of the clinical evaluation will need data from and cross references to the manufacturer's risk management documents. The risk management documents are expected to identify the risks associated with the device and how such risks have been addressed. The clinical evaluation is expected to address the significance of any clinical risks that remain after design risk mitigation strategies have been employed by the manufacturer.		4.6.3 4.6.4
•	The current knowledge/ state of the art in the corresponding medical field, such as applicable standards and guidance documents, information relating to the medical condition managed with the device and its natural course, benchmark devices, other devices and medical alternatives available to the target population.	V	3 8
•	Data source(s) and type(s) of data to be used in the clinical evaluation. • Data relevant to the clinical evaluation may be generated and held by the manufacturer or available from scientific literature.	V	4.3 4.4 4.5.3
•	Whether the manufacturer has introduced/ intends to introduce any relevant changes, including -design changes, -changes to materials and manufacturing procedures, -changes to the information materials supplied by the manufacturer (label, IFU, available promotional materials including accompanying documents possibly foreseen by the manufacturer) or other claims, -and whether the claim of equivalence to an existing device is still appropriate. Whether there are any specific clinical concerns that have newly emerged and need to be addressed.	V	4.2
•	PMS aspects that need regularly updating in the clinical evaluation report: -new clinical data available for the device under evaluation; -new clinical data available for the equivalent device (if equivalence is claimed); -new knowledge about known and potential hazards, risks, performance, benefits and claims, including -data on clinical hazards seen in other products (hazard due to substances and technologies); -changes concerning current knowledge/ the state of the art, such as changes to applicable standards and guidance documents, new information relating to the medical condition managed with the device and its natural course, medical alternatives available to the target population; -other aspects identified during PMS./PMCF	V	4.3
•	Needs for planning PMS/PMCF activities.	V	4.3

3. Clinical background, current knowledge, state of the art

3.1 Applied standard:

The present evaluation was performed according to the requirements and guidance of

- MDD 93/42/EC Annex I and Annex X.

- EN ISO 10993-1:2009 Biological evaluation of medical devices- Part 1: Evaluation and testing within a risk management process.
- EN ISO 14791:2012 "Medical devices- Application of risk management to medical devices".
- MEDDEV 2.7.1 rev 4, June 2016: Evaluation of clinical data: A guide for the manufacturers and notified body.
- ISO 8637-2:2018: Extracorporeal systems for blood purification —Part 2: Extracorporeal blood circuit for haemodialysers, haemodiafilters and haemofilters
- ISO 8536-4:2010: Infusion equipment for medical use- Part 4: Infusion sets for single use, gravity feed.
- ISO 11135:2014: Sterilization of health-care products- Ethylene Oxide-Requirements for the development, validation and routine control of sterilization process for medical devices.
- ISO 11607-1: 2014 Amendment 1 Packaging for terminally sterilized Part 1: Requirements for materials Sterile barrier systems and packaging Medical devices systems.
- ISO 15223-1:2016 Medical devices- Symbols to be used with medical device labels, labeling and information to be supplied- Part 1: General requirements
- ISO 80369-7:2016 Small- bore connector for liquids and gases in healthcare applications- Part 7: Connectors for intravascular or hypodermic applications.

3.2 The benefits and risk when use Blood lines product.

- Support the patient through the renal dialysis process, help patient to reduce the paints caused by kidney failure.
- There are health damages if used for a long time due to the residues of EtO and ECH in the sterilization process, as well as the residues produced from the nature of materials being used and from the production process

3.3 Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common genetic nephropathies, affecting one in every 800-1000 individuals in the worldwide general population and 5-10% of hemodialysis patients (refer by PubMedresource).

3.4 The recommended dialysis pattern in the West is at least three sessions weekly with high-flux dialyzers. Studies from Shanghai and Taiwan might however indicate a benefit of twice versus thrice weekly sessions. In less developed Asian countries, a twice weekly pattern is common, sometimes with dialyzer reuse and inadequate water treatment. A majority of patients decrease session frequency or discontinue the program due to financial constraint. (3) As convective therapies are gaining popularity in Europe, penetration in Asia is low and limited by costs. (4) In Asian countries, in particular in the South and South-East, hepatitis and tuberculosis infections in HD patients are higher than in the West and substantially increase mortality. (5) Progress has recently been made in countries like Thailand and Brunei to provide universal HD access to all patients in need. Nevertheless, well-trained personnel, reliable registries and better patient follow-up would improve outcomes in low-income Asian countries(refer by PubMed resource).

4 Device under evaluation

4.1 Type of evaluation

The clinical evaluation is based on:

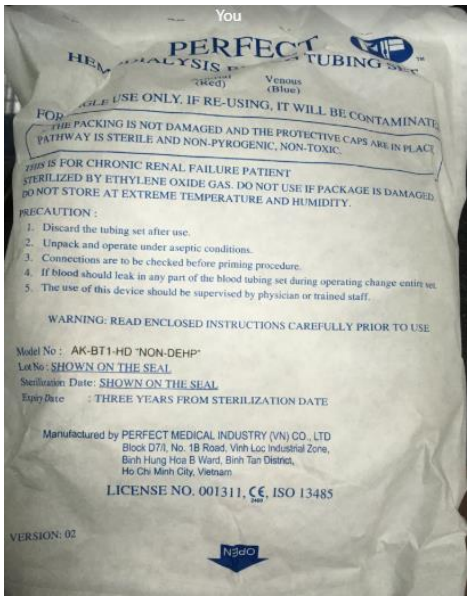
- Scientific literature databases as: (MEDLINE) PubMed, ,CENTRAL, IRIS.
- FDA U.S.Food & Drug
- Pre-clinical testing databases as:

1. Physical test:
   The device met the ISO 8638 criterion on Physical requirements:
   - Pump Segment performance
   - Positive- pressure test
   - Negative-pressure test
   - Pull test
   - Injection site
   - Locked test
   - Transducer protector test
   - Conical fitting
2. Chemical test:
   The device met the ISO 8638 criterion on chemical requirements:
   - Acidity or alkaline
   - Heavy metals
   - Residue on evaporation
   - Reducing substance $KMnO_4$

3. The device met the ISO 10993-1 criterion on biocompatibility:
   - Acute systemic Toxicity test with ISO 10993-11
   - Cytotoxicity test with ISO 10993-5
   - Sensitization test with ISO 10993-10
   - IntracutaneousReactivity Test with ISO 10993-10
   - Hemocompatibility (Hemolysis test) with ISO 10993-4
   - ENDOTOXIN test with USP <85>
4. The device met the ISO 11737-2 &ISO 10993-7 criterion on sterilization
   - Sterile test
   - EO residual test report

4.2 Demonstration of equivalence:

DORA Tubing Sets for Hemodialysis



PF Bloodline

This Clinical evaluation document used The Equivalent device is DORA Tubing Sets for Hemodialysis, it is manufacture by Bain Medical Eqiupment (Guangzhou) Co.,Ltd, product Code BIAN- BL-005.

DORA Tubing Sets for Hemodialysis are single-use sterile medical devices intended to connect the patient to the hemodialyzer and the hemodialysis delivery system in hemodialysis treatment.

The configuration of the DORA Tubing Sets for Hemodialysis areArteria Line Venous Line, Drip Chamber,Branch Lines,Female Luer Lock,Clamps,Filter,Drain Bag Recirculating Connector.

The proposed devices, DORA Tubing Sets for Hemodialysis, mainly consists of two tubes, which are arterial line with certain components in red and venous line with certain components in blue, as well as two accessories which are recirculate connector and drainage bag.

Bench performance testing of the DORA Tubing Sets for Hemodialysis were conducted in accordance with the performance testing described in ISO 8638:2010 ISO 80369-7

- **Technological Characterisyics**:
  The perfect Blood line is single use, Blood line is equivalent to that of the DORA Tubing Sets for Hemodialysis in intended use, material and performance characteristics.

•

Category		Blood line	Tubing Sets for Hemodialysis
1. Trade name		Perfect Blood lines	DORA Tubing Sets for Hemodialysis
2.Model Number		V06203 refer FSC No. 42/2017/BYT-TB-CT	BAIN-BL-005
3.Manufacturer		Perfect medical Industry(VN) Co., Ltd	Bain Medical Eqiupment (Guangzhou) Co.,Ltd,
4. Regulatory Class		Class IIa	Class IIa
5. Inten	6.	The Blood lines is Blood lines is	The DORA Tubing Sets for

ded Use/ Indication for use		designed to transfer blood from patient to the hemodialyzer via the arterial blood tubing and from the hemodialyzer back to the patient via the venous blood tubing. The Blood lines isintended for single patient use only and is to be discarded at the end of each usage.	Hemodialysis are single-use sterile medical devices intended to connect the patient to the hemodialyzer and the hemodialysis delivery system in hemodialysis treatment.
6.Material	Drip Chamber	Polyvinyl chlorua	Polyvinyl chlorua
	Branch Lines	Polyvinyl chlorua	Polyvinyl chlorua
	Female Luer Lock	Polyvinyl chlorua	Polyvinyl chlorua
	Clamps	Polypropylene	Polypropylene
	Filter	Polypropylene	Polypropylene
	Drain Bag	Polyvinyl chlorua	Polyvinyl chlorua
	Recirculating Connector	Polypropylene	Polypropylene
	Pillow	Polyvinyl chlorua	Polyvinyl chlorua
	HDF line	Polyvinyl chlorua	Polyvinyl chlorua
	Transducer protector	Polyvinyl chlorua	Polyvinyl chlorua
	I.V.set	Polyvinyl chlorua+ Acrylonitrin Butadien Styren	
	needleless	Polyvinyl chlorua+silicone	Polyvinyl chlorua+silicone
	Drip chamber cap	Polyvinyl chlorua	Polyvinyl chlorua
7. Single use		Yes	Yes
8. CE mark		2460	0197
9. Sterilization		EO Sterilization SAL (10^{-6})	EO Sterilization SAL (10^{-6})
10. Shelf life		3 Years	3 Years

