International Water Standards

How they effect the design of a water treatment

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International Water Standards

- What are the applicable standards in Canada and Europe?
- In what way are they different?
- What equipment is needed to comply with the standards?

Specific standards for water and water treatment for HD and related therapies

Canada	Europe	ISO International Organization for Standardization	
Z364.2.2-03	ERA/EDTA	26722: 2009 CD 23500*	Design
Z364.2.2-03	ERA/EDTA EDTNA	CD 23500* *CD status 10/09	Operation
Z364.2.2-03	Ph. Europe ERA/EDTA EDTNA National	13959: 2009	Product quality

Regulatory Background

Canada (MDR)	European Union (MDD)
RO Systems:	
Medical Device Class 3 (MD Licence required)	Medical Device Class IIb (MD Licence required)
Heat Disinfection:	
MD Class 2 (MD Licence required)	MD Class IIa (MD Licence required)

Specific Standards

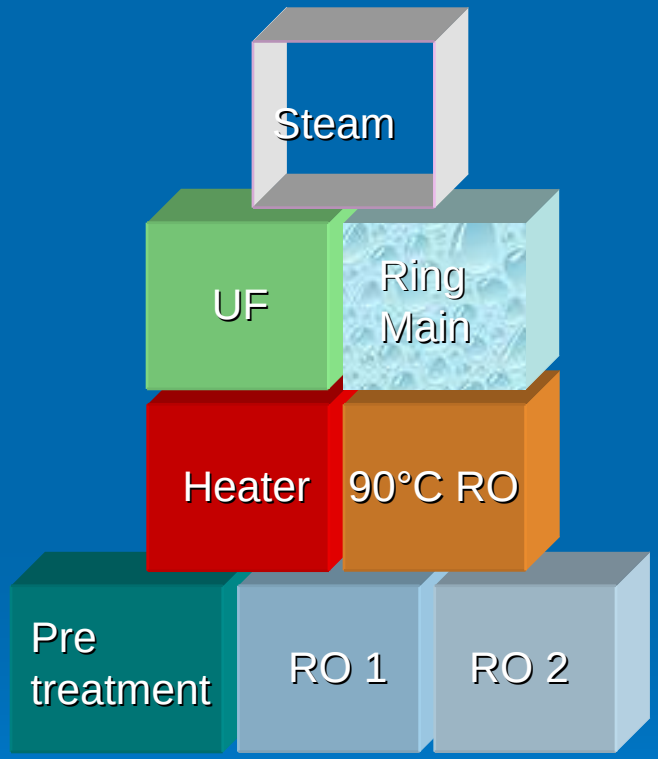
Canada	European Union
Q.- System ISO 13485	Q.- System ISO 13485
CSA Z364.2.2-03 Water Treatment Equipment and Water Quality	European Pharmacopoeia and National standards
CAN/ CSA C22.2 No. 601.1	EN 60601-1-2 (2006) for EMC
CAN / CSA C22.2 No.61010-1 Safety Requirements for Electrical Equipment	EN 61010-1 (2001) Safety Requirements for Electrical Equipment

Microbiological parameters

	Ph. Europ. (2009)	ERA/EDTA (2002)	ISO 13959 (2009)	CSA Z364.2.2 (2003)
HD: CFU/ml	< 100	<100 (25)	<100 (50)	<100 (50)
UP: CFU/ml	< 0.1 (HP water)	< 0.1		
HD: IU/ml	< 0.25	<0.25 (0.125)	< 0.25 (0.125)	<2.0 (1.0)
UP: IU/ml	< 0.03 (HP water)	< 0.03		

HD: Hemodialysis; UP: Ultrapure water/ highly purified water

Water Treatment Modules



- Conductivities < 2µs/cm (1TDS) require permeate-staged RO systems.
- Heat disinfection of the ring main became a standard for automated sanitization.
- Heat disinfection of the RO was a further development
- Depending on local preferences UF is a common process step.
- Ring main DI with steam has already been realized in various installations.

