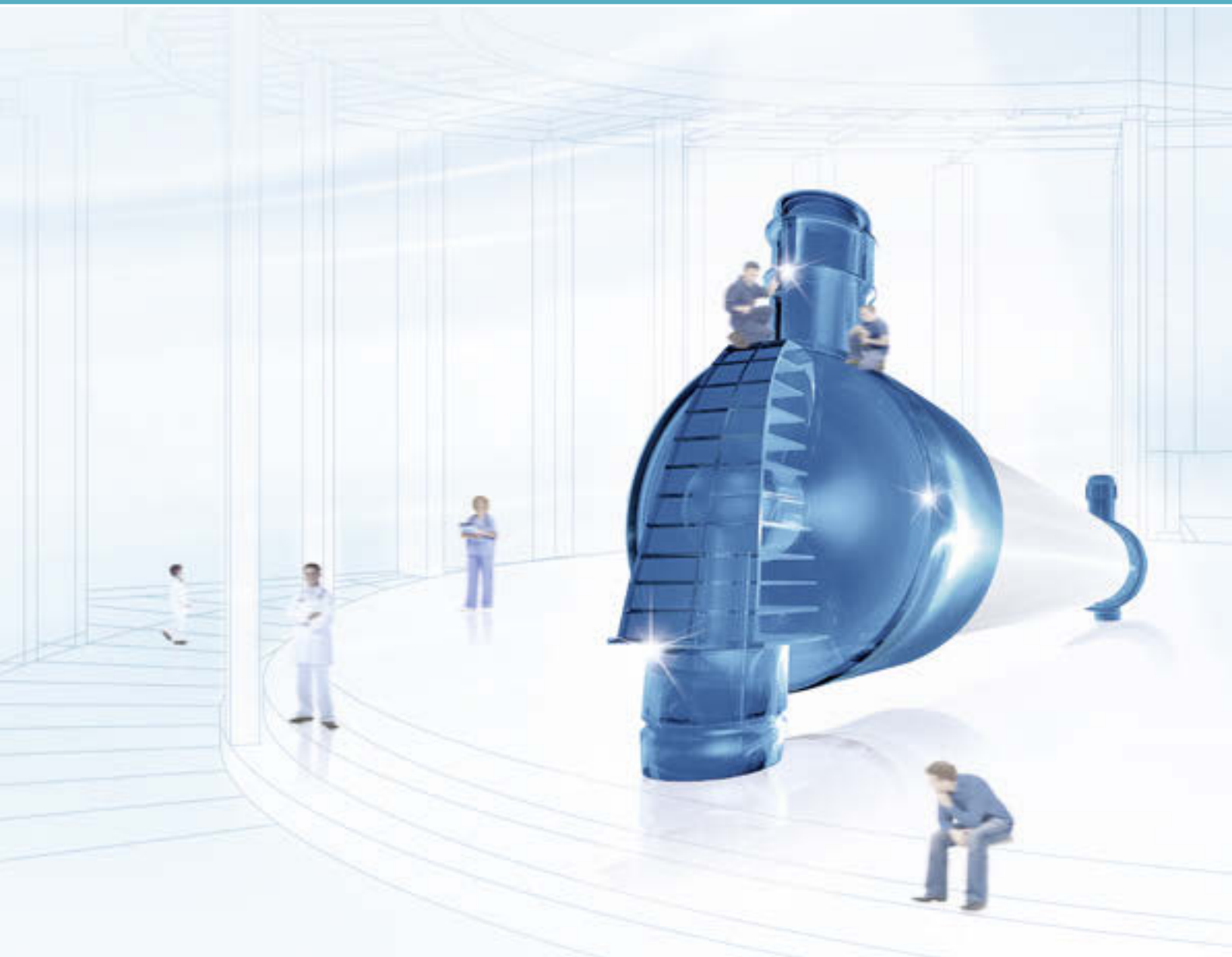


Cardioprotective Haemodialysis

FX classix

High-Flux Dialysis for Improved Survival



Cardioprotective Haemodialysis **SPOT**



**FRESENIUS
MEDICAL CARE**

Protect your Patient

Cardioprotective Haemodialysis

The reduction of risk factors for cardiovascular diseases (CVD) is core to the development of dialysis systems and products at Fresenius Medical Care. Outstanding cardioprotection must be reflected in all levels of product development and application.