❖ Biological

11. Biocompatibility	Conforms to ISO 10993-1: • Acute systemic Toxicity test Cytotoxicity test • Sensitization test • IntracutaneousReactivity Test • Hemocompatibility (Hemolysis test) • ENDOTOXIN test with USP <85>	• Cytotoxicity • Sensitization • Intracutaneous reactivity • Acute systemic toxicity • Hemolysis • Partial Thromboplastin Time Complement System • In vitro Chromosomal Aberration • Bacterial Reverse Mutation • Mouse Bone Marrow Micronucleus • Pyrogen

❖ Pre-clinical testing

12. Performance	Conforms to ISO 8637-2(ISO 8638) ISO 80369-7	Conforms to ISO 8638 ISO 594-2（equivalent ISO 80369-7)

	Refer : Equivalent device comparison test report	Refer: Equivalent device comparison test report

Equivalent device comparison test report:

Test Item	Specification	Test Result				Standard
		DORA Tubing Sets for Hemodialysis Mode: BAIN-BL – 005 Lot: 201701030165 MFD: 2017.08 EXP: 2019.07		Perfect Blood lines Mode:V0625310620002 Lot:181524 MFD:2018.12.05 EXP: 2021.12.05		
Physical Test						
Appearance	Clarity observation	Pass		Pass		ISO 8638
Pump Segment performance	0mmHg to -250mmHg	Pass		Pass		
Positive- Pressure Test	to apressure of 1,5 times the manufacturer's recommended pressure	Pass		Pass		
Negative- Pressure Test	-50KPa	Pass		Pass		
Anti-heat and anti-cold test	Resist 50^0c and less than 0^0c	Pass		Pass		QW-V189
Injection site	Using a hypodermic needle with an outside diameter of 0.8mm· There is no fluid leakage underpressure 1.5kgf/cm^2 and the disconnection of component	Pass		Pass		ISO 8638
Locked test	There is no fluid leakage underpressure 1.5kgf/cm^2 and easily flow when locking and open the clamp respectively	Pass		Pass		
Transducer protector test	No leakage underpressure 1.5kgf/cm^2	Pass		Pass		
Pull Test	Resist to 2.0 kgf(20N)	4.24~20.05kgf	Pass	4.12~19.56kgf	Pass	
Conical fitting	Fit with reference female gauge	Pass		Pass		ISO 80369-7
Chemical Test						
Acidity or Alkaline	≤1.0 ml NaOH M/100 (0.01M) ≤1.0 ml HCl M/100 (0.01M)	0.50ml HCl	Pass	0.46ml HCl	Pass	QW-V190
Heavy metals	< 1ppm	The color of the tested solution is lighter than the comparing solution, the standard is <1ppm		The color of the tested solution is lighter than the comparing solution, the standard is <1ppm		QW-V190
Residue on evaporation	≤5.00mg/50ml	0.6mg	Pass	0.8mg	Pass	
Reducing substance KMnO4	≤2.00ml	0.5ml	Pass	0.4ml	Pass	
Sterile test	No Growth	Pass		Pass		ISO 11737-2

Substantial Equivalence :

The PF Bloodline is substantially equivalent to the DORA Tubing Sets for Hemodialysis in intended use, principles of operation, technology, design, materials and performance.

Discussion:

The PF Blood line has been verified to meet the established performance criteria above. The results of the Per-clinical testing/design verification testing demonstrate that the PF Bloodline performs as intended and performs as well as the DORA Tubing Sets for Hemodialysis

The blood line with safety type is a Bloodline that uses a needle-free type to replace the rubber pad at the sampling place. The purpose is to reduce the risk of minimize risk of accidental needlestick when use needle.

4.3 Clinical data generated and held by the manufacturer.

4.3.1 Risk management report for Blood lines (Hemodialysis Blood tubing sets) (refer # RD 001).

Risk management report is implemented by Perfect Medical to identify the hazards associated with Blood lines to estimate and evaluate the associated risks, to control these risks, and to monitor the effectiveness of controls. This report is applicable to all stages of the life-cycle of Hemodialysis Blood Tubing Set a in accordance with EN ISO 14971:2012.

The risk management file shall provide traceability for each identified hazardto

- Risk Analysis
- Risk Evaluation
- Risk Control
- Evaluation of overall residual risk acceptability

Each given hazard shall be controlled by actions to reduce risk and these actions shall be validated.

According to company's quality policy, risk acceptance criteria shall be established and represented

Risk management shall be maintained implementation and verification of the effectiveness of relevant actions based on the results of collecting data in production and post-production, and at least once a year, the risk management report should be revised and reviewed.

Documents for assessing the results of risk management activities are based on statistic data in production as well as technical changes, customer feedbacks, customer complaints, recall notices, product returns, etc.

According to the intended use, we will have identified about characteristics related to the safety of the medical device.

Blood lines have some hazards below:

- Biological hazards and contributory factors:

No	Item	Y/N	No	Item	Y/N
2.1	Bacteria	Y	2.3	Viruses	Y
2.2	Re-and/or cross infection	Y			Y

- Chemical Hazards.

No	Item	Y/N	No	Item	Y/N
3.1	Chemical properties of some material	Y	3.3	Toxicity of chemical constituents (biocompatibility)	Y
3.2	EO sterilizing agents residues	Y	3.4	PHT DINP	Y

- Information hazards

No	Item	Y/N	No	Item	Y/N
4.1	Inadequate Specification of intended use	N	4.4	Re –sterilize	Y
4.2	Inadequate with warning single-use medical device	Y	4.5	Inadequate instruction for use	Y
4.3	Inadequate specification of accessories to be use with the medical device	Y	4.6	Inadequate specification of pre-use check	Y
4.4		Y			

- Operational hazards

No	Item	Y/N	No	Item	Y/N
5.1	Disposal and scrapping after use	Y	5.2	Use error by knowledge-based failure	

- Manufacturing processes hazards

No	Item	Y/N	No	Item	Y/N
6.1	Manufacturing(injection/ printing/assembly) process cause the loss of function of product	Y	6.5	The post- production storage/ storage process cause the loss of the safety of performance of product	Y
6.2	Sealing process cause the loss of the safety of performance of product	Y	6.6	Delivery process cause the loss of the safety of performance of product	Y
6.3	Packaging process cause the loss of the lose function of product	Y	6.7	Post delivery process cause the loss of the safety of performance of product	Y
6.4	Sterilization process cause the loss of the safety of performance of product	Y			

For each hazard identified as potential affected to the safety and performance of the product, an analysis and assessment of its impact was made. At the same time, appropriate methods has been chosen to control and minimize the risk to the lowest possible where the benefit are greater than the residual risk.

The results before and after the implementation of risk reduction are described as follow:

Risk Analysis (before Risk Reduction)

Severity levels (X) Probability levels(Y)	Negligible (1)	Minor (2)	Major (3)	Serious (4)	Critical (5)
Frequent (5)	6.1(1); 6.2(1); 6.3;	6.1(2); 6.2(2); 6.5(1);			
Probable (4)		4.3; 6.5(2);			
Occasional (3)		6.7(2)	5.2;	2.1(1); 3.1; 3.2; 3.3; 5.1; 6.2(3); 6.4;	
Remote (2)		4.4; 6.7(1)		2.1(2); 2.1(3); 6.6;	
Improbable (1)					

Risk Analysis (after Risk Reduction)

Severity levels (X) Probability levels(Y)	Negligible (1)	Minor (2)	Major (3)	Serious (4)	Critical (5)
Frequent (5)					
Probable (4)					
Occasional (3)	6.2(1); 6.3;				
Remote (2)	6.1(1);	4.3; 4.4; 6.1(2); 6.2(2); 6.5(1); 6.7(2)			
Improbable (1)		6.5(2); 6.7(1);	5.2	2.1(1);2.1(2); 2.1(3);2.2;3.1; 3.2;3.3;4.2;4.4; 5.1; 6.2(3);6.4; 6.6;	

Note:

Insignificant risk 不嚴重的風險(white color 白色)

Unacceptable risk 不可接受的風險(red color 紅色)

The conclusion:

The Blood lines and relevant components has been approved by the competent and qualified staffs by means of risk analysis, risk evaluation, risk control, evaluation of overall residual risk acceptability, risk management report, and production and post-production procedures to conduct the risk assessment and risk management review during the product's full life cycle.

Before releasing the products to the market, Perfect Medical Industry has reviewed the risk control procedure to ensure the risk management plan has been conducted properly. The intended medical benefits exceed all residual risks; therefore, all residual risks are

determined as acceptable. Results of this review are recorded as the risk management report included in the risk management file

4.3.2 Medical device Post- Market Surveillance& Post-market clinical follow-up for Bloodline (refer to PMS/PMCF report No. PMS/PMCF 01)

The Post-market Surveillance & Post-market clinical follow-up are implemented by Perfect Medical to gather post-market data of the medical device – Disposable Syringes to control and to monitor safety and effectiveness of controls.