Water for hemodialysis

Basic configuration:

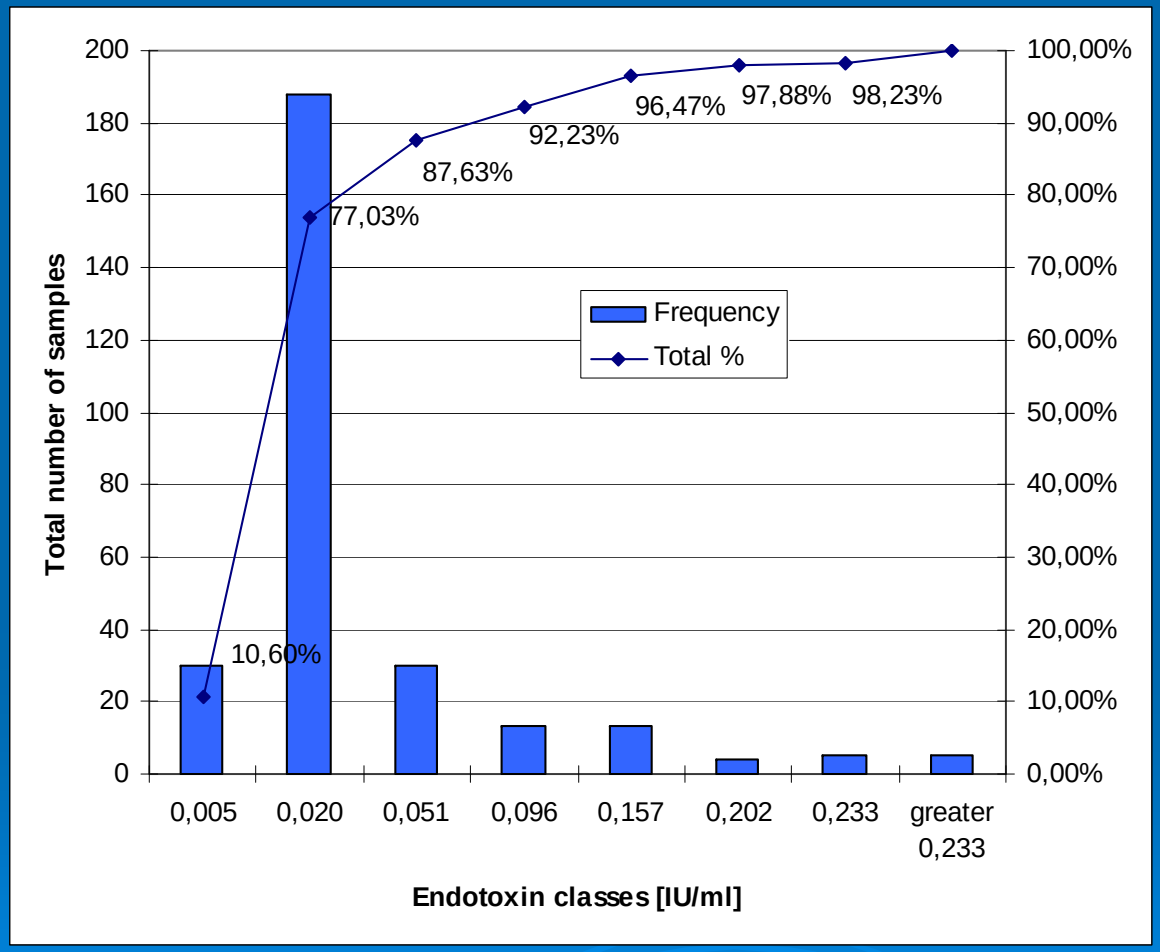
1. Pre-treatment (carbon, softener, particle filter)
2. Single staged RO
3. Ring main

The basic configuration of a water treatment and distribution system provides water for hemodialysis.

Permeate staged RO systems

- Double membrane barrier
- 2 x 100% redundancy
- Avoids bacterial growth of standby RO
- Second RO w/o water losses
- Direct feeding

Endotoxin – Permeate staged RO



Average:	0,027 IU / ml
Standard deviation:	0,045 IU / ml
# samples:	283

General design requirements

- All inner surfaces must be smooth and w/o grooves to prevent bacterial growth (Stainless steel, PVDF).
- All water contact materials must not change their physical properties or chemical characteristics during DI.
- No leach out.
- High velocity and low temperature during operation to prevent bacterial growth.

