FX-class®
High-Flux Dialysis for Improved Survival
The benefits of High-Flux membranes – the essence of the MPO Study:

- A 37% reduction of the relative risk of death was observed for patients having a serum albumin level ≤ 4.0 g/dL.
- Significantly improved survival for diabetes patients.

As between 56% and 86% of dialysis patients worldwide have a serum albumin level < 4.0 g/dL, the majority of patients on dialysis would benefit from High-Flux dialysis\(^\text{2}\).

The MPO Study is supported by other studies\(^{3,4,5,6}\) showing a beneficial effect of High-Flux membranes for dialysis patients like the recently published data by Krane et al. (2007) from the database of the German Diabetes and Dialysis (4D) Study\(^7\):

- A beneficial effect of biocompatible High-Flux membranes on patients’ outcome compared to cellulosic membranes and Low-Flux membranes was shown for patients with type 2 diabetes.

During the study, additional enrolment of patients with serum albumin > 4.0 g/dL was allowed.
Several state-of-the-art technologies have been combined to create the distinctive functional features of the FX-class® dialysers:

The fibre bundle geometry, the membrane nanostructure, the flow port and the housing design all provide advantages in terms of performance, haemodynamics, dialysate flow as well as safety and handling.

**Optimised fibre array**

The higher packing density of the fibre bundle together with the special wavy fibre structure regulates a homogeneous distribution of dialysate over the whole cross-section of the dialyser. This is evident in the superior clearance values of the FX-class®®.

**Refined haemodynamics**

The lateral blood-inlet port defines a homogeneous blood flow-path, avoiding low velocity stagnation zones in the header region. Furthermore, the risk of accidental twisting of bloodlines is virtually eliminated.
Helixone® is the advanced High-Flux polysulfone membrane of the FX-class® dialysers. Helixone® has been designed specifically to meet the present-day demands of High-Flux dialysis and convective therapies:

- Larger average pore size (3.3 nm)
- More even distribution of pores
- High membrane porosity for enhanced hydraulic permeability

The result of these structural refinements is the smooth and unrestricted transport of larger uremic toxins across the membrane wall, as exemplified by the significantly increased sieving coefficient for larger solutes (e.g. $SC_{\text{ß2m}} = 0.8$) – but with minimal leakage of useful proteins like albumin ($SC_{\text{albumin}} \leq 0.001$).

Radial dialysate flow

The pinnacle structures at both ends of the polypropylene housing together with the potting technology ensure an even, radial flow of the dialysate around the individual fibres of the bundle.

Fibres designed for High-Flux HD

The reduced inner diameter and wall thickness of the fibre increase the internal filtration and minimise the diffusion resistance. A significant increase of both the diffusive and convective clearances is therefore achieved, allowing the efficient removal of a broad spectrum of uremic toxins.
Superior Production Process Involving INLINE Steam Sterilisation

The FX-class® dialysers are sterilised by the unique INLINE steam sterilisation process specifically developed by Fresenius Medical Care.

During the INLINE steam sterilisation process, both blood and dialysate compartment of the dialysers are rinsed continuously for 15 minutes with steam at a temperature of 121 °C. \(^2\)

This extensive rinsing of FX-class® dialysers with hot steam and without chemicals results in extremely low levels of residuals.

Every dialyser is then tested for fibre integrity. Fresenius Medical Care carries out its 100% fibre leak testing procedures using a bubble-point test: Air pressure is applied to the fibre bundle from one side while the other side contains sterile water. If there were leakages in the membrane, air would pass the membrane and create bubbles, which are then detected by automated camera systems. \(^3\)

The dialysers failing the integrity test are discarded. Finally, the dialysers are dried with warm, sterile air.

After INLINE steam sterilisation the dry dialysers get labeled, are visually inspected and finally fully automatically packed.

During every production step, all Fresenius Medical Care dialysers are undergoing various automated in-process controls.
Advantages of INLINE Steam Sterilised Dialysers

The INLINE steam sterilisation process leads to:

- Highly purified dialysers
- Dialysers free of any toxic chemicals or sterilisation by-products
- Low rinsing volumes

In contrast to INLINE steam sterilisation, gamma-irradiation may physically and/or chemically alter the membrane as high-energy radiation produces ionisation and excitation in polymer molecules such as polysulfone. This process may result in physical or chemical cross-linking or degradation of the material and cytotoxic substances may be generated\(^9\).\(^{10}\)

Among others, it has been shown that 4,4’-methylene-dianilin, a substance of known carcinogenic potential, may be generated in the polyurethane potting material of capillary dialysers during gamma-radiation\(^{11}\).

Furthermore, chemically active or pyrogenic substances and residuals from sterilisation or production may remain within the fibre. Intensive priming and rinsing procedures are needed with irradiated filters.

A recent study carried out by the Fraunhofer Institute, Germany, shows the effects of test extracts obtained from dialysers after undergoing different sterilisation procedures on the viability of cells in culture:

- Samples from different irradiated dialysers inhibited metabolic activity (determined with a cell proliferation assay) of cells by 70% to 97%. The samples of INLINE steam sterilised FX80 dialysers showed only a negligible influence.
- DNA synthesis was determined after incorporation of the base analogue BrdU (5-bromo-2’-deoxyuridine): The extracts from FME dialysers affected the cells only in a non-significant manner, whereas irradiated dialysers contain cytotoxic residuals killing a majority of the cells. \(^4\)

Therefore, highly intensive rinsing is recommended before use of irradiated dialysers.
Advantages of FX-class® High-Flux Dialysers

- Highly purified dialysers – sterile and pyrogen-free
- Excellent haemobiocompatibility, unaffected by sterilisation
- Dry packed, “light-weight” products
- Dialysers without pore-fillers or sterilising agent residues
- Safe and comfortable treatment for your patients
- Environmentally friendly sterilisation method

All production steps from the manufacturing of the membrane to the finished dialyser are adjusted to each other resulting in constant highest quality.