Feedback is analyzed, and determinations are made whether improvement action needs to be taken to fix the problem, through product design or manufacturing changes, product labeling and/or training, etc. Feedback and data also need to be evaluated to determine whether regulatory action such as Medical Device Reporting (FDA), Medical Device Vigilance Reporting (EU), advisory notices.

Generally explain how the data is collected and analyzed often include measurement and analysis, management review meetings, risk management, etc. These explain how the feedback (gathered from the above procedures) is analyzed and evaluated, identify the frequency for evaluation and reporting and describe how this post-market surveillance data is used:

- To update the benefit-risk determination and to improve the risk management
- To update the design and manufacturing information, the instructions for use and the labelling;
- To update the clinical evaluation;
- To update the summary of safety and clinical performance
- For the identification of needs for preventive, corrective or field safety corrective action;
- For the ensuring the continued acceptability of the benefit-risk ratio.
- For the identifying previously unknown side-effects and monitoring the identified side-effects and contraindications,

4.3.2.1 Responsibilities & Authorities for PMS/PMCF Inputs and Training of personnel

a. PMS/PMCF Inputs

Information on the adverse event reports for own and similar devices; results from published literature review relevant to the device in question and equivalent devices; feedback from sales and marketing; proactive follow-up through customer surveys; identifying previously unknown side-effects and monitoring the identified side-effects and contraindications.

The following table identifies the PMS/PMCF Report Inputs for Hemodialysis blood tubing sets.

Item #	Description of Input	Responsible Person	Frequency of Review
1	feedback from sales and marketing	Sales and QA	Monthly. For extraordinary cases, immediately handling

2	proactive follow-up through customer surveys	Sales	Every 6 months.For extraordinary cases, immediately handling
3	Information on the adverse event reports for own products	Sales and Regulatory Affair	Every 6 months For extraordinary cases, immediately handling.
4	Information on the adverse event reports for similar devices	Regulatory Affair	Every 6 months. For extraordinary cases, immediately handling
5	Results from published literature review relevant to the device in question and equivalent devices	Product RA	Every 1 year
6	identifying previously unknown side-effects and monitoring the identified side-effects and contraindications	Product RA	Every 1 year

b. Training of personnel

All personnel that are involved in the review of PMS/PMCF data shall be trained on the following procedures:

- Procedure for distribution of records;
- Procedure for feedbacks and complaint handling;
- Procedure for product recall;
- Procedure for controlling regulatory appraisal;
- Procedure for controlling design changes.
- SOP for Post-Market Surveillance control.

(a) Data collection & Data Summary

Each person responsible for gathering PMS/PMCF data shall summarize the data as mentioned in the item #1 to #6 above on the frequency identified in the table in Section (a) PMS/PMCF Inputs.

- ❖ Sales history

Year / Country	2014	2015	2016	2017	2018
Bangladesh	42,008	25,008	12,000	-	12,360
Indonesia	244,416	360,504	541,296	691,656	851,880
India	5,448	109,584	170,232		59,904
Korea	13,152	130,104	184,776	240,744	233,208
Malaysia	440,232	431,448	171,262	122,400	149,688
Philippines	200,544	214,296	507,432	245,520	158,232
Thailand	116,424	102,552	13,008	340,104	457,920
China	419,712	269,760	56,680	149,996	127,328
Pakistan	214,448	178,344	176,928	361,800	111,720
Peru	114,072	-	-	-	-
Taiwan	448,080	586,392	631,176	1,238,080	1,323,492
Vietnam	354,960	586,723	646,848	722,832	771,048
South Africa	-	-	-	18,280	60,144
Germany	-	-	-	30,000	70,008
Total	The total sale number since product is CE marked: 24,431,732pcs				

❖ Table for adverse events and Regulatory actions undertaken

Year	Q'ty	pcs	ECN/ECN	CAPA	Customer complaint	Recall	Advisory notice and complication	Returned
2014	Total	2,612,449	"N" 4 case	0	"N" 7	0	0	0
2015	Total	2,994,715	"N" 12 case	0	"N" 3	0	0	0
2016	Total	3,111,638	"N" 4 case	0	"N" 4	0	0	0
2017	Total	4,131,412	"N" 2 case	0	"N" 5	0	0	0
2018	Total	4,386,932	"N" 4 case	0	"N" 5	0	0	0

Note "N" Mean "happen without impact on the risk analysis result or performance/safety of Disposable Syringe".

❖ Information on the adverse event reports for similar devices

➢ Collection method:

- Collecting adverse event and product recalls in the last three years from the network of medical device Authority as MAUDE, CANADA, AUSTRAULIA.
- From the web source of equivalent product manufacturers, Google scholar, scientific literature including: PubMed; Medline; CENTRAL; IRIS; EMBASE; MEDION; MAUDE Looking for product-related research.

➢ Record:

- Basic on the information as above mentioned, it is very clear that no any MAUDE, Health - Canada.ca of Blood lines in Vietnam
- There is 1 recall case relative to Blood lines product on MAUDE (FDA) from 2017 to now.

Year	Link	Adverse event/ product recalls contents	Product model	Manufacture
FDA				
20180515	https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?id=163665	Nipro Blood Tubing set with Priming Set and Transducer Protectors. Each device is packaged in a film pouch with 24 lines per cas There is a possibility of the heparin line is occluded.	Model No. BL+A223D/V 809D, Vendor Batch No. 17I06-9, 17I16-9, 17I18-9, 17J17-9, 17J19-9 , 17J20-9 , 17J21-9, 17I19-9, 17K07-9 , 17I01-9, 17J12-9, 17J16-9, 17I21-9, 17I25-9, 17I26-9, 17J09-9, 17J11-9, 17K15-9, 17K16-9.	Nipro Medical Corporation 3150 NW 107th Ave Doral FL 33172-2135

❖ Results from published literature review relevant to the device in question and equivalent devices

Link	Astract	Inventor
https://patentimages.storage.googleapis.com/b1/8b/b4/86f31817d6c4da/US8980094.pdf	A method for the filling and flushing of a blood tube set including a pump segment for a blood pump, an arterial line connected to an inlet of a dialyser, a venous line connected to an outlet of a dialyser, a substituate line connected to a sub stituate port and having a pump segment for a substituate pump, and a three-way connector connected to the arterial line, the venous line and a rinse port. The method includes the steps of opening the rinse port, filling and simultaneously flushing the arterial and venous lines with the substituate Supplied from the Substituate line via the	Max Fischer, Frankfurt (DE)

	Substituate pump, while substituate is drained off via the rinse port, closing the rinse port, and circulating the Substituate in the circuit of arterial line, dialyser and venous line by the blood pump.	
https://patents.google.com/patent/US20180024022A1/en	The disclosure relates to a method for checking a connection between a compressed air outlet of a blood treatment apparatus and a pressure measuring line of an extra corporeal blood tubing set. The methods disclosed include providing a blood treatment apparatus having a compressed air line. A compressed air device is in fluid communication with the compressed air line for generating pressure within the com pressed airline. A compressed air outlet is in fluid communication with both the compressed air line and an exterior of the blood treatment apparatus. The compressed air outlet is connectable with a pressure measuring line and a pressure sensor. The method also includes building up a pressure and an air flow in the compressed air line and / or at the com pressed air outlet, measuring a pressure at the compressed air outlet or in the compressed air line, and evaluating an increase of the measured pressure.	Josef Beden , Mainz - Kastel (DE

- ❖ Identifying previously unknown side- effects and identified side- effects:

  There are twos The side-effect of device are :

  - The side-effect of device in production process
  - The side-effect of device with user

4.3.2.2 Analysis and Discussion benefits/risks from collection data

❖ **Feedback from sales and marketing**

➢ **Data:**

- The PVC tube fold.
- Detect wires with problematic connectors and T-connectors of arteries, have 1 set on the surface and have small ankles in the host tube (detected as insoluble plastic beads).
- Recirculation Connector is not well assembled so it is dropped
- Filter assembly is not fixed position.

➢ **Analysis:**

- Due to the production in packaging process cause the tube is fold.
- Due to injection process, production conditions cause defects.
- Assembly process component assembly is not positioned.

The defects in the complaint data have been identified as risks in the production process and have been included in risk control in 6.1~6.3 of the risk management report..

❖ **Proactive follow-up through customer surveys**

No any case

❖ **Information on the adverse event reports for own products:**

No any case

❖ **Information on the adverse event reports for similar devices:**

➢ **Data:**

From the collected information, there is: 1 case of leakage due to manufacturing process.

➢ **Analysis:**

Adverse event /recall of similar medical devices in the market is caused by the assembly process. These defects have been identified and control in the risk management process by Perfect and until now the control method is still valid so continue to maintain the method that has taken control in RMR.

❖ **Results from published literature review relevant to the device in question and equivalent devices:**

➢ **Data:**

- A method for the filling and flushing of a blood tube set including a pump segment for a blood pump, an arterial line connected to an inlet of a dialyser, a venous line connected to an outlet of a dialyser, a substituate line connected to a substituate port and having a pump segment for a substituate pump, and a three-way connector connected to the arterial line, the venous line and a rinse port. The method includes the steps of opening the rinse port, filling and simultaneously flushing the arterial and venous lines with the substituate Supplied from the Substituate line via the Substituate pump, while substituate is drained off via the rinse port, closing the rinse port, and circulating the substituate in the circuit of arterial line, dialyser and venous line by the blood pump.