Wide-ranging cardioprotection

There have been tremendous improvements in the quality and efficacy of haemodialysis (HD) therapy in recent years. Despite this, cardiovascular diseases (CVD) remain the leading cause of death for patients with end-stage renal disease (ESRD).

SF

Cardioprotective

Services

Over 30 years of experience in dialysis at your service.

- Project Planning and Consulting
- Training and Education
- Technical Services
- Water Quality Service (WQS)
- Medical Information Services

Products

State-of-the-art technologies enable advanced cardioprotective therapies.

- CorDiax product line:
 - 5008 CorDiax and 5008S CorDiax
 - FX CorDiax haemodiafilter
 - BCM-Body Composition Monitor
- Classix product line:
 - 4008S classix
 - FX classix dialysers
- Therapy Data Management System (TDMS)
- Online Purification Cascade (OPC)

Moreover, both overall and cardiovascular mortality are markedly greater in ESRD patients than in the general population. This is why we put Cardioprotective Haemodialysis on the SPOT. A comprehensive approach that includes services, products and therapies is needed to

achieve the best therapeutic performance – meaning improved clinical outcomes and better quality of life, enhanced control of therapy costs, and simpler, safer handling.



Haemodialysis

Outcomes

Achieving better outcomes with cardioprotective therapies.

- Reduced mortality risk
- Fewer cardiovascular complications
- Optimised use of resources

Therapies

Cardioprotective therapies designed by the world market leader in haemodialysis.

- High-Flux dialysis
- HighVolumeHDF®
- Advanced Fluid Management

Protect your Patient

Cardioprotection at the heart of long-term haemodialysis

Chronic kidney disease (CKD), as well as the effects of dialysis itself, can lead to cardiovascular diseases (CVD) such as atherosclerosis and left ventricular hypertrophy (LVH), the largest causes of death in haemodialysis patients.¹

Fresenius Medical Care's mission is to enable nephrologists to provide the best possible therapy for their long-term haemodialysis patients in order to minimise the risk of CVD.

In addition to the efficient removal of uraemic toxins, protecting patients through a high level of membrane biocompatibility and endotoxin retention is crucial in Cardioprotective Haemodialysis.

Therefore, Fresenius Medical Care has developed a new class of dialyser, which opens the door to cardioprotective renal replacement therapy – the FX classix:

FX classix – highest level of biocompatibility

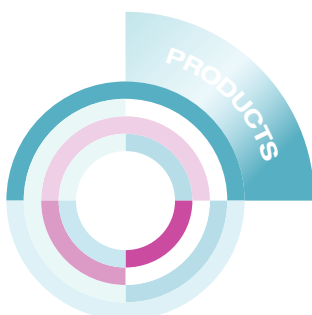
- INLINE steam sterilisation enables the production of sterile and pyrogen-free dialysers and ensures high biocompatibility.²

FX classix – maximum endotoxin retention

- The Helixone® membrane has a high endotoxin retention capacity, which minimises the risk of inflammation.³

FX classix – cost saving potential

- FX classix dialysers provide an additional cost saving potential thanks to the lower rinsing volumes enabled by INLINE steam sterilisation as well as the lower weight of the dialysers, which could result in lower waste management costs.



References

1. de Jager D. et al., JAMA (2009); 302: 1782–1789.
2. Müller T. F. et al., Nephron (1998); 78: 139–142.
3. Weber V. et al., Blood Purif (2003); 21: 365.