Design requirements for UP water

- Direct feed
- Storage tanks should be avoided
- Polisher (Second RO, EDI).
- High shear stress, small diameters, high flow rates.
- Avoid dead space and lateral arms

ERA / EDTA (2002)

Pipe disconnection to avoid retrograde contamination

- To avoid a retrograde contamination of the dialysis machines from the drain an air gap is strongly recommended

Hidden dead spaces

- Throughout the installation ball valves must be avoided.
- Due to their design these valves cannot be dead space free.

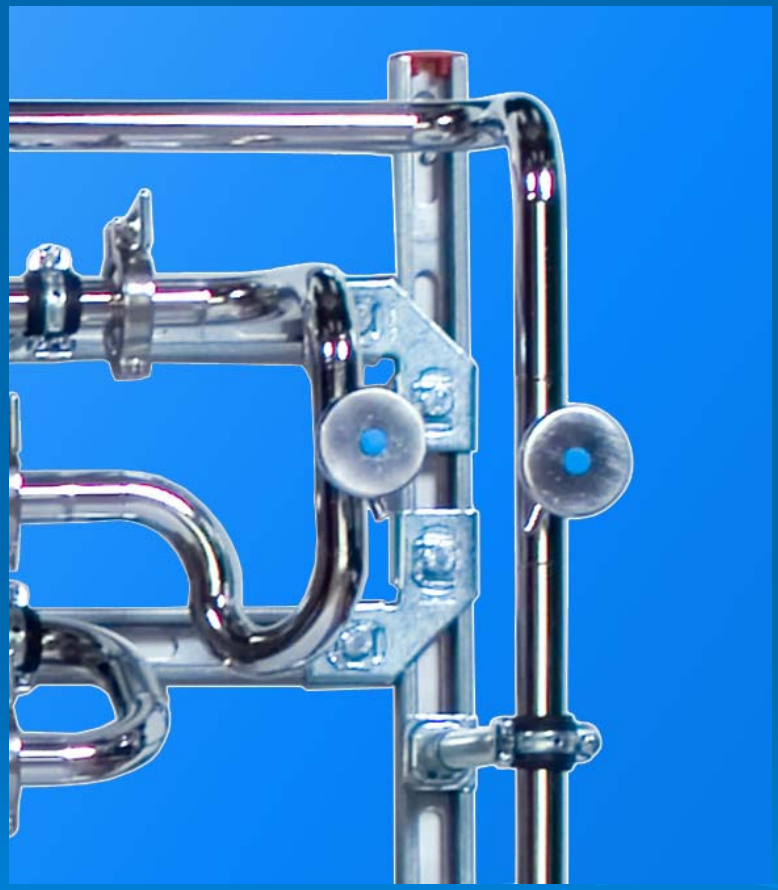
Hidden dead spaces

- The design of a compression fitting includes dead spaces.

Sterile clamps and fittings

- Sterile clamps and fittings minimize bacterial growth in the ring main.

Professional sampling methods



- Easy access to the sampling ports.
- Sampling ports are integrated in the sanitization process

Dead leg free ring mains

- Permeate circulates through the ring main to the point of use.
- High velocity / shear forces (0.5 – 1 m/s)
- Ring main shall not affect permeate quality in any way.
- Material and design must follow the same design guidelines as they are valid for the RO.

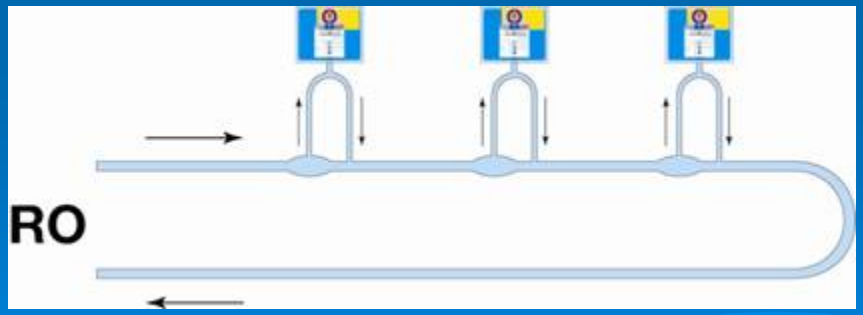
Water distribution system

Materials of the distribution system that contact the purified water shall not interact chemically or physically so as to affect the purity or quality of the product water adversely.