Refer https://patentimages.storage.googleapis.com/b1/8b/b4/86f31817d6c4da/US8980094.pdf

- The disclosure relates to a method for checking a connection between a compressed air outlet of a blood treatment apparatus and a pressure measuring line of an extra corporeal blood tubing set. The methods disclosed include providing a blood treatment apparatus having a compressed air line. A compressed air device is in fluid communication with the compressed air line for generating pressure within the com pressed airline. A compressed air outlet is in fluid communication with both the compressed air line and an exterior of the blood treatment apparatus. The compressed air outlet is connectable with a pressure measuring line and a pressure sensor. The method also includes building up a pressure and an air flow in the compressed air line and / or at the com pressed air outlet, measuring a pressure at the compressed air outlet or in the compressed air line, and evaluating an increase of the measured pressure.

Refer https://patents.google.com/patent/US20180024022A1/en

➢ **Analysis:**

- That was the conclusion of a method for the filling and flushing of a blood tube set including a pump segment for a blood pump. After the connection of the patient, the substituate is displaced by the inflowing blood such that a possible contact of the blood with air is reduced to a minimum.
- The methods disclosed include providing a blood treatment apparatus having a compressed air line. A compressed air device is in fluid communication with the compressed air line for generating pressure within the com pressed airline. A compressed air outlet is in fluid communication with both the compressed air line and an exterior of the blood treatment apparatus. The compressed air outlet is connectable with a pressure measuring line and a pressure sensor. The method also includes building up a pressure and an air flow in the compressed air line and / or at the com pressed air outlet, measuring a pressure at the compressed air outlet or in the compressed airline, and evaluating an increase of the measured pressure.

❖ **Identifying previously unknown side- effects and identified side- effects**:

The side-effect of device in production process:

➢ Data:

The product in the manufacturing process occurs unexpected incidents that cause the product to lose performance as a leaked. According to statistics on MAUDE web in the past 3 years with 1 cases of product recall have been generated due to the above defective products. (refer clause 4c).

➢ **Analysis:**

Bloodline is design, production and controlled according to ISO 8637-2, ISO

80369-7 and SIP, SOP issued by Perfect.

According to statistical results, there are some cases of product complaints of loss of performance, this rate has been controlled to decrease from 2016 to a rate of $6.6 * 10^{-7}$, 2017 has a ratio of $1.65 * 10^{-6}$ and continues decreased at a rate of $2.2 * 10^{-7}$ in 2018 (refer refer customer complain docunent).

The side-effect of device with user

- Data:

According to data collected from Pubmed source, the results of clinical investigation showed that:

Link: https://pubmed.ncbi.nlm.nih.gov/10760102/

Citation: R Duffy[1], K Tomashek, M Spangenberg, L Spry, D Dwyer, T J Safranek, C Ying, D Portesi, H Divan, J Kobrenski, M Arduino, J Tokars, W Jarvis

Abstract

Background: Hemolysis associated with hemodialysis is rare. The most frequent causes of hemodialysis-associated hemolysis are chemical contamination, heat, or mechanical injury of erythrocytes from occluded or kinked hemodialysis blood lines. When patients in three states developed hemolysis while undergoing hemodialysis between May 13 and 23, 1998, an investigation was initiated.

Methods: A case-patient was defined as any patient at healthcare facilities A (Nebraska), B (Maryland), or C (Massachusetts) during May 13 through 23, 1998 (epidemic period), who had hemolysis diagnosed > or =48 hours after undergoing hemodialysis. To identify case-patients and to determine background rates, the medical records of patients from facilities A, B, and C who were undergoing hemodialysis during the epidemic and pre-epidemic (that is, May 5 through 19, 1998) periods were reviewed. Experiments simulating hemodialysis with the same lot numbers of hemodialysis blood tubing cartridge sets used on case- and control-patients were conducted.

Results: The rates of hemolysis among patients at facilities A, B, and C were significantly higher during the epidemic than the pre-epidemic period (13 out of 118 vs. 0 out of 118, P < 0.001; 12 out of 298 vs. 0 out of 298, P = 0.001; and 5 out of 62 vs. 0/65, P = 0.03, respectively). All case-patients had hemolysis. Twenty (66%) had hypertension. Eighteen (60%) had abdominal pain, and 10 (36%) were admitted to an intensive care unit. There were two deaths. The only commonality among the three outbreaks was the use of the same lot of disposable hemodialysis blood tubing from one manufacturer. Examination of the implicated hemodialysis blood tubing cartridge sets revealed narrowing of

an aperture through which blood was pumped before entering the dialyzers. In vitro experiments with the hemodialysis blood tubing revealed that hemolysis was caused by increased pressure on erythrocytes as they passed through the partially occluded hemodialysis blood tubing.

Conclusions: Our investigation traced the multiple hemolysis outbreaks to partially occluded hemodialysis blood tubing produced by a single manufacturer. On May 25, 1998, the manufacturer issued a voluntary nationwide recall of the implicated lots of hemodialysis blood tubing cartridge sets

- **Analysis:**

This study indicated that. Examination of the implicated hemodialysis blood tubing cartridge sets revealed narrowing of an aperture through which blood was pumped before entering the dialyzers. In vitro experiments with the hemodialysis blood tubing revealed that hemolysis was caused by increased pressure on erythrocytes as they passed through the partially occluded hemodialysis blood tubing

4.3.2.3Conclusion:

The PMS/PMCF report is based upon these inputs. The results show that:
No new clinical adverse event is gathered during the period, and then there is no need to update the clinical evaluation report.
There are no new risks identified, and there is no need to update the current risk management report.
Product is safety and performance throughout its expected lifetime are evaluated in CER
Ensuring the continued acceptability of the benefit-risk ratio and the side-effect and the residual risk are evaluated and acceptance in the Risk Management Report.
Identifying possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct are evaluated in the Usability engineering report.

4.3.3 Pre-clinical testing (refer Pre-clinical test report)

Item test	Standard	Test report number/date	Criteria/ result	Test organization
Physical test	ISO 8638	Certificate of Analysis/QA-COA-2019071501	Performance meet the ISO 8638	PF (QA Dep.)
Conical fitting	ISO 80369-7	Certificate of Analysis/ QA-COA-2019071501	Performance meet the ISO 8638	PF (QA Dep.)

Chemical test	PF's SOP QW-41-992 & E.P 9.0	Certificate of Analysis/ QA-COA-2019071501	Performance meet the ISO 8638	PF (QA Dep.)
Sterile test	ISO 11737-2	Certificate of Analysis/0145-0219/TTKN	Performance meet the ISO 8638	PF (QA Dep.) & Ho Chi Minh City Centre for the quality control of Food, Drug and Cosmetics
Ethylene Oxide Sterilization residuals	ISO 10993-7	UB/2019/20044	Safety meet the ISO 10993-7	TW SGS Centre
Hemolysis test	ISO 10993-4	UB/2016/90070A-01	Safety meet the ISO 10993-4	TW SGS Centre
Cytotoxicity test	ISO 10993-5	UB/2018/40147	Safety meet the ISO 10993-5	TW SGS Centre
Intracutaneous Reactivity test	ISO 10993-10	UB/2016/90070A-02	Safety meet the ISO 10993-10	TW SGS Centre
Sensitization test	ISO 10993-10	UB/2016/90070A-04	Safety meet the ISO 10993-10	TW SGS Centre
Acute systemic toxicity test	ISO 10993-11	UB/2016/90070A-03	Safety meet the ISO 10993-11	TW SGS Centre
Endotoxin test	USP <85><161>	UB/2018/340146	Safety meet the USP class <85>	TW SGS Centre
Usability test	IEC 62366-1	Usability engineering report	Safety meet the IEC 62366-1	PF's RD
Drop test	ASTM D9416	Disposable syringe and Disposable blood donor set drop test	Performance meet the ASTM D9416	PF's QA
Packaging validation report	ISO 11607-1	Packaging actual aging report	Performance meet the ISO 11607-1	PF's QA
Packaging accelerated aging report	ASTM F1980	Packaging accelerated aging report	Performance meet the ASTM F1980	PF's QA

4.4 Clinical data from literature

4.4.1 Device name/Model：

Bloodline or Hemodialysis Blood tubing sets (standard type and safety type).

4.4.2 Scope of the literature search:

The scope of the literature review was to demonstrate the performance and safety of the products Bloodline or safety Bloodline, based on equivalence to the well establish products Bloodline, Safety Bloodline used in medical.

4.4.3 Methods:

- Date of search: 2020.04.01~2020.04.29.
- Name of persons undertaking the literature search
  Ms: Phan, Thi Thanh Tuyen
  Mr: Cao, Chánh Bảo Tín
- Period covered by search
  in the past 5 years
- Literature sources used to identify data:
  Following scientific database was used: MEDLINE, Pubmed.
  Following database for sysmatic review was used:
  Bookshelf database, pubmed database

4.4.4 Database search details:

- Search keyword used:
  Bloodline; Hemodialysis Blood tubing sets, Safety Bloodline, Hemodialysis blood tubing sets performance.
  For each of the search terms above a literature search is performed separately or in rational combination. The results are combined in a single database, duplicates are removed.

4.4.5 Medium used:

Online: https://www.ncbi.nlm.nih.gov/pubmed.
https://www.nlm.nih.gov/

4.4.6 Selection criteria used to choose articles:

Only literature is selected describing the treatment/ use of Hemodialysis blood tubing set.
Afterwards the literature selected is separated to the following categories:

- Literature demonstrating the performance of Hemodialysis blood tubing set
- Literature pointing out safety aspect, describing complications of Hemodialysis blood tubing set in medical.
- Literature outlining state-of-the-art of safety feature of Hemodialysis blood tubing set after use.
  - Data were requied to be the most comprehensive and up-to-date available, and that it should preferably come from recognized, scientific, peer-reviewed journals in the field ,and
  - Data were gathered from the following sources:
    - Independent review papers
    - Reports of significant experience with relation process.

