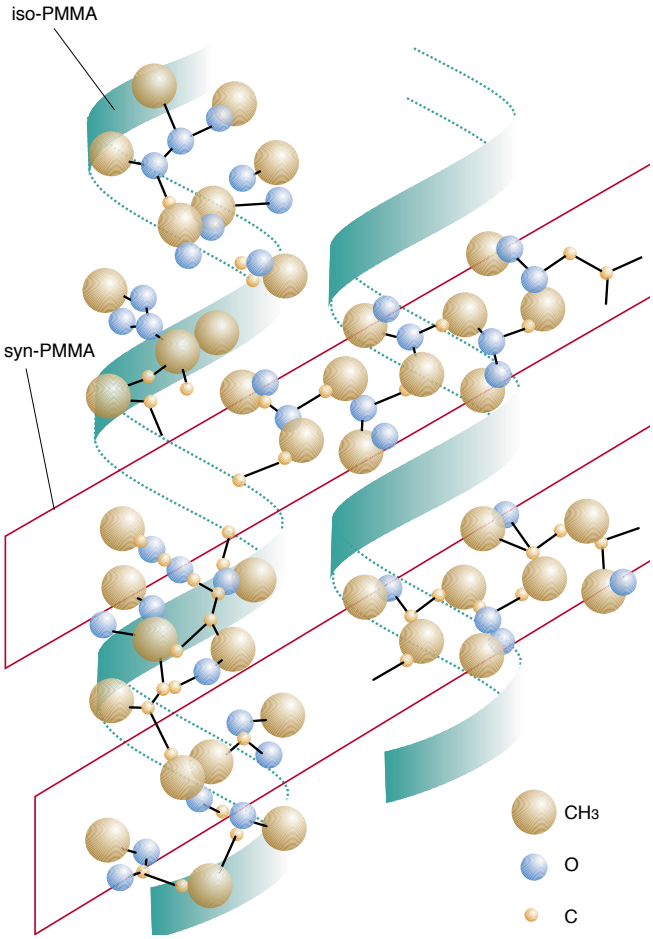
'TORAY'

New PMMA Membrane for Better Quality of Life

Hollow Fiber Dialyzer

Filtryzer BG-U Series

New Membrane Structure by "Sophisticated Pore Controlling Technology"



"FILTRYZER" is made with Polymethylmethacrylate (PMMA) membrane and TORAY is the only manufacturer which succeeded in developing it as a dialysis membrane. FILTRYZER was introduced in 1977 and it has enjoyed a good reputation all over the world due to its excellent biocompatibility, high removal performance, wide range of UFR, and unique adsorption characteristics for various proteins.

The membrane consists of 2 kinds of polymers, isotactic PMMA (iso-PMMA) and syndiotactic PMMA (syn-PMMA). These polymers form the stereocomplex structure as shown in the picture. The pore structure in the membrane can be widely adjusted by controlling the process conditions including the chemical structure, the composition of the PMMAs (i.e., ratio of iso-PMMA to syn-PMMA), the concentration, cooling speed of dope solution, and the heat setting.

With this wide range of pore structure, FILTRYZER has met diversified requirements of physicians and has been used in many clinical studies for more than 20 years.

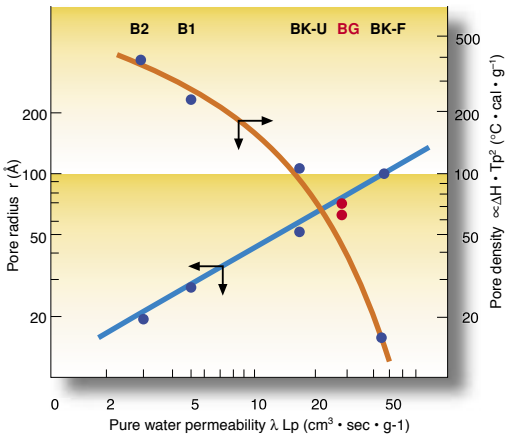
FILTRYZER has established excellent reliability in its long history based on many kinds of clinical data and accumulated technology. For further improvement of the patient's quality of life, TORAY has been investigating the potential of FILTRYZER through research and clinical trials.