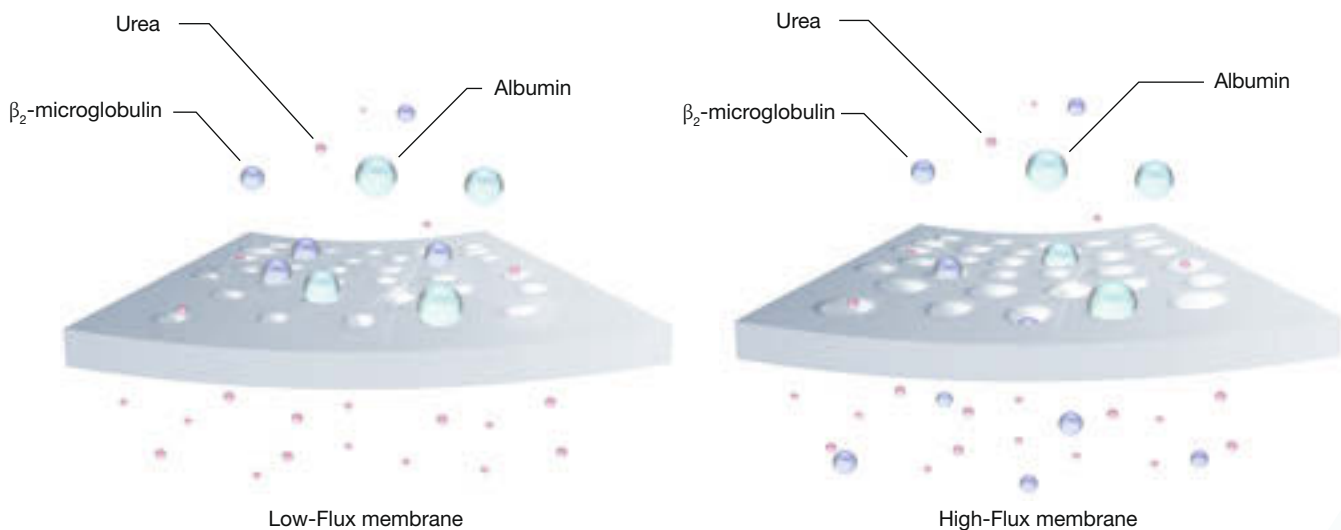
FX classix – high performance

- Performing High-Flux dialysis has advantages over Low-Flux dialysis: thanks to the larger pores on the inner surface of the innovative Helixone® membrane, High-Flux dialysers also remove middle molecules such as β_2 -microglobulin while preventing the loss of essential blood components such as albumin. In addition, the permeability to water is much higher than in Low-Flux dialysers.

These benefits reduce the risk of CVD and help to improve the long-term outcomes of your patients.

SPOT on:

- Highest biocompatibility due to INLINE steam sterilisation.²
- High endotoxin retention of Helixone® membrane.
- Cost saving potential due to lower rinsing volumes.



Protect your Patient

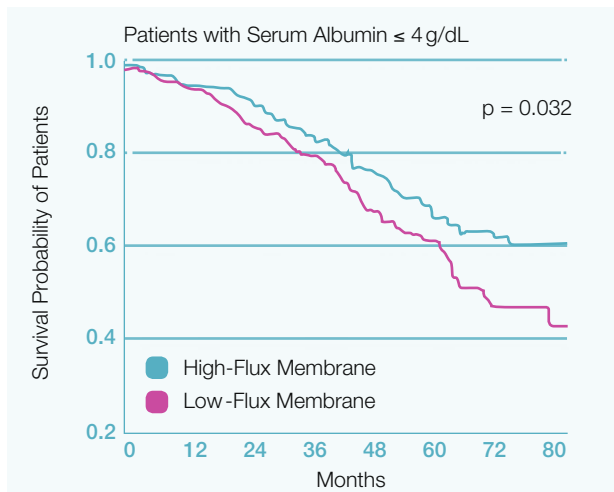
Clinical benefits of High-Flux dialysers

Improved survival

The Membrane Permeability Outcome Study (MPO) revealed superior survival rates in high-risk patients when treated with High-Flux membranes compared to Low-Flux membranes. For patients with hypoalbuminaemia (≤ 4 g/dL of serum albumin) or diabetes mellitus, a reduction in the relative risk of death of up to 37% was observed.¹

Up to 86% of dialysis patients worldwide have a serum albumin level ≤ 4 g/dL, underlining the relevance of these risk factors in dialysis.²

During the first 4 years of the MPO study, one in eleven events of death was prevented when hypoalbuminaemic patients were treated with High-Flux dialysers instead of Low-Flux dialysers.