- The articles should clearly evaluate the criteria applied to ensure the product sare safe and effective during use process.

Publications were only included in the clinical evaluation if they contain sufficientinformation for objective and rational assessment and if their study design was appropriate. Suitability of data for demonstration of performance and safety of the product under evaluation is evaluated in according to MEDDEV 2.7.1 rev 4, A5.3.

Criterion	Group	Grade 1	Grade 2	Grade 3
Test device	D	Actual device	Equivalent device	Other device
Intended use	A	Same use	Similar use	Other use
Patient population	P	Applicable	Limited	Other
Quality of information	R	High quality	Acceptable	Insufficient quality

In principle, the same appraisal criteria are used for literature addressing state of the art. However, inparticular cases, e.g. when the epidemiology, pathomechanisms, or the clinical symptomatology of thecondition to be treated are described, the criteria "test device", "intended use", and "patient population" may be non-relevant for data selection.

Selection process:

Step 1: Abstracts of all retrieved publications are reviewed and graded according the appraisal criteria given above. Publications that are assigned to grade 3 for at least one criterion are excluded from further evaluation

Step 2: All remaining publications are subject to a more detailed evaluation based on full texts. Only literature is included in the clinical evaluation that is assigned to grade 1 at least once and that is not assigned to grade 3 for any criterion after full text evaluation.

4.4.7 Outputs:

- Literature retrieved from each database search:

Literature Source	Key word	Filter condition	Hits found
PUBMED https://www.ncbi.nlm.nih.gov/pubmed	Bloodline	5 years filter	136
	Hemodialysis blood tubing set	5 years filter	449

MEDLINE https://www.nlm.nih.gov/	Bloodline	Health information filter	16
	Hemodialysis blood tubing set	Health information filter	2

The publication was retrieved by manual search in literature databases.

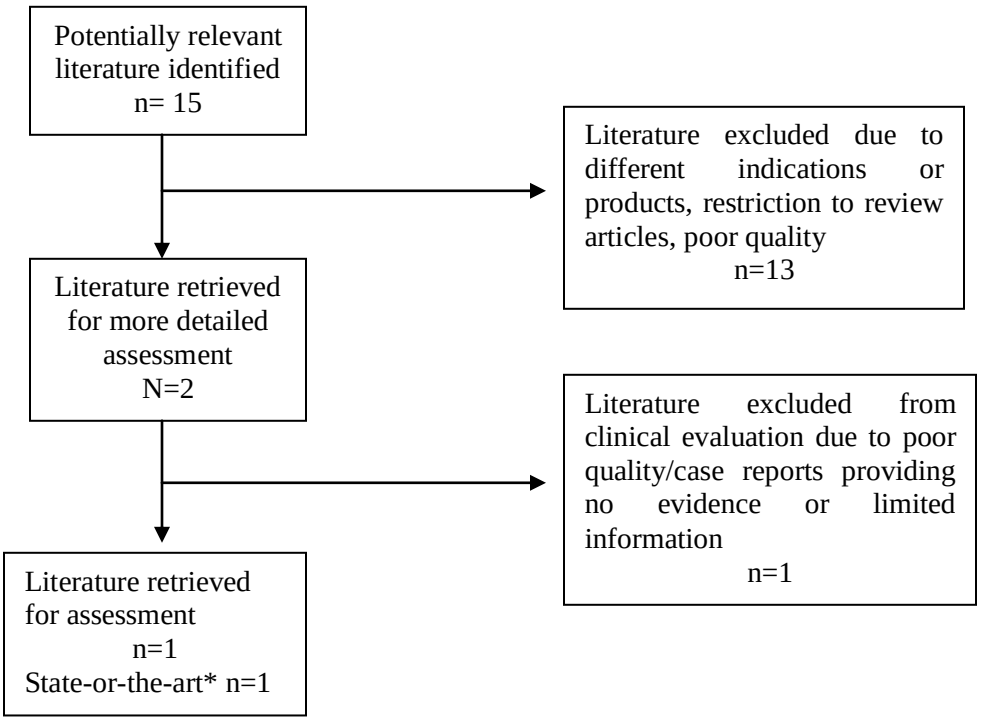
Total 603 publications could be found, there are 98 publications are the duplicates have been removed.

After collecting the literature the duplicates have been removed. In summary 15 publications could be detected, and their abstracts were reviewed. Based on this results 13 articles were considered as being not relevant for this clinical evaluation. These publications deal with different indications, different products, or has been excluded due to poor scientific validity. A total of 2 publications were evaluated in more detail and 1 publication was removed since they were considered to contain limited relevant information only.

- Data selection process:

  Finally the selected literature was separated according to the following aspects:

Literature outlining state-of-the-art	1



4.5. Summary and appraisal of clinical data:

4.5.1 Summary of clinical data：

Optical and Electrical Characterization of Biocompatible Polymeric Lines for Hemodialysis Applications

Website: https://pubmed.ncbi.nlm.nih.gov/29547575/

Citation: Enrico Ravagli [1], Stefano Severi

Abstract

During hemodialysis (HD), blood is circulated through an extracorporeal tubing system (bloodline) made of medical-grade polymeric material. Sensors of various types that do not come into contact with blood (optical, electromagnetic, etc.) are applied directly across the bloodline for clinical purposes and for therapy customization. Thus, a detailed knowledge of the bloodline's physical properties is useful for the development of next-generation HD sensors. In this work, we performed a novel comparative analysis of the materials used by the manufacturers of the bloodlines. We focused on signals and characterization techniques matching those of the abovementioned sensors; consequently, this is an application-specific study of the optical and electrical characterization of bloodline material. Such properties are analyzed and compared for bloodlines from seven different manufacturers by optical absorbance spectroscopy and electrical impedance spectroscopy (EIS). Absorbance spectrum measurements are carried out in the VIS-NIR range. Absorbance spectra are pre-processed and data from both types of analyses are normalized with respect to sample thickness. Optical analysis shows that all bloodlines except one have similarly shaped spectra with slight quantitative differences. In all optical spectra, we find a decreasing trend of specific absorption from 0.14 mm^{-1} at 400 nm to 0.06 mm^{-1} at 1000 nm, with an absorption peak at 915 nm. In one case, a large absorption peak centered at ≃600 nm is found. Electrical analysis shows that all bloodlines have the electrical properties of a constant-phase element (CPE), with statistically significant differences in parameters' values. Estimation of electrical CPE parameters for all bloodline returns a range of 0.942-0.957 for parameter n and a range of 12.41-16.64 for parameter Q_0'. In conclusion, we find that, although some statistically significant differences are present, bloodlines from a representative group of manufacturers share similar electrical and optical properties. Therefore, contactless sensing devices developed for HD will work on different bloodlines if a simple recalibration is performed.

Literature’content analysis table

Article No.	The content of Literature have related with product’s safety and performance	Conclusion
Article 1	This study presents important data for those scientists and engineers involved in contactless sensor design for hemodialysis. A comparison of the optical and electrical	The thickness of the blood tubing set design and the selection of raw materials must meet the monitoring

	properties of several bloodlines from different manufacturers has not, to our knowledge, been performed before in an academic context. Our conclusions are the following: • All bloodlines from the analyzed brands share similar optical spectra in the VIS-NIR range, with one exception of increased absorbance in the VIS region. • All bloodlines from the analyzed brands share the same electrical behavior, that of the constant-phase element (CPE). • Significant differences are present in CPE parameters among bloodlines. • ontactless devices developed for use on one specific bloodline could be used with bloodlines of different manufacturers with proper recalibration	sensor measurement function

4.5.2 The appraisal plan:

To ensure systematic and unbiased appraisal of the data, the company set up an appraisal plan that describes the procedure and the criteria to be used for the appraisal.

The appraisal plan includes:

- Criteria for determining the methodological quality and the scientific validity of each data set.
- Criteria for determining the relevance to the clinical evaluation (relevance to the device and to the different aspects of its intended purpose).
- Criteria for weighting the contribution of each data set to the overall clinical evaluation.

  Following are the criteria and appraisal level set for the Methodological quality and the scientific validity, Relevance of data set for clinical evaluation, Contribution weighting of clinical data.

The following appraisal criteria are used:

Items	Criteria	Levels	Level description
Methodological quality	Shall consider followings aspects: - confounding influences;	M4	High methodological quality and the scientific validity

and the scientific validity	- bias - random error - inadequate disclosure of information - misinterpretation -risk related to device materials, use methods, contraindication, and other hazards happen in clinical use. -risks related to production process. -inadequate information on label, IFU. -state of art of the device.	M3	Middle methodological quality and the scientific validity
		M2	Low methodological quality and the scientific validity
		M1	No methodological quality and the scientific validity
Relevance of data set for clinical evaluation	a. Pivotal data Pivotal data must have the data quality necessary for demonstration of adequate clinical performance and clinical safety of the device under evaluation; be generated either with the device under evaluation or with an equivalent device used in its intended purpose. b. Other data	R4	Complete relevance, pivotal data
		R3	High relevance, pivotal data
		R2	Normal relevance, other data
		R1	No relevance.
Contribution weighting of clinical data	Typically, well designed and monitored randomized controlled clinical investigation should receive the highest weighting. More important clinical data, shall have more weighting.	C4	High contribution, clinical investigation data
		C3	High contribution, no clinical investigation data
		C2	Normal contribution
		C1	No contribution.