Our "Sophisticated Pore Controlling Technology", which combines the process conditions and copolymerization, made it possible to create brand new PMMA membrane "FILTRYZER BG-U series". This new PMMA membrane has obtained both the controlled pore radius around 70Å and uniform distribution of pore size.

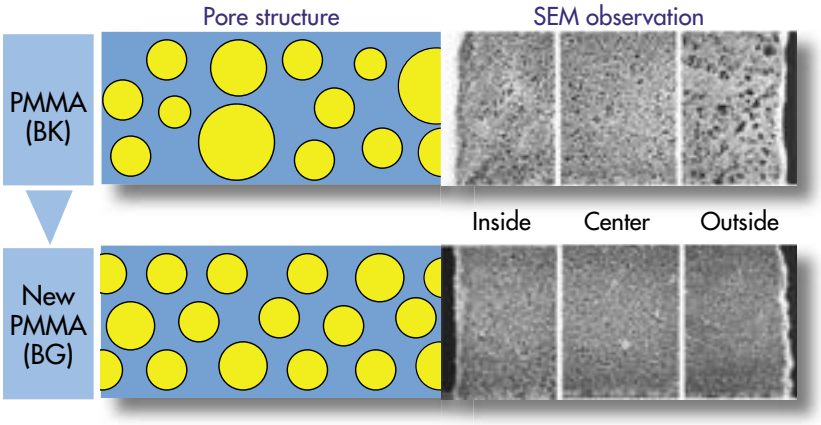
At the same time, this membrane has higher porosity and unprecedented adsorption capability.

This structure can improve UFR, permeability of small molecules, and permeability of not only low molecular weight proteins but also higher molecular weight proteins like cytokines.

Relationship of pore radius, pore density and water permeability of PMMA membranes



Structure of new PMMA membrane BG

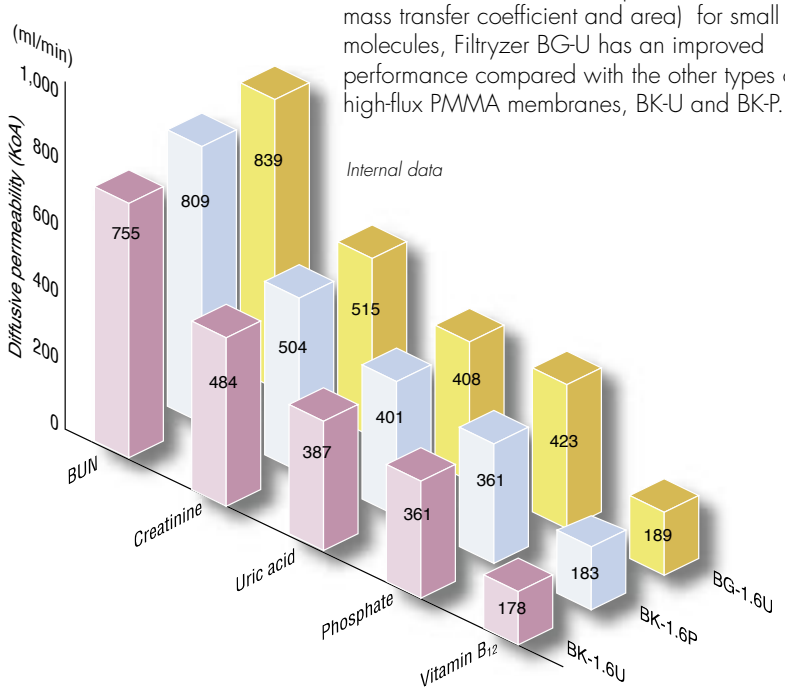


As shown in the figure, BG membrane is designed by homogenizing the pore size and increasing the number of pores, resulting in the improvement of the removal through small molecules to low molecular weight proteins such as β2-MG.

Improved diffusive permeability (KoA)

As for several KoAs (the product of overall mass transfer coefficient and area) for small molecules, Filtryzer BG-U has an improved performance compared with the other types of high-flux PMMA membranes, BK-U and BK-P.