The FX-class® of dialysers is – like all other products from Fresenius Medical Care – produced with quality foremost in mind. Production and quality control systems are ISO 9001 and EN 45001 certified; the product specifications are also determined and controlled according to the acknowledged EN standards.

There has been an increasing interest in the development of more efficient haemodialysis treatment modalities in recent years. The main objective of these efforts has been primarily to remove a wide range of uremic retention solutes – particularly the middle molecules – in the most efficient way.

The FX-class® possesses outstanding clearances for both low-molecular weight solutes but also for larger uremic toxins.

An extended clinical experience worldwide has established that the efficient removal of a wide range of toxins by High-Flux is a significant contributing factor for improved long-term results for dialysis patients (EBPG 2.2), for example in terms of

- better control of renal anemia
- delayed onset of amyloidosis
- reduced inflammation
- improved immune response
- prolonged preservation of residual renal function
To utilise a dialyser to its full capacity and achieve optimal blood flow conditions in the dialyser, it is important to consider the relationship between its effective surface area and the achievable blood flow rate.

At low blood flow rates, large dialyser surface areas are not exploited to their full extent.

### In-vitro Performance Data

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At low blood flow rates, large dialyser surface areas are not exploited to their full extent.

### Optimal application for the FX-class® dialysers

![Diagram](image)

### In-vitro performance data

<table>
<thead>
<tr>
<th>Ultrafiltration coefficient (mL/h x mmHg)</th>
<th>FX 40</th>
<th>FX 50</th>
<th>FX 60</th>
<th>FX 80</th>
<th>FX 100</th>
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<tbody>
<tr>
<td>Clearance: Q = 200 (mL/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urea</td>
<td>20</td>
<td>33</td>
<td>46</td>
<td>59</td>
<td>73</td>
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<tr>
<td>Creatinine</td>
<td>170</td>
<td>189</td>
<td>193</td>
<td>197</td>
<td>*</td>
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<tr>
<td>Phosphate</td>
<td>144</td>
<td>170</td>
<td>182</td>
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<tr>
<td>Vitamin B₁₂</td>
<td>138</td>
<td>165</td>
<td>177</td>
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<tr>
<td>Inulin</td>
<td>84</td>
<td>115</td>
<td>135</td>
<td>148</td>
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<tr>
<td>* Refer to recommended blood flow range.</td>
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</table>

The in-vitro performance data were obtained with Qₑ = 500 mL/min, Q₀ = 0 mL/min and T = 37 °C (EN 1283, ISO 8637).

The ultrafiltration coefficients were measured using human blood, Hct 32 %, protein content 6 %.

<table>
<thead>
<tr>
<th>Sieving coefficient Q₀ = 300 mL/min, Qₑ = 60 mL/min</th>
<th>Inulin</th>
<th>β₂-microglobulin</th>
<th>Albumin</th>
<th>1</th>
<th>0.8</th>
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<td>Effective surface area (m²)</td>
<td>0.6</td>
<td>1.0</td>
<td>1.4</td>
<td>1.8</td>
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<td>KDA∞</td>
<td>489</td>
<td>824</td>
<td>977</td>
<td>1292</td>
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<tr>
<td>Wall thickness/inner diameter (µm)</td>
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<td>35/185</td>
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<tr>
<td>Blood filling volume (mL)</td>
<td>32</td>
<td>53</td>
<td>74</td>
<td>95</td>
<td>116</td>
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<tr>
<td>Membrane</td>
<td></td>
<td>Polypropylene</td>
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<td>Housing material</td>
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<td>Polyurethane</td>
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<tr>
<td>Potting compound</td>
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Ever since the conception of haemodialysis therapy, nephrologists worldwide have addressed the factors contributing towards the poor long-term outcome of dialysis patients.

The task has been complicated by the fact that many dialysis patients suffer from multiple co-morbid conditions, particularly hypertension, diabetes and malnutrition – all of which contribute to the high incidence of cardiovascular disease in this population group.

The central function of haemodialysis therapies is to remove a broad range of ‘uremic toxins’ efficiently – like the natural kidney.

Over the last years there has been an increasing body of evidence pointing towards a reduced death risk in patients undergoing High-Flux dialysis as well as advanced treatments such as haemodiafiltration (HDF).^{[13]}

Both High-Flux dialysis and HDF require dialysis membranes that are highly permeable to large toxins and water. In addition, such membranes must be biocompatible and have a high endotoxin retention capacity.

Fresenius Polysulfone® and Helixone® membranes – the most widely used dialysis membranes worldwide – have specially been designed to fulfil these essential criteria.

Together with nephrologists and nurses, Fresenius Medical Care continues to contribute towards the improved quality of life of HD patients, and ultimately their survival.
"The positive results of the MPO Study validate our efforts to offer innovative dialysis products such as our High-Flux dialysers with Helixone® membranes so that dialysis patients can look toward the future with more confidence. And we are proud that the majority of the patients in the study’s High-Flux group were treated with our dialysers,” said Dr. Emanuele Gatti, Fresenius Medical Care’s Chief Executive Officer for Europe, Latin America, Middle East and Africa.

Literature


15. Koda Y et al., Switch from conventional to High-Flux membrane reduces the risk of carpal tunnel syndrome and mortality of hemodialysis patients. Kidney Int (1997); 52: 1096-1101

16. Locatelli F et al., Comparison of mortality in ESRD patients on convective and diffusive extracorporeal treatments. Kidney Int (1999); 55: 286-293