4.5.3 Appraisal of clinical data

According to the appraisal plan defined in 4.5.2, we conduct appraisal for those clinical data collected as follows:

M: Methodological quality and the scientific validity.

R: Relevance of data set for clinical evaluation

C: Contribution weighting of clinical data

Accepting the Appraisal with the results meet the conditions with a level of 2 or more

Clinical data	Brief description of clinical data	Appraisal			Appraisal result
		M	R	C	
Clinical data generated and held by the manufacturer					
Risk management report	Describe the structure and expected intended use of the product, the risks involved in the design and using process, as well as measures to	3	4	3	accepting

	reduce the risk as far as to ensure safety and performance of the product				
PMS/PMCF report	The changes arose in design that affect product performance and safety, product information in and post- market, adverse events, etc.	3	3	3	accepting
Pre-clinical testing	Pre-clinical testing items demonstrate that the product is safety and performance during use	3	3	3	accepting
The appraisal plan of literature:					
Article 1	This study presents important data for those scientists and engineers involved in contactless sensor design for hemodialysis. A comparison of the optical and electrical properties of several bloodlines from different manufacturers has not, to our knowledge, been performed before in an academic context. Our conclusions are the following: • All bloodlines from the analyzed brands share similar optical spectra in the VIS-NIR range, with one exception of increased absorbance in the VIS region. • All bloodlines from the analyzed brands share the same electrical behavior, that of the constant-phase element (CPE). • Significant differences are present in CPE parameters among bloodlines.	4	2	2	accepting

Products have long-term production technology, products have low risk, therefore the safety and performance of the product is mainly based on the results of pre-clinical testing to conclude.

Based on the data collected from literatures, there are some relevant information on the safety performance of the product and the actual results of pre-clinical testing for Disposable Syringes product proved that the product fully complied with safety and performance.

The product of Performance (conforms with ISO 8638/8637-2 & ISO 80369-7):

- Pump Segment performance

- Positive- pressure test
- Negative-pressure test
- Pull test
- Injection site
- Locked test
- Transducer protector test
- Conical fitting
- Acidity or alkaline
- Heavy metals
- Residue on evaporation
- Reducing substance $KMnO_4$

The product of safety(conforms with ISO 11737-2 & ISO 10993-7):

- Sterile test
- EO/ECH residue test report
- Endotoxin test with USP <85>

Sterile Barrier Packaging testing performed

- Seal strength according to ASTM F88
- Dye penetration according to ASTM F1929
- Burst Test according to ASTM F1140

Biocompatibility (conforms with ISO 10993-1):

- Acute systemic Toxicity test with ISO 10993-11
- Cytotoxicity test with ISO 10993-5
- Sensitization test with ISO 10993-10
- Intracutaneous Reactivity Test with ISO 10993-10
- Hemocompatibility (Hemolysis test) with ISO 10993-4

4.6 Analysis of the clinical data:

Perfect Hemodialysis Blood Tubing set/ Bloodline has performed clinical evaluation basic on:

- Risk management
- PMS/PMCF report
- Pre-clinical testing
- Clinical evaluation comparison with Equivalence device
- The literature data from PubMed resource

To analysis conducted and the results of these tests demonstrate that Perfect Hemodialysis Blood tubing sets/ Bloodlines are safety and performance with user. The Clinical Evaluation was perform by Perfect Clinical Evaluation team.

4.6.1 Requirement on safety:

The devices must be designed and manufactured in such a way that, when used under the conditions and for the purposes intended, they will not compromise the clinical condition or the safety of patients, or the safety and health of users.

The products was designed and manufactured with purpose reducing, as far as possible, the risk of use error due to the ergonomic features of the device and the environment in which the device is intended to be used, the residue of risks was acceptable when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.

- The products was designed and manufactured according to ISO 8638/8637-2, ISO 80369-7and applied to control by pre-clinical testing:
  - Pump Segment performance
  - Positive- pressure test
  - Negative-pressure test
  - Pull test
  - Injection site
  - Locked test
  - Transducer protector test
  - Conical fitting
  - Acidity or alkaline
  - Heavy metals

- Residue on evaporation
- Reducing substance $KMnO_4$

The product of safety(conforms with ISO 11737-2 & ISO 10993-7):

- Sterile test
- EO/ECH residue test report
- Endotoxin test with USP <85>

Sterile Barrier Packaging testing performed

- Seal strength according to ASTM F88
- Dye penetration according to ASTM F1929
- Burst Test according to ASTM F1140

Biocompatibility (conforms with ISO 10993-1):

- Acute systemic Toxicity test with ISO 10993-11
- Cytotoxicity test with ISO 10993-5
- Sensitization test with ISO 10993-10
- Intracutaneous Reactivity Test with ISO 10993-10
- Hemocompatibility (Hemolysis test) with ISO 10993-4

➢ The product is applied to the risk management process according to EN ISO 14971: 2012.

Identification of risks including:

Identified hazard	Yes/No	Identified hazard	Yes/No
Energy	No	operation	Yes
Biological	Yes	Manufacturing	Yes
Chemical	Yes	Storage & Delivery	Yes
Information	Yes	Post- Delivery	Yes

(1). Biological hazards: Bio-contamination – Bacterium，Virus，Other pathogen; Re- use,

- ➢ For Bio-contamination – Bacterium，Virus，Other pathogen: The product is assembled in a clean environment of 100,000class, the product is periodically inspected for cleanliness according to ISO 11737-1 method and the product is sterilized according to ISO 11135 method and finally re-verified amount by sterile test according to ISO 11737-2.
- ➢ For Re-use hazard：with precaution in the label “Single use only, if reusing, it will be contamination”.

(2). Chemical hazards: The possibility of a harm arising from a particular exposure to a chemical substance, under specific conditions (e.g., acids or alkalis, residues,

contaminates, EO sterilizing agents residues, substances).

- For input materials selected to be suitable for medical use, conduct the necessary chemical tests for the input materials and finished products by ISO 8638/8637-2 and ISO 10993-18.
- For Ethylene oxide sterilization residual E.O： The finished product meet with EN ISO 10993-7.
- For biocompatibility hazard: In the production process, the selection suitable of the raw materials and the finished product are tested according to EN ISO 10993-1 to confirm that the quality of the product meets the requirements.

(3). Information hazards: Inadequate labeling; Inappropriate with warning single-use medical device; Inadequate specification of accessories to be use with medical devices.

- For Inadequate specification of accessories to be use with medical devices: in the design and production process according to the intended use of the product to design in accordance with ISO 8638/8637-2, ISO 9626
- With precaution in the label "Single use only, if reusing, it will be contamination" for Re-use
- Using EN ISO 15223-1 symbol to make caution information to user
- With do not re- sterilization using symbol of EN ISO 15223-1 to make caution information to user.

(4). Operation hazards: Device use is affected by the use environment and the impact is not recognized or understood by the user. Device is misused in the ways that were not anticipated or anticipates but risk control measures were not applied.

- Use usability assessment according to EN 62366 to assess and control risks arising during use process by users.
- Use IFU to guide product Disposal and scrapping safely in accordance with the law.

(5). Manufacturing hazards:

Some hazards in the production process will affect the safety and performance of the products. These hazards should be listed first and used to control the risk reduction.

Hazards in production, warehouse and delivery processes are as follows:

- Injection/ Printing/Assembly Process: use of wrong materials, poor injection of parts (black spots, scratches, burrs, lack of material, impurities, blocked, cracks, 6% connector is failed, dimension failed, leak), Use parts that are not correct, assembly is not positioned, assembly is poor, leak, pinch, rupture, missing parts, part separation, empty package, bad packaging process, lot number/date wrong, tearing too short, there are smash when tearing, incorrect packing quantity, deterioration, printing failed, 6% cracking, component cracking,.ect…

- Sealing process:

  The performance of the process of sealing are faults, which cause the product sterilization incomplete or factors of machinery, conditions that cause defective products (eg: difficult to tear, or whentearing off the product generates paper dust, or Showing unclear lot number, MFD, Sealing mold clamping products causes product is crack, leakage).
- Packaging process:

  Factors of machinery, person that cause defective products (quantity in each box is too much or not enough) or use wrong label
- Sterilization process: Factors of machinery, conditions person that is causing the product is sterile not completed causes the product contaminated
- The post-production storage /storage: Environmental conditions within storage areas (temperature, space, location) are not suitable lead to damage the product or Storage without clearly organized confuses the state of the product, resulting in the wrong product to be took.
- Delivery process:

  Using inappropriate container size, inappropriate shipping method and product organization during transport cause product damage (torn bags, broken box) in shipment or distribution process.
- Post delivery process:

  Post-delivery product, storage does not comply with the original conditions. This leads to damage to the product or/and Post-delivery product , use does not in accordance with their intended use, causing the product to lose its function.

- The above all hazards were controlled by QA department under SIP/ SOP issued by Perfect.
- Use the ISO 15223-1 symbols to make warning safety information to users.
- Use international standards from the product design stage and incorporate controls throughout the manufacturing process and warnings according to EN ISO 15223-1 and manufacturer's supplied information. Addition according to EN 1041 on the packaging and on the IFU to control and safety warnings for users.

4.6.2 Requirement on acceptable benefit/ risk profile.

a. The risk profile:

- Biological hazards:

  Sources of biological hazards may include bacteria, are-or cross-infection…. These sources can cause infection.