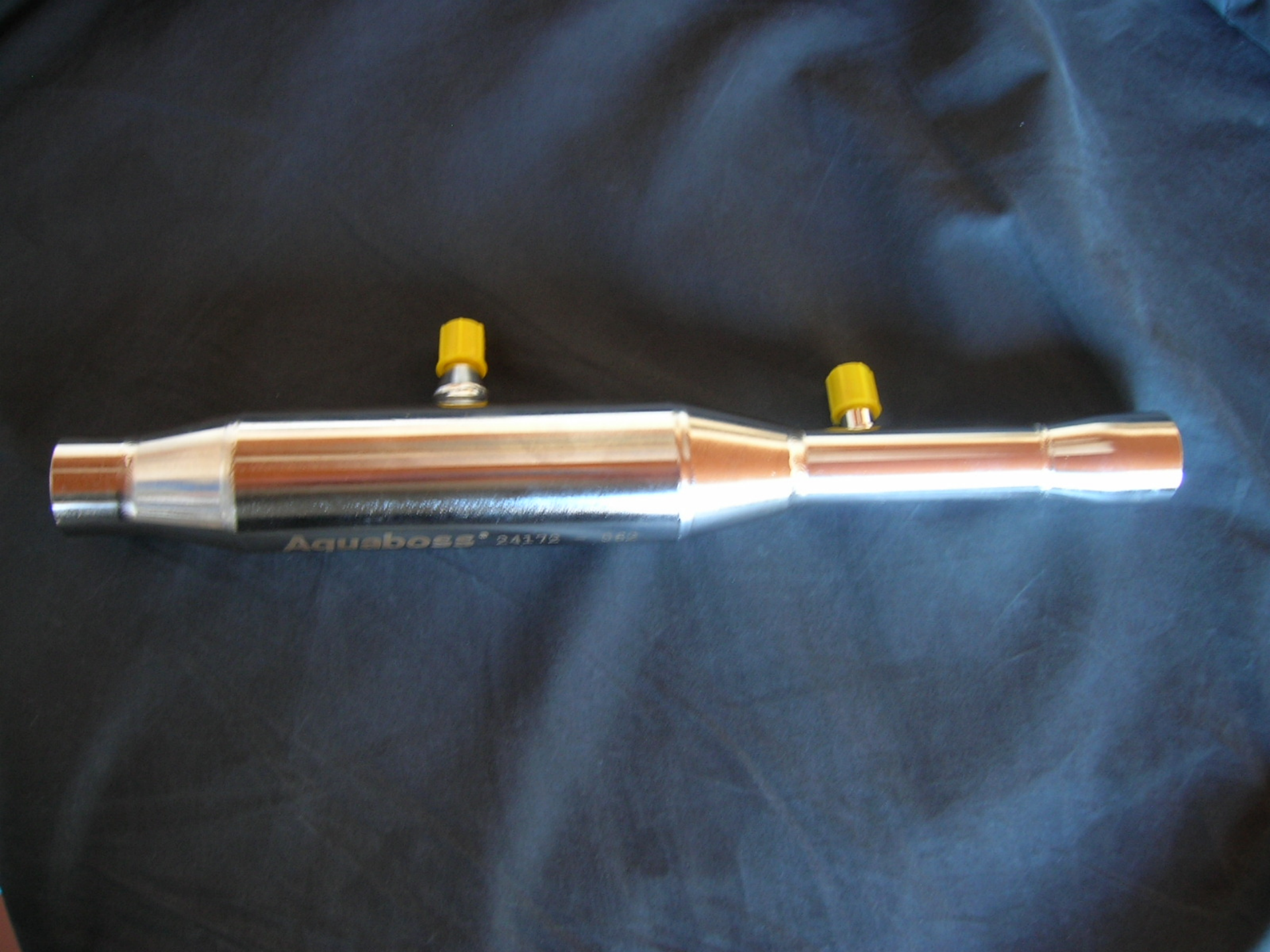
Water distribution system

- Most common materials for distribution systems in Europe are :
  - **PVC** (☺ inexpensive, ☹ embrittles, not heat resistant)
  - **Stainless steel** (☹ complex installation, ☺ ☺ dead space free, heat resistant up to 120°C, Standard in pharmaceutical industry)
  - **PEX** (☺ Easy to install, heat resistant 90°C; ☹ compression fittings with dead spaces)
  - **PVDF** (☹ complex installation, ☺ dead space free, heat resistant up to 90°C, Standard in semi conductor industry)