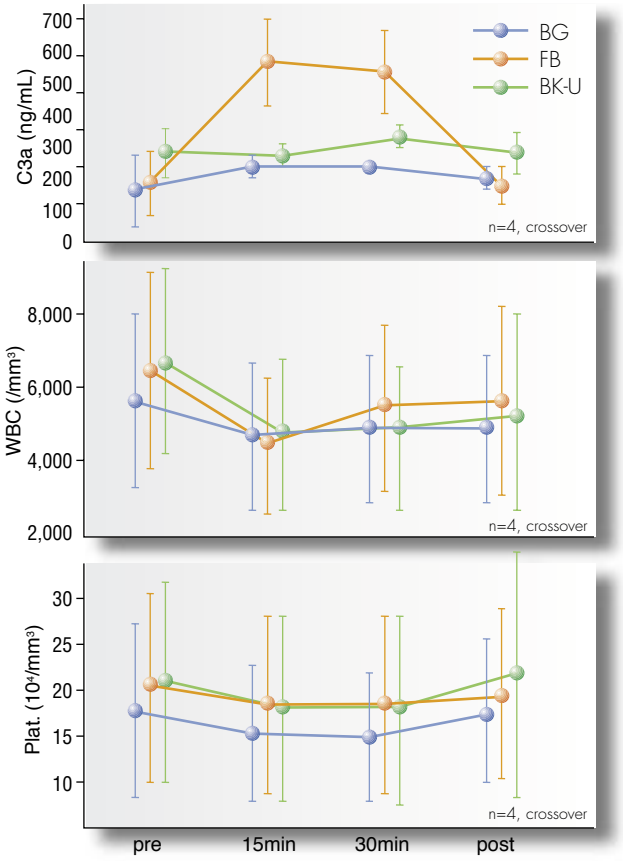
Internal data



Proven Biocompatibility

The time course of complement fragment C3a, white blood cell count and platelet count.

Modified from Touma S, Kidney & Dialysis, Suppl.,132-134, 1997



Excellent biocompatibility

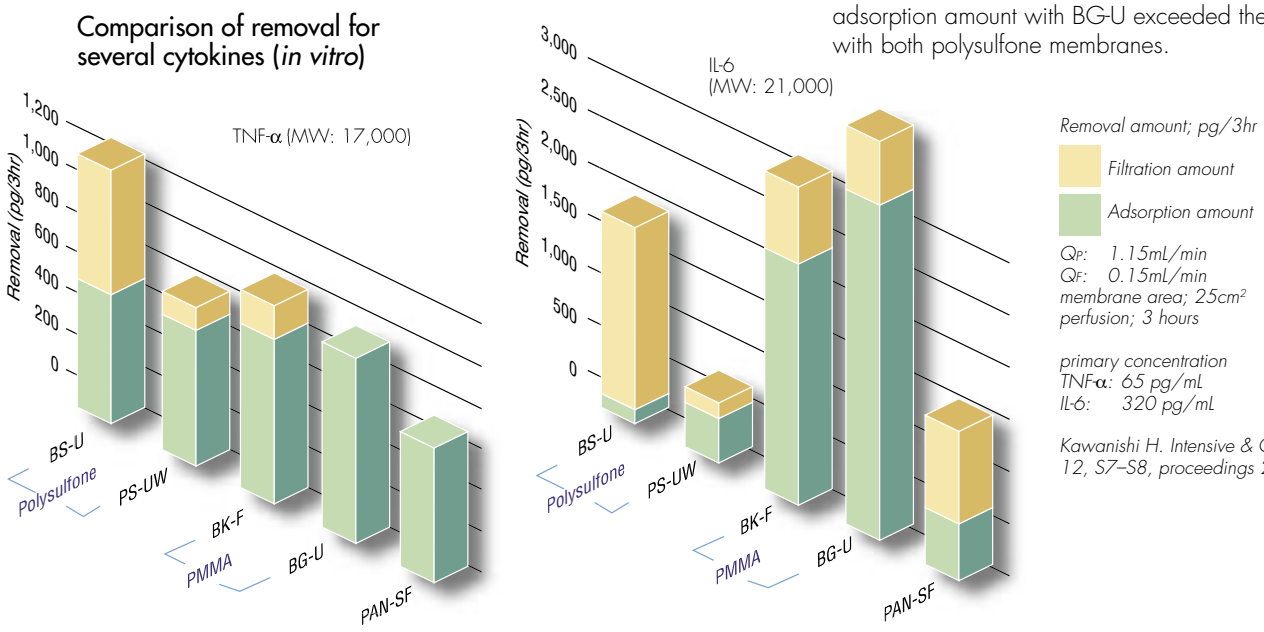
Touma studied the biocompatibility of BG-U (BG) membrane based upon the time course of complement fragment C3a, WBC count and platelet count in comparison with cellulose tri-acetate membrane, FB, and the previous PMMA membrane, BK-U.