- Chemical hazards:

  The possibility of a harm arising from a particular exposure to a chemical substance, under specific conditions (e.g., acids or alkalis, residues, contaminates, EO sterilizing agents residues , substances…)which has the potential to threaten the surrounding natural environment / or adversely affect people's health

  Any single or combination of toxic chemical, biological, or physical agents in the environment, resulting from human activities or natural processes, that may impact the health of exposed subjects. Addition Toxicity of chemical constituents (allergenicity/ Irritancy, pyrogenicity) teratogenic, the toxin affects the reproduction process.

- Information hazards:

  The manufacturer provides inaccurate, unclear information, which is cause:

  - Reuse
  - Re sterilization
  - Incorrect storage conditions
  - Inadequate specification of accessories to be used with the medical device
  - Inadequate specification of intended use.

- Operational hazards:

  Improperly for disposal and scrapping

  Incorrect or inappropriate output or functionality

  Incorrect measurement

  Device use is affected by the use environment and the impact is not recognized or understood by the user.

  Device is misused in the ways that were not anticipated or anticipates but risk control measures were not applied.

- Manufacturing processes hazards:

The risks are arising in the production process that can cause product loss of performance and unsafe for users.

b. The benefit profile:

Nearly 750,000 patients per year in the United States and an estimated 2 million patients worldwide are affected by end stage renal disease (ESRD).

Internationally the numbers are staggering. Estimates are that 2 million people worldwide suffer from ESRD, and the number of patients diagnosed with the disease continues to increase at a rate of 5-7% per year. Taiwan, Japan, Mexico, the United States, and Belgium currently have the highest prevalence of ESRD.

At present, ESRD patients have two treatment options:

- Transplantation: live and deceased donor kidneys
- Dialysis: hemodialysis or peritoneal dialysis

The only alternative today to kidney transplantation is dialysis.

Hemodialysis involves pumping a patient's blood through an external circuit for filtration before it is pumped back into the body. A typical hemodialysis schedule is three sessions per week, for 3-5 hours per session at a medical facility.

When choosing a treatment solution that is a dialysis method, you must use Bloodline products.

Hemodialysis is the far more common type of dialysis—about 90% of all dialysis patients.

4.6.3Requirement on performance:

The Blood lines are designed to transfer blood or other fluids from a patient's vascular access device to the dialyser/ haemodialyser unit for the circulation. Blood lines used together with the A.V. Fistula Needle, Dialyzer and Hemodialysis machine during hemodialysis therapy for patients with renal failure. The Blood lines is intended for single patient use only and is to be discarded at the end of each usage.

Bloodline must to connect with others medical device such as A.V Fistula needle, infusion deliver system, dialysis machine, Dialysis filter….

- Desinged:
  - Product is designed according to the ISO 8638/8637-2, the connections to related devices are based on international standards such as ISO 80369-7（refer Product test report Doc No. COA）.
  - The materials used are assessed and selected according to the requirements

of EN ISO 10993-1 or USP class VI (refer PP material USP class VI Doc No 707-41102-02 PO.No 75708007).

- Packaging material are meet with EN ISO 11607-1 (refer Technical data sheet issue Januaty 22,2015)
- Use error: Applied EN 62366 to assesment To reduce product usage errors or incorrect use by environment or users (refer Engineering usability report Report No. RD 001).

- Manufactured:
  - Production environment meet with class 100,000 (refer Dust particals mesuarement report No. 809Q-PF-HTB/MTLD-REC).
  - Injection Process/ Asembly process are control by QA dept. under SOP, SIP which are issued by Perfect (refer production process validation for injection, Document history record).
  - Sealing process: perform validation for sealing process according to EN ISO 11067-2.
  - Packaging process is control by QA dept. under SOP, SIP which are issued by Perfect
  - Sterilization: The product was sterilized by Ethylene Oxide accordance with ISO 11135, The sterilization is meet with SAL 10^{-6} (refer Sterilization validation report), EO residual meet with EN ISO 10993-7 (refer UB/2019/20044).

    Finished product inspection (chemical, physical, sterile) meet with ISO 8638/8637-2-1, ISO 80369-7 and ISO 11737-2 (refer Document history record).

    Finished product will be test Hemolysis test ISO 10993-4(refer UB/2016/90070A-01), Cytotoxicity test ISO 10993-5 (refer UB/2018/40147), Intracutaneous Reactivity test ISO 10993-10 (refer UB/2016/90070A-02), Sensitization test ISO 10993-10 (refer UB/2016/90070A-04), Acute systemic toxicity test ISO 10993-11 (Refer UB/2016/90070A-03), and Endotoxin test USP <85> (refer UB/2018/40146) perform by SGS Centre
  - The post-production storage /storage:

    Storage and use EN ISO 15223-1 to mark in the label

    Zoning to store for each type of material - semi-finished product - finished

product according to Warehousing control procedure QP-V029.

Perform storage products with according to Warehousing control procedure QP-V029

- Delivery process:

  Apply ASTM D6149 standard to test product quality for shipping process. (refer Label and Drop test report No. QA-BCT-2019051508).

- Post Delivery process:

  Apply EN 62366 for usability engineering evaluation refer Usability engineering repost Doc No. RD 005

  Use symbols according to EN ISO 15223-1 on the packaging to alert for safety during storage refer Label

  Provide IFU for customers to use refer IFU

4.6.4 Requirement on acceptability of side- effect:

The side-effect of device in production process:

- The product in the manufacturing process occurs unexpected incidents that cause the product to lose performance as a leaked. According to statistics on MAUDE web in the past 3 years with 1 cases of product recall have been generated due to the above defective products. (refer PMS/PMCF report Doc No. PMS/PMCF 001).
- Bloodline is design, production and controlled according to ISO 8637-2, ISO 80369-7 and SIP, SOP issued by Perfect.

According to statistical results, there are some cases of product complaints of loss of performance, this rate has been controlled to decrease from 2016 to a rate of $6.6 * 10^{-7}$, 2017 has a ratio of $1.65 * 10^{-6}$ and continues decreased at a rate of $2.2 * 10^{-7}$ in 2018 (refer PMS/PMCF report Doc No. PMS/PMCF 001).

The side-effect of device with user

- According to data collected from Pubmed source, the results of clinical investigation showed that:

Link: https://pubmed.ncbi.nlm.nih.gov/10760102/

Citation: R Duffy[1], K Tomashek, M Spangenberg, L Spry, D Dwyer, T J Safranek, C Ying, D Portesi, H Divan, J Kobrenski, M Arduino, J Tokars, W Jarvis

Abstract

Background: Hemolysis associated with hemodialysis is rare. The most frequent causes of hemodialysis-associated hemolysis are chemical contamination, heat, or mechanical injury of erythrocytes from occluded or kinked hemodialysis blood lines. When patients in three states developed hemolysis while undergoing hemodialysis between May 13 and 23, 1998, an investigation was initiated.

Methods: A case-patient was defined as any patient at healthcare facilities A (Nebraska), B (Maryland), or C (Massachusetts) during May 13 through 23, 1998 (epidemic period), who had hemolysis diagnosed > or =48 hours after undergoing hemodialysis. To identify case-patients and to determine background rates, the medical records of patients from facilities A, B, and C who were undergoing hemodialysis during the epidemic and pre-epidemic (that is, May 5 through 19, 1998) periods were reviewed. Experiments simulating hemodialysis with the same lot numbers of hemodialysis blood tubing cartridge sets used on case- and control-patients were conducted.

Results: The rates of hemolysis among patients at facilities A, B, and C were significantly higher during the epidemic than the pre-epidemic period (13 out of 118 vs. 0 out of 118, P < 0.001; 12 out of 298 vs. 0 out of 298, P = 0.001; and 5 out of 62 vs. 0/65, P = 0.03, respectively). All case-patients had hemolysis. Twenty (66%) had hypertension. Eighteen (60%) had abdominal pain, and 10 (36%) were admitted to an intensive care unit. There were two deaths. The only commonality among the three outbreaks was the use of the same lot of disposable hemodialysis blood tubing from one manufacturer. Examination of the implicated hemodialysis blood tubing cartridge sets revealed narrowing of an aperture through which blood was pumped before entering the dialyzers. In vitro experiments with the hemodialysis blood tubing revealed that hemolysis was caused by increased pressure on erythrocytes as they passed through the partially occluded hemodialysis blood tubing.

Conclusions: Our investigation traced the multiple hemolysis outbreaks to partially occluded hemodialysis blood tubing produced by a single manufacturer. On May 25, 1998, the manufacturer issued a voluntary nationwide recall of the implicated lots of hemodialysis blood tubing cartridge sets

5**. Conslusions:**

Based on the result from the Medical Device Post-Market Surveillance and Post-market clinical follow-up (PMS/PMCF report), the residual risk assessment data from the implementation of risk control action conveyed in the risk management report, and the data from the Literature source from the equivalent product, and

Basic on Pre-clinical testing report of Blood lines Perfect medical concludes that Blood lines product group is safe and performs are claimed when used and applied intended and that the claims

as laid dowm in the Instruction for Use are in consistence with the outcome of these studies.

Blood lines will be used in Dialysis system, That process can help patients with end stage renal disease to increase quantity and quality of life.

The primary benefit of hemodialysis is that it only involves a dialysis session three times a week, with four days each week with require the patient need to go to a medical clinic for dialysis.

Hemodialysis is recommended for people who are unable to carry out the dialysis procedure themselves, due to visual impairment, dementia, or other conditions.