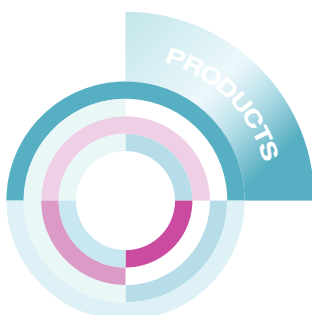
Kaplan-Meier survival curves for the population of patients with serum albumin levels ≤ 4.0 g/dL (log-rank test $p=0.032$).¹

(Graph adapted from original publication)

Guidelines recommend High-Flux dialysers

As a consequence of the results of the MPO study, High-Flux membranes **are now recommended by the European Renal Best Practice Advisory Board for all haemodialysis patients:**

“Guideline 2.1: Synthetic High-Flux membranes should be used to delay long-term complications of haemodialysis therapy ... even in low-risk patients...”³



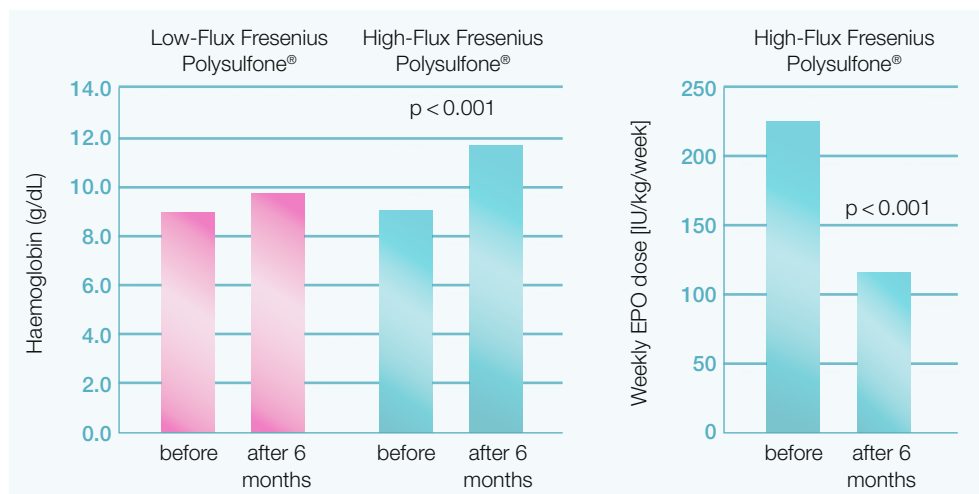
Improved anaemia management

In patients with ESRD, it is often necessary to administer EPO to treat anaemia. In addition to this, inflammation often contributes to EPO hypo-responsiveness.⁴ It was shown that High-Flux membranes improved control of anaemia while allowing a progressive reduction in the exogenous EPO dose by 25 to 45%.⁵

Hence, High-Flux membranes offer the potential to reduce EPO costs.

SPOT on:

- Improved patient survival with High-Flux dialysis.¹
- Relative risk reduction of 37% for hypoalbuminemic patients with High-Flux dialysis.¹
- Improved anaemia control through High-Flux dialysis.⁵



Recovery of haemoglobin (Hb) levels was significantly better after 6 months for patients treated with High-Flux vs Low-Flux membranes. Further, in this patient group the mean EPO dose was significantly lower.⁵

(Graph adapted from original publication)

References

1. Locatelli F. et al., Journal of American Society of Nephrology (2009); 20: 645–654.
2. The DOPPS report 2004; http://www.dopps.org/pdf/dopps_report_2004.pdf.
3. Tattersall J., Nephrol Dial Transplant (2010); 25: 1230–1232.
4. Gunnell J. et al., Am J Kidney Dis (1999); 33(1): 63–72.
5. Ayli D. et al., J Nephrol (2004); 17: 701–706.

Protect your Patient

Proven benefits of the FX-class® design

Fresenius Polysulfone® has long been the »gold standard« in dialysis membranes. For over 30 years, Fresenius Polysulfone® has stood for outstanding safety and performance. Derived from established Fresenius Polysulfone® technology, the Helixone® membrane is at the core of FX-class® dialysers.