As shown by the blue line, the changes on these biocompatibility parameters of BG were more stable than that of FB and almost the same as BK-U. So the biocompatibility of BG membrane is judged to be superior similarly to that of the previous PMMA membrane, which obtained a reputation for excellent biocompatibility during the long period of its history.

Higher adsorptive removal for cytokines

Removal of cytokines with BG-U membrane and others were investigated in an *in vitro* perfusion test. The removal of cytokines with BG-U is mainly conducted by adsorption as shown in the graph: the green bar was the major portion of total amount removed with BG-U. As for removal of IL-6, the adsorption amount with BG-U exceeded the total amounts with both polysulfone membranes.

Comparison of removal for several cytokines (*in vitro*)



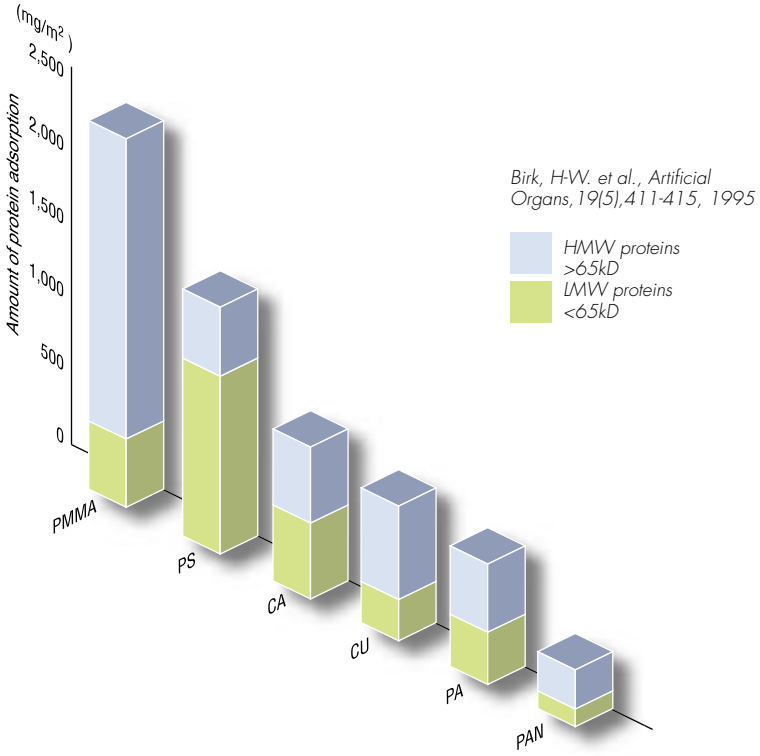
Kawanishi H. Intensive & Critical Care Medicine 12, S7–S8, proceedings 2000