Secondary loops



- Tubing between ring main and HD machines must be integrated in routine disinfection.
- Secondary ring mains eliminate dead legs between the main loop and the HD machine.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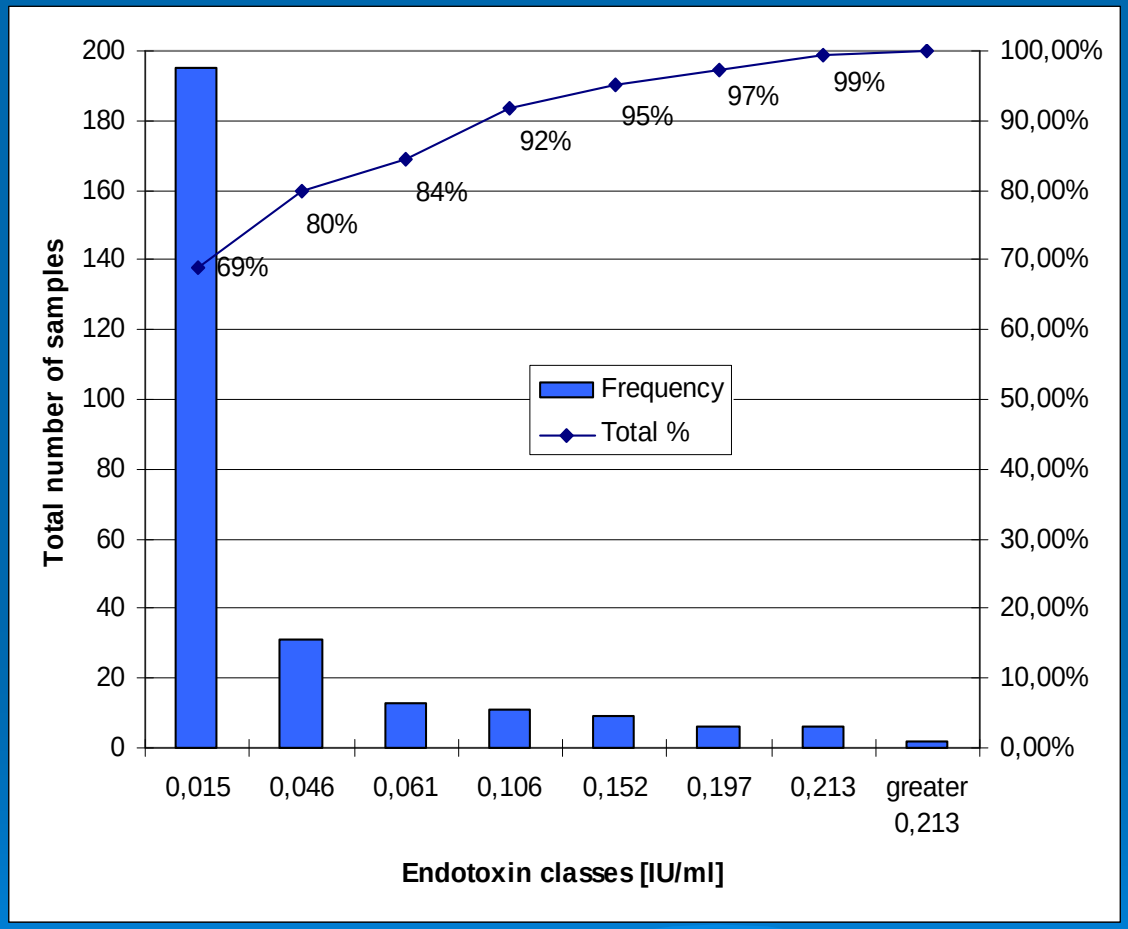
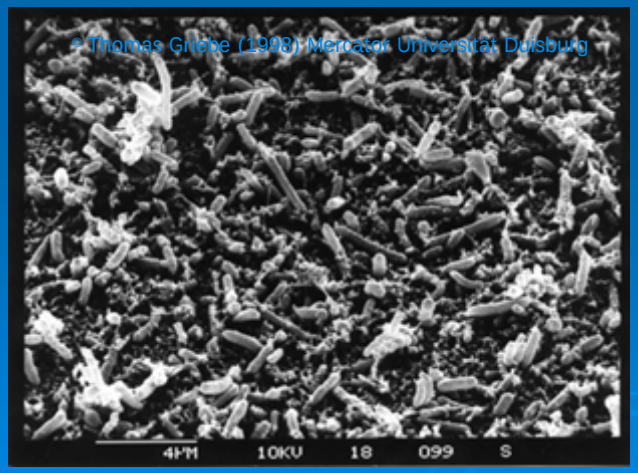
Freigabe durch QS