The new FX classix dialysers are part of the FX-class® series. More than 177 million treatments have been performed with FX-class® dialysers proving the record of success of the Helixone® membrane.

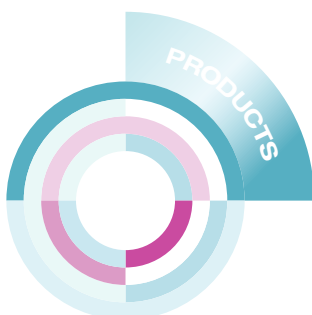
The unique design of the FX-class® dialyser is based on refined and optimised performance and handling. Several state-of-the-art technologies have been combined to offer distinctive benefits:

Helixone® membrane – optimised performance

- Optimised membrane permeability enables efficient removal of low molecular weight substances and middle molecules
- Minimal loss of essential blood components
- Produced with Nano Controlled Spinning (NCS™) technology

Optimised haemodynamics

- Homogenous blood flow in the dialyser header through lateral blood-inlet port
- Fewer stagnation zones in the header region
- Risk of bloodline kinking is diminished



Optimised dialysate flow for higher clearances

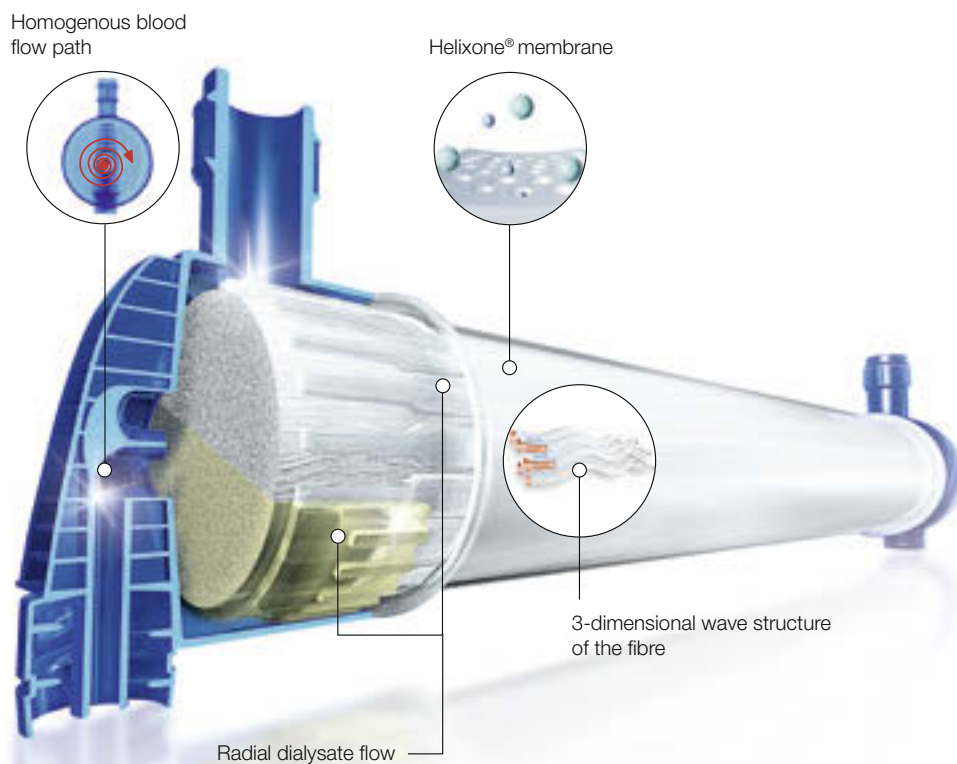
- 3-dimensional microwave structure of the fibres, together with a higher packing density, ensures a homogenous distribution of dialysate over the entire cross-section of the dialyser
- Radial flow of the dialysate around each fibre within the bundle

Kind to the environment

- Usage of ecologically-friendly plastics
- Lower carbon-footprint as a result of fewer materials, less packaging and less fuel for transport

SPOT on:

- Proven and trusted Helixone® membrane.
- Optimised haemodynamics.
- Optimised dialysate flow.
- Environmental-friendliness.