Unique Adsorption of Proteins

Adsorption of ^{125}I-labeled plasma proteins on the various membranes

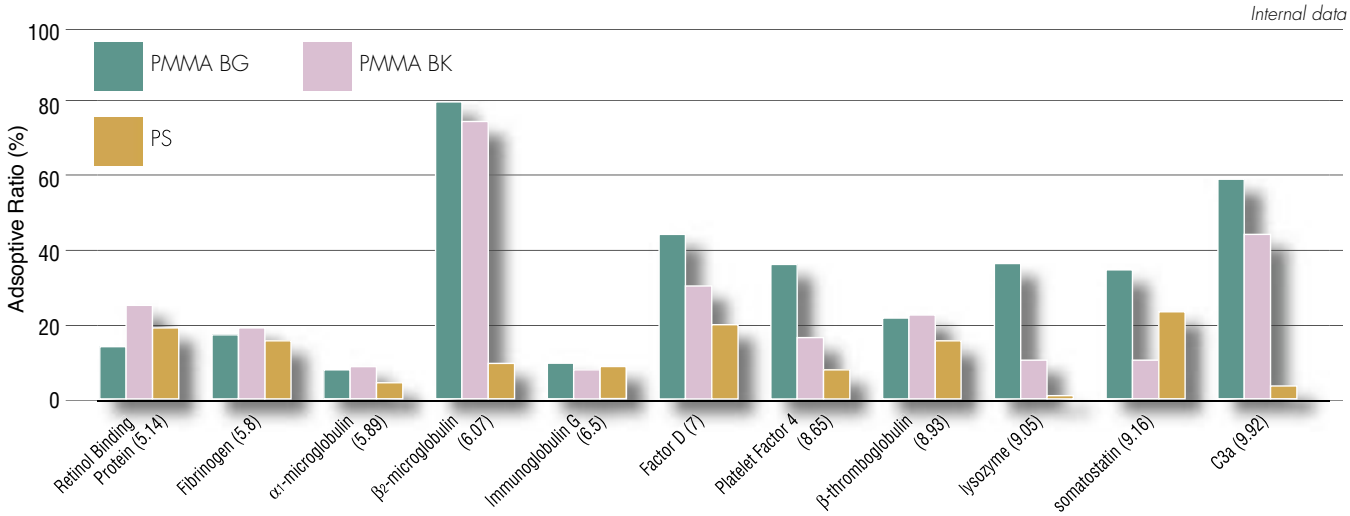
Using the 6 kinds of dialyzers, Birk et al., conducted the adsorption experiment of plasma protein labeled with radio-isotope *in vitro*. The PMMA membrane showed the maximum amount of protein adsorption per unit surface area.

Furthermore, the analysis on the molecular weight of adsorbed proteins revealed that PMMA adsorbed higher molecular weight proteins (HMW proteins) than albumin compared with other membrane materials as shown by the blue bars. When the PMMA membrane was used, the removability by adsorption tended to increase for proteins with higher molecular weights.

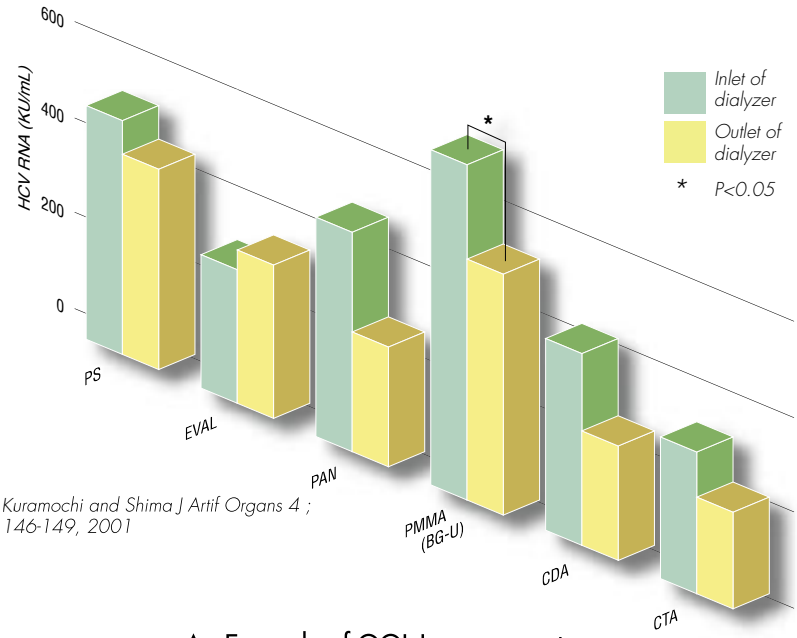


Adsorption of plasma proteins with mini-module

The below figure shows the internal data for adsorption of plasma proteins with mini-module with 3 kinds of synthetic membranes. On the X axis, plasma proteins in the order of iso-electric point are shown. For example, the adsorptive ratio of β2-MG on BK and BG membranes are in the high level. But towards the target proteins with more cationic iso-electric point, BG membrane adsorbed more of them than BK membrane such as PF-4, lysozyme and somatostatin. So these data suggest the adsorption of cationic proteins are enhanced by the electric interaction with the BG membrane.