Endotoxin measurement ring main return



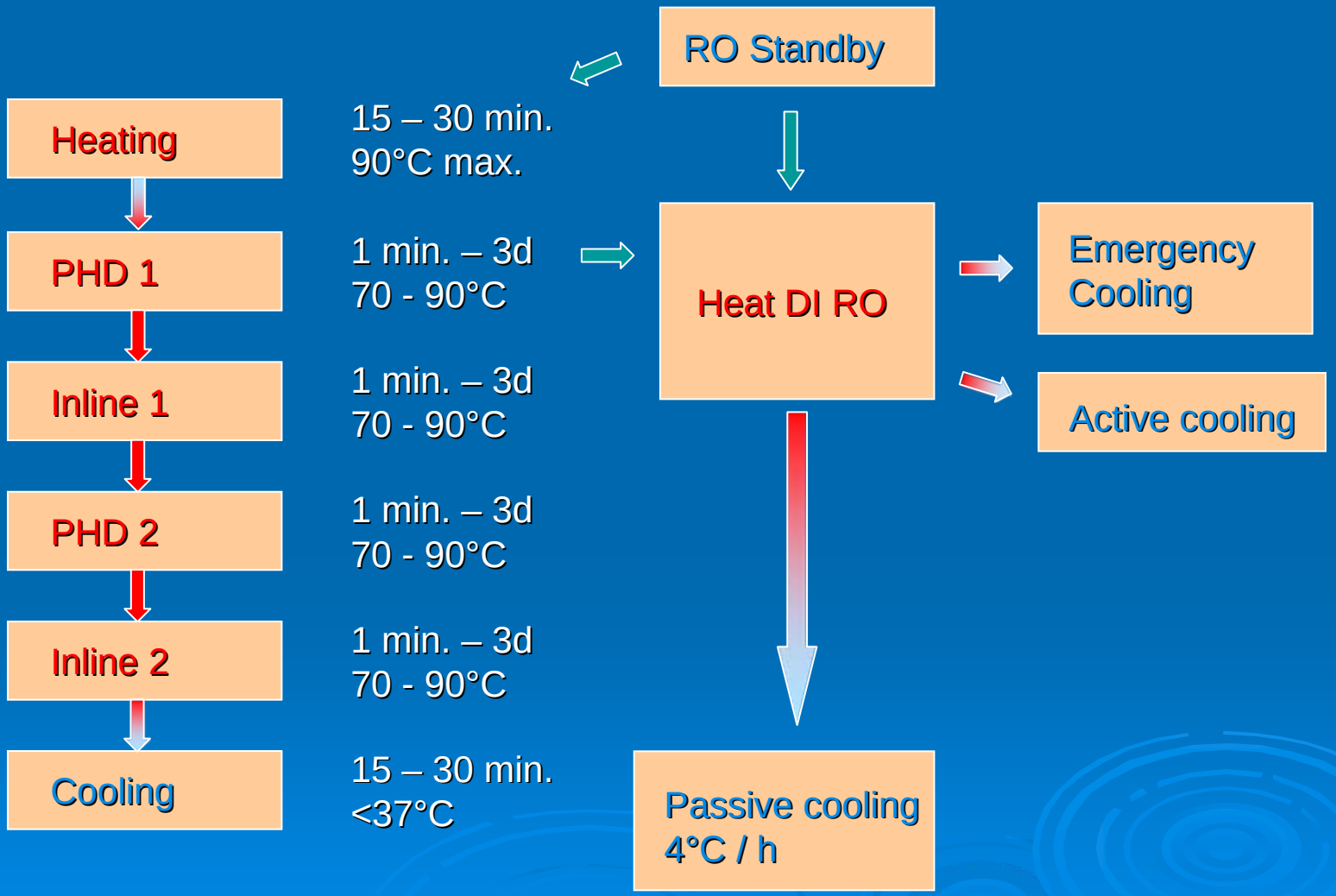
Average:	0,032 IU / ml
Standard deviation	0,047 IU / ml
# samples	283