Protect your Patient

Purity ensured – with steam

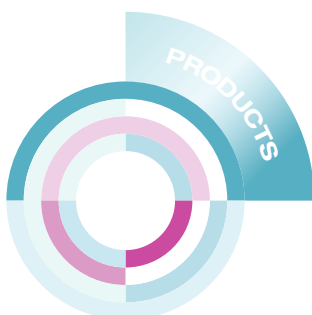
INLINE steam sterilisation

Product safety means patient safety. In the manufacturing process of our dialysers, we comply strictly with highest quality standards. Thus, all the FX classix dialysers pass through the unique INLINE steam sterilisation process specifically developed by Fresenius Medical Care.

The blood and dialysate compartments of the dialysers are rinsed with hot steam > 121°C for 15 minutes. Following this, all dialysers undergo a fibre leakage test to ensure the integrity of every single fibre.

No chemical residuals

INLINE steam sterilisation reduces potential hazards from residuals. The basic principle of this method is extensive rinsing with hot steam – without the need for chemicals or gamma sterilisation processes. Gamma irradiation may induce the degradation and alteration of the material chemistry and generate cytotoxic substances.¹ INLINE steam sterilisation therefore leads to highly purified dialysers free from chemical, cytotoxic and carcinogenic residuals and with excellent haemocompatibility.



INLINE steam sterilisation process and integrity test

SPOT on:

- Rinsing with hot steam leads to highly purified dialysers.



INLINE steam sterilisation process.



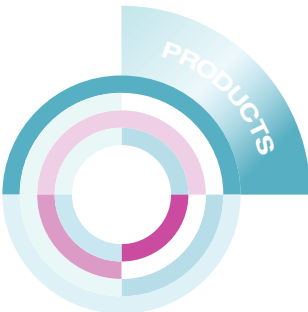
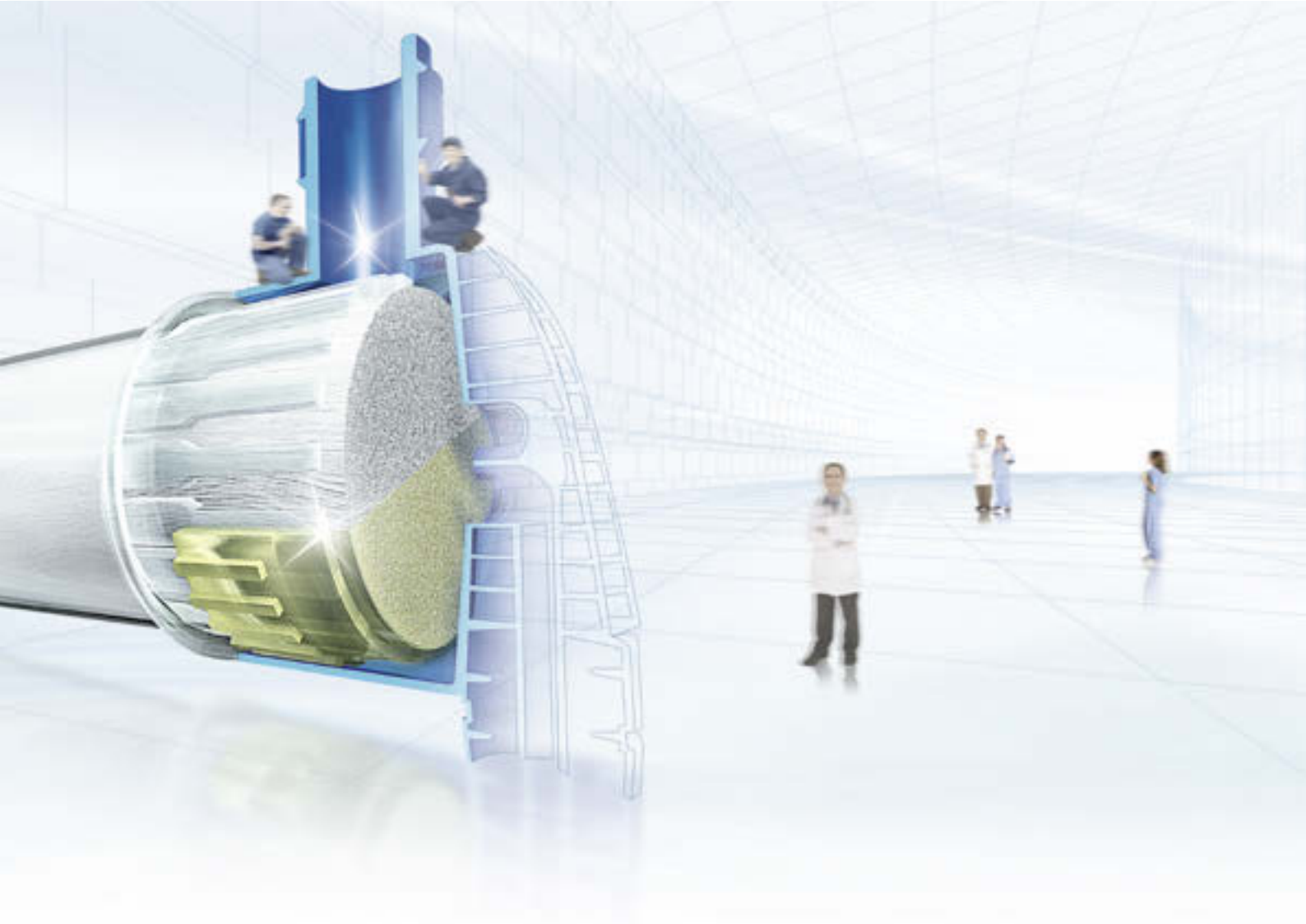
Integrity test: air pressure is applied to the fibre bundle from one side while the other side contains sterile water. If any leakages were present in the membrane, air would pass through the membrane and create bubbles.