Excellent Clinical Benefits to Renal Failure Patients

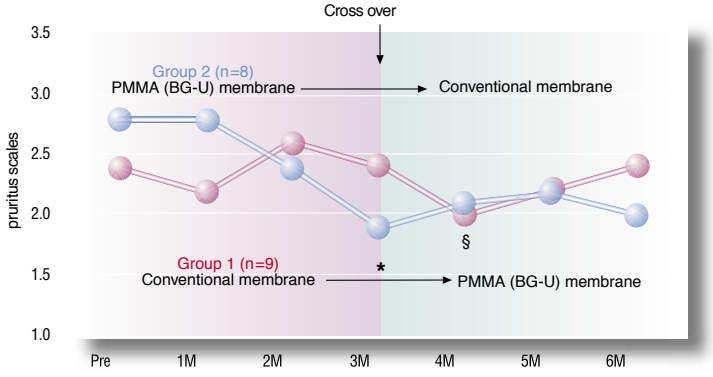


Kuramochi and Shima J Artif Organs 4 ; 146-149, 2001

The possibility in decrease of HCV particles in HD patients over hemodialysis therapy

In HD patients, the positive rate of anti-HCV antibody seems to be high. However the number of HCV RNA in blood is lower compared to the above rate of antibody. Furthermore, the symptomatic liver failure is not so frequently observed. It may be due to extracorporial treatment through dialyzer use every 2 days. Kuramochi reported that the viral particles decreased in the blood through dialyzer, above all, through PMMA membrane. The viral particles were not detected in the filtrate or dialysate, and were rather thought to be adsorbed on the dialyzer membrane surface.

An Example of QOL Improvement



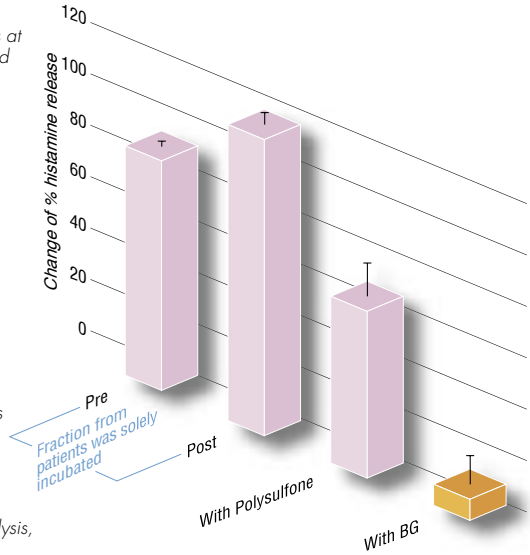
Kato A. et.al., Artificial Organs 25(6);441-447, 2001
§p=0.049 as compared to scores at 2 months, *p=0.047 as compared to scores at the beginning.

Efficacy in amelioration of renal itching in hemodialysis patients (cross over study)

In group 1, one month after changing to PMMA (BG-U) membrane, the pruritus scales decreased to 1.9 ±0.4 which is significantly lower compared to those at 2 months when the conventional membranes were used (§p=0.049).

In group 2, the PMMA (BG-U) membrane gradually and significantly reduced pruritus scales from 2.8 ±0.2 to 1.9 ± 0.4 3 months later (*p=0.047). The degree of pruritus did not worsen during the next 3 months despite returning to the conventional dialyzers.

Confirmation of removal of pruritus generating substances assayed with mast cells



Pre: Before incubation
Post: After incubation without fibers

Yamada S. et al., Kidney and Dialysis, suppl.; 167-171, 2003

The left figure shows the results of change in histamine release from mast cells which were coincubated with hollow fibers for 3 hours.

With BG membrane the activity was massively reduced compared with that of polysulfone membrane.

These data suggest the adsorption of the substances generating pruritus and correspond well to the observation of clinical amelioration in pruritus with BG membrane.

Technical Data

		BG-U Series			
Type		**BG-1.3U**	**BG-1.6U**	**BG-1.8U**	**BG-2.1U**
Housing	Material	Polystyrene			
Fibers	Material	Polymethylmethacrylate			
	Inner diameter (μm)	200			
	Membrane thickness (μm)	30			
	Effective surface area (m^2)	1.3	1.6	1.8	2.1
Potting Material		Polyurethane			
Sterilization		Gamma-ray Irradiation			
Blood Volume (mL)		77	95	113	124
Clearance *in vitro* (mL/min)*					
	Urea	184	189	191	192
	Creatinine	182	188	188	191
	Phosphate	155	165	172	179
	Vitamin B_{12}	106	118	123	133
	Inulin	60	67	72	81
UFR *in vitro* {mL/hr, at 13.3kPa (100mmHg)}**		2,900	3,300	3,500	4,300
Max. TMP {kPa (mmHg)}		66 (500)			