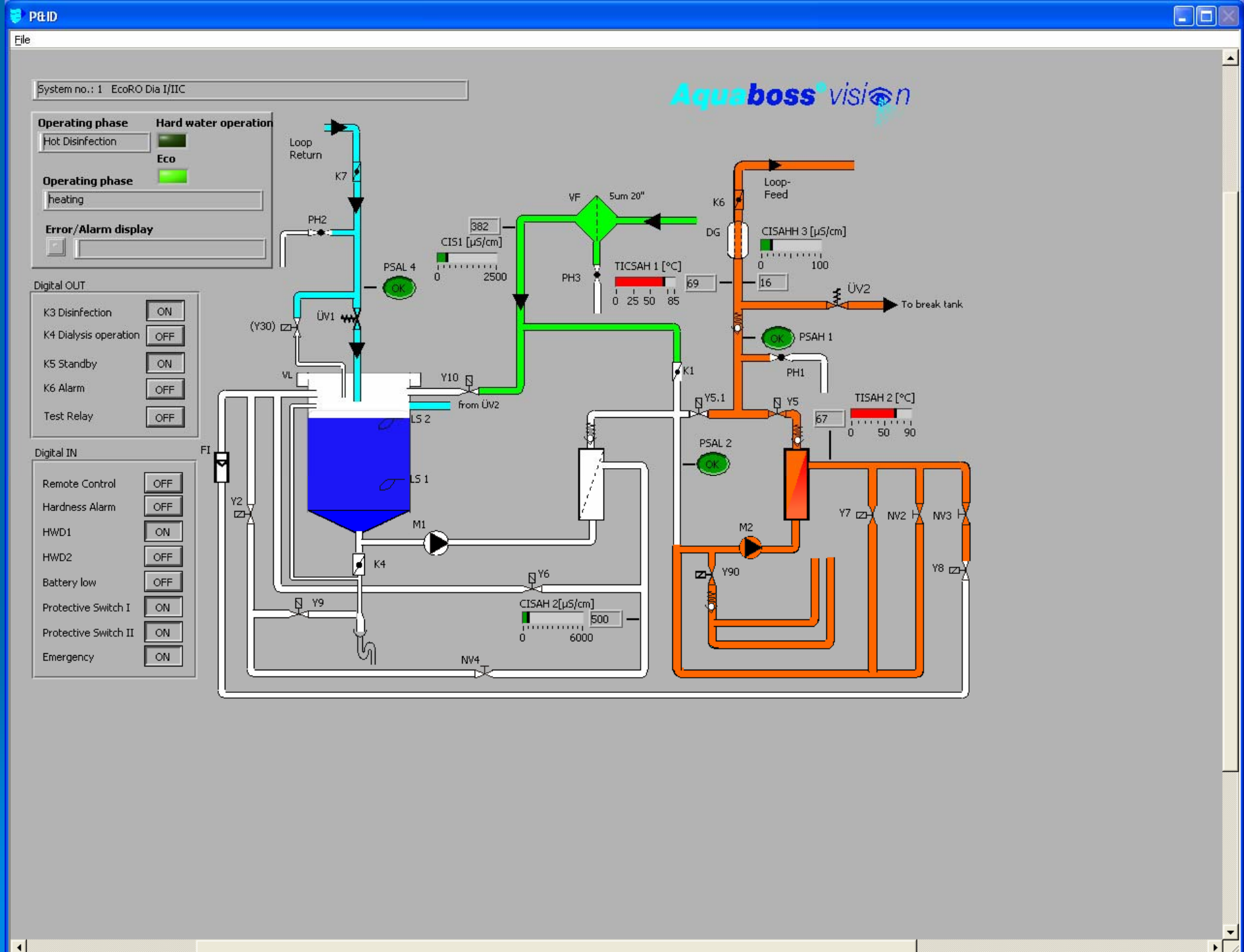
Prevention of biofilm



- Automated heat disinfections of the RO and ring main minimize growth of biofilms.

Heating process diagram

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