References

1. Shintani H. et al., Journal of Analytical Toxicology (1989); 13: 354–357.

Protect your Patient

Greater protection through active prevention



Superior endotoxin retention

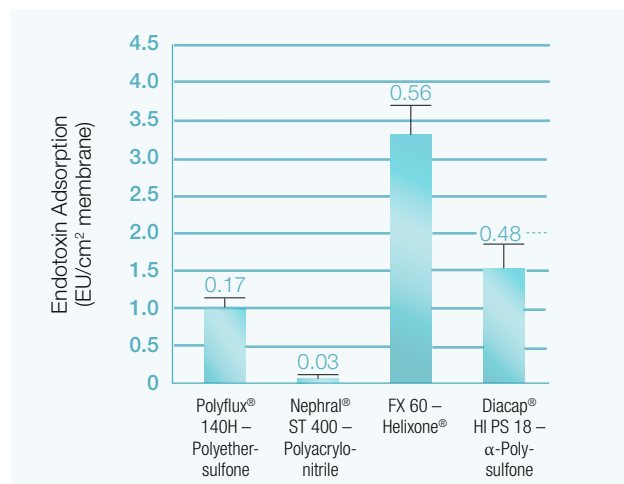
Endotoxins are large molecules from the outer membrane wall of gram-negative bacteria. They are able to enter dialysis fluid, and thus the bloodstream, via the microbial contamination of water or fluid conduits. Once in the patient's blood, endotoxins can induce inflammatory responses and – in the longer term – complications such as amyloidosis or accelerated atherosclerosis.

Membranes, such as Helixone[®], which have a high endotoxin retention capacity, protect the patient from inflammation, particularly when ultrapure dialysate is not available.¹ Therefore, it is crucial to prevent endotoxins entering the bloodstream by adopting the following hygiene regime:

- Use of dialysis membranes with high endotoxin retention capacities, such as Helixone[®], to protect the patient from inflammation.
- Use of dialysis fluid filters to create ultrapure dialysis fluid free from residual endotoxins.
- Overall hygiene of water supply system.

SPOT on:

- High endotoxin retention of Helixone[®] membrane.
- Improved patient protection through ultrapure dialysis fluid.