The cost is very cheap, and it is suitable for patients who do not have enough financial resources to pay for the transplanted kidney or cannot use the transplanted kidney treatment.

6. **Date of the next clinical evaluation:**

- Re-evaluate when the intended use can be change.
- Re-evaluate when the products carries significant risks.
- Re-evaluate when the design, materials, production process, storage and so on have changed in compared to the original.
- Re-evaluate when there are adverse information about the device after put into the market or from the equivalent device.
- Clinical evaluations will be re-evaluated every 3 years if there are not any of the above issues occurring during the manufacturing process.

7. Dates and signatures

Based on the data from the market (PMS/PMCF report), the residual risk assessment data from the implementation of risk control action conveyed in the risk management report, and the data from the Literature sourcefrom the equivalent device, and

Taken the intended use, application and indication of Blood lines product group into considerationPerfect medical concludes that for all listed claim the clinical safety and performance data demonstrate conformity with the Essential requirement of Annex1, MDD 93/42/EC.

This report was prepared by:

Management, Rep.: Phan, Thi Thanh Tuyen

Sign :_____

RD Director: Chen, Tung Shun; RD Section Chief: Huynh, Thi Xuan Diem

Sign:_____

QA Director : Hsu, Shun Chieh; QA Vice Manager: Tran, Thi Phuc Hau

Sign:_____

Production Manager: Lu Chih Chien

Sign:_____

Clinical person Internal medicine Doctor

Reviewed by: Ho, Viet Ai

Approved by: G.M: Chen Hung Jen

Sign: CHEN HUNG JEN

8. Qualification of the Responsible evaluators

Clinical evaluation team	Department/ Position	Education	Work experience	Role in the clinical evaluation
Chen, Hung Jen	General Manager	Engineer	5 years on G.M position	Clinical evaluation Report Approved
Chen,Tung Shun	RD Director	Bachelor Chemical Synthetic fibers	QA, RD : 26 Years -South Asia Institute of Technology 1983 Huaxing Chemical -Pharmaceutical Co., Ltd. / 1985 ~ 1993. -Perfect Medical Industry 1993 ~ 2014 Manager QA, RD, Factory -Perfect Medical Industry 2014 ~ 2018 QA&RD Manager -Perfect Medical Industry 2019 ~ now RA,RD Manager	Clinical evaluation Prepared team
Hsu, Shun Chieh	QA Director	Master BSc in Pharmacy from Chia Nan University of Pharmacy and Science(2001~2006) -MSc in Pharmaceutical Science from Chia Nan University of Pharmacy and Science(2007~2009)	Medical and Pharmaceutical Industry Technology and Development Center Project Manager(2011~2012) -Metal Industries Research & Development Centre Project Manager(2012~2016)) -Perfect Medical Industry Regulatory Affairs Senior Specialist(2016~2017) Regulatory Affairs Assistant Manager(2017~2018) Regulatory Affairs Manager(2018)	Clinical evaluation Prepared team

		-EMBA from National Chiao Tung University(2017~2019)	Regulatory Affairs Director(2018~2019) Quality Assurance Director(2019~now)	
Lu, Chih Chien	Production Manager	Bachelor Human resource management department	- Perfect Medical Industry（VN) CO., Ltd ： 2011 ~ 2013 :Director of production - Perfect Medical Industry（VN) CO., Ltd： 2014 ~ 2016: Management Director - Perfect Medical Industry（VN) CO., Ltd： 2017 ~ now: Factory chief	Clinical evaluation Prepared team
Phan, Thi Thanh Tuyen	Management, Rep	Bachelor Organic Synthesis Chemical	QA，RD, RA：16 years Perfect Medical Industry（VN) CO., Ltd： 12/2002 ~ 6/2009:QA head officer - Perfect Medical Industry（VN) CO., Ltd： 7/2009 ~ 01/2013: QA Manager - Perfect Medical Industry（VN) CO., Ltd： 01/2013 ~ 05/2014 :QA Vice Manager - Perfect Medical Industry（VN) CO., Ltd： 05/2014~ 07/2016: RD Manager & QMS Representative -Perfect Medical Industry（VN) CO., Ltd： 07/2016 ~ 10/2017 : RA Manager & QMS Representative - Perfect Medical Industry（VN) CO., Ltd： 10/2017~ 01/2019: Audit Vice Manager& Special Assistant of General Manager. -Perfect Medical Industry（VN) CO., Ltd 01/2019~now Audit Manager, RA Manager and QMS	Clinical evaluation Prepared team

			Representative	
Huynh, Thi Xuan Diem	RD Section Chief	Bachelor Food department	QA，RD：15 years Perfect Medical Industry（VN) CO., Ltd：2002 ~ 2013 :QA technician - Perfect Medical Industry（VN) CO., Ltd：2014 ~ 2015 :RD Staff - Perfect Medical Industry（VN) CO., Ltd：2016 ~ 2017 :RD Deputy of Department - Perfect Medical Industry（VN) CO., Ltd：2018 ~ now :RD Head of Department	Clinical evaluation Prepared team
Tran, Thi Phuc Hau	QA Vice Manager	Bachelor Biology	QA: 12 years Perfect Medical Industry（VN) CO., Ltd：07/2006 ~ 6/2007:QA personnel - Perfect Medical Industry（VN) CO., Ltd：7/2007 ~ 03/2014: QA Staff - Perfect Medical Industry（VN) CO., Ltd：04/2014 ~ 07.2015 :QA Deputy of Department - Perfect Medical Industry（VN) CO., Ltd：08/2015~ 04/2017: QA Head of Department - Perfect Medical Industry（VN) CO., Ltd：05/2017 ~ now: Vice Director of QA	Clinical evaluation Prepared team
Declarations of interests				

I, clinical doctor Ho,Viet Ai			
Name	Ho, Viet Ai	Age	51
Gender	Male	Position	Surgery – Anaesthesiology & Recovery Department Deputy Dean Of The Department in The Saigon International Maternity Hospital

Education:

The degree of Doctor of Medicine, University of medicine and pharmacy, Ho Chi Minh City.

Professional Experience:

17 years Doctor of The Saigon International Maternity Hospital in Ho chi minh City

https://www.sihospital.com.vn/en/team-of-doctors/;

PERSONAL INFORMATION

Date of birth 10/04/1968

Gender Male

Place of birth Quang Tri Province

EDUCATION INFORMATION

1996 Graduation at Ho Chi Minh City Medicine and Pharmacy University

WORK EXPERIENCES

1989-1993 Physician at Long Khanh hospital

1996-1999 Working at Long Khanh health center

2002-2008 Doctor at the Saigon International Maternity Hospital

2009-2019 Surgery – anesthesiology & recovery department Deputy Dean of The Department in the Saigon International Maternity Hospital

I reviewed clinical evaluation report for the some medical devices are manufactured by Perfect medical as below :

- Blood lines
- Disposable Infusion sets
- Disposable Transfusion sets
- Disposable Syringes
- Extension Tubes
- Scalp Vein Sets
- Winged needle sets

- A.V Fistula needle sets
- I.VLocks
- Rinse (Priming Tubing sets).

I declare no conflict interest as below:

I and my family members are included never have gotten or get promised any grants, sources of income or benefits from Perfect medical .

I'm not a：

- Perfect medical's employment .
- Perfect medical 's participation as an investigator in clinical studies of the device, or in pre-clinical testing of the device

I don't have :

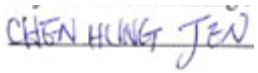
- Any ownership/ shareholding possibly affected by the outcome of the evaluation .
- Grants sponsored by Perfect Medical.
- Benefits such as travelling or hospitality .
- Interests in connection with the manufacturing of the device or its constituents.
- Interests in connection with intellectual property, such as patents, copyrights and royalties (whether pending, issued or licensed) possibly affected by the outcome of the evaluation .
- Other interests or sources of revenues possibly affected by the result of the evaluation.

I committed to ensuring the independence and integrity of my content.

Declarations of interests issue on Feb 10th, 2020 by Clinical Doctor HoViet Ai

Signed by :Ho Viet Ai

Signed by: Perfect Medical Industry（VN）Co., Ltd
General Manager



9. References:
   1. MEDDEV 2.7/1 Rev 4Medical devices directives clinical investigation.
   2. MDD 93/42/EEC Medical device directive.
   3. EN ISO 14971:2012 Medical devices- Application of Risk management to medical devices
   4. ISO 8636:2010 Cardiovascular implants and extracorporeal Systems- Extracorporeal blood circuit for Haemodialysiers, haemodiafilters and haemofilters.
   5. EN ISO 10993-1:2018 Evaluation and testing within a risk management process.
   6. ISO11135:2014 Sterilization of Health- Care products- Ethylene oxide- Requirement for the development, validation and routine control of a sterilization process for medical devices.
   7. MEDDEV 2.12/2 Rev2 Guidelines on medical devices Post market clinical Follow-up studies.
   8. MEDDEV 2.12/1 Rev 8 Guidelines on a medical devices vigilance system.
   9. Risk managementfile #RD 001 (for Blood line).
   10. PMS/PMCF report (for Blood line).
   11. COA (for Blood line).
   12. Biocompatibility test reports(for Blood line).
   13. K161582, DORA Tubing sets for Hemodialysis 510(K)
   14. Guidance for industry and FDA staff Hemodialysis Blood tubing set- Premarket Notification [510(k)] Submissions.
   15. Article 1: Optical and Electrical Characterization of Biocompatible Polymeric Lines for Hemodialysis Applications.