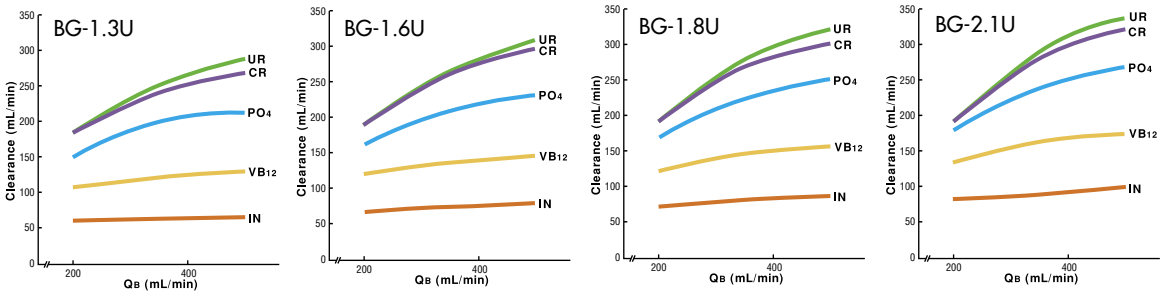
* *Clearances are measured with aqueous solution. Q_B: 200 ±4mL/min, Q_D: 500 ±10mL/min, Q_F: 10 ±2mL/min, Temp.: 37 ±1°C*

** *UFRs are measured data with bovine blood. (Ht 30 ±3%, TP 6.0 ±0.5g/dL) Q_B: 200 ±4mL/min, TMP: 13.3 ±1.3kPa (100 ±10mmHg), Temp.: 37 ±1°C*

"Instructions for Use" should be read thoroughly prior to the use of these medical devices.

Specifications and designs are subject to change without notice for improvements.

Clearance



BG-1.3U			
Q_B	300	400	500
UR; Urea	234	267	289
CR; Creatinine	228	253	269
PO_4; Phosphate	184	202	213
VB_{12}; Vitamin B_{12}	119	123	129
IN; Inulin	63	63	64

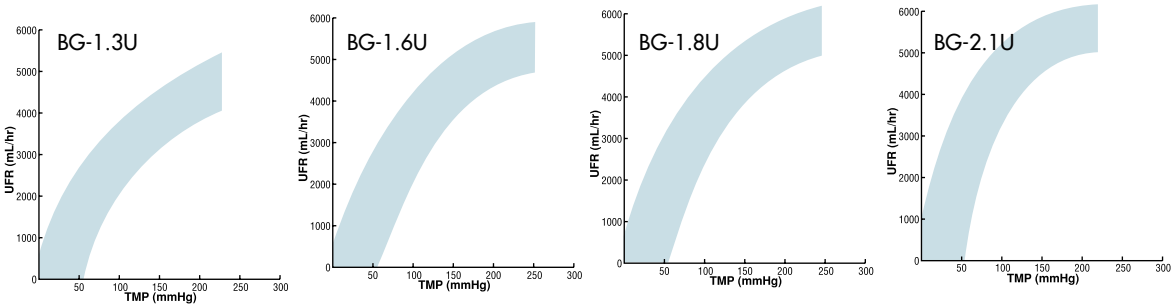
BG-1.6U			
Q_B	300	400	500
UR; Urea	249	283	310
CR; Creatinine	247	276	298
PO_4; Phosphate	202	221	236
VB_{12}; Vitamin B_{12}	134	140	146
IN; Inulin	73	74	79

BG-1.8U			
Q_B	300	400	500
UR; Urea	258	301	321
CR; Creatinine	250	285	300
PO_4; Phosphate	217	236	253
VB_{12}; Vitamin B_{12}	142	152	155
IN; Inulin	80	83	86

BG-2.1U			
Q_B	300	400	500
UR; Urea	265	312	335
CR; Creatinine	262	300	318
PO_4; Phosphate	223	248	268
VB_{12}; Vitamin B_{12}	155	169	172
IN; Inulin	86	90	99

Measured data with aqueous solution

UFR



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Printed in Japan 1401 G