Endotoxin adsorption per cm² membrane surface area after 120 min in-vitro dialysis with contaminated dialysate (endotoxin from bacterial culture filtrates; initial concentration 50 EU/mL).¹

(Graph adapted from original publication)

References

1. Weber V. et al., Blood Purif (2003); 21: 365.

The new FX classix

Optimised use of resources

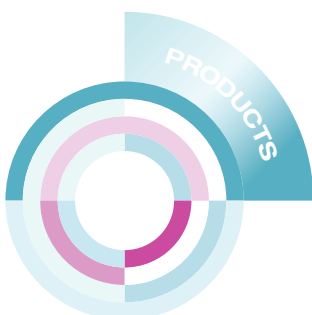
Lower weight – reduced costs

The reduced weight of the FX classix dialysers – due to less packaging and decreased use of processed materials – allows cleaner, more cost-effective waste management and thus conserves valuable resources.

Less rinsing – reduced costs

Since FX classix dialysers are INLINE steam sterilised, rinsing volumes of only 500 mL are needed per treatment. Consequently, it is possible to apply the dialysers quickly with decreased preparation time.

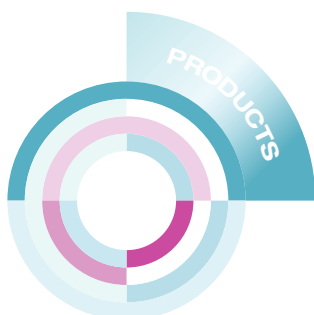
Moreover, the reduced rinsing volume represents an average cost saving of 50 % for the priming fluid.



The new FX classix

Performance data

FX classix High-Flux dialysers	Molecular weight (Dalton)	FX 50 _{classix}	FX 60 _{classix}	FX 80 _{classix}	FX 100 _{classix}
Clearance (Q _B = 300 mL/min)					
Cytochrome c	12,230	55	74	89	100
Inulin	5,200	72	95	113	122
Vitamin B ₁₂	1,355	137	162	185	201
Phosphate	132	204	225	244	253
Creatinine	113	224	243	259	264
Urea	60	253	266	279	280
Clearance (Q _B = 400 mL/min)					
Cytochrome c	12,230	-	76	92	105
Inulin	5,200	-	99	119	129
Vitamin B ₁₂	1,355	-	175	202	222
Phosphate	132	-	252	279	291
Creatinine	113	-	277	300	309
Urea	60	-	312	334	336
Ultrafiltration coeff. (mL/h x mmHg)		27	38	53	68
Sieving coefficients					
Albumin	66,500		< 0.001		
Myoglobin	17,053		0.1		
β ₂ -microglobulin	11,731		0.7		
Inulin	5,200		1		
<i>In vitro performance: Q_D = 500 mL/min, Q_F = 0 mL/min, T = 37 °C (EN 1283, ISO 8637). Ultrafiltration coefficients: human blood, Hct 32 %, protein content 6 %.</i>					
Membrane material				Helixone®	
Sterilisation method				INLINE steam	
Housing material				Polypropylene	
Potting compound				Polyurethane	
Units per box				24	
Effective surface (m ²)		1.0	1.4	1.8	2.2
K ₀ A Urea		866	1,068	1,394	1,429
Priming volume (mL)		53	74	95	116
Article number		F0002385	F0002386	F0002387	F0002388



Protect your Patient

High-Flux dialysis – improved survival. Better outcomes

Almost one in two patients with ESRD dies as a result of cardiovascular disease. That is why Cardioprotective Haemodialysis is a core principle at Fresenius Medical Care, as we work and learn to solve the challenges of modern dialysis. Each step we take is focused on minimising cardiovascular risks and extending patients' lives. In recent years, several studies have demonstrated that patients show improved long-term survival when treated with High-Flux dialysers. Hence, the new FX classix dialysers are a fundamental component of our SPOT programme and help you to protect your patient – day by day.

State-of-the-art technologies enable advanced cardioprotective therapies.



✓ Efficient removal of uraemic toxins

✓ Higher clearances by design

✓ Optimised haemodynamics

✓ INLINE steam sterilisation

✓ Optimised use of resources

SPOT on:

- High-Flux dialysis and design benefits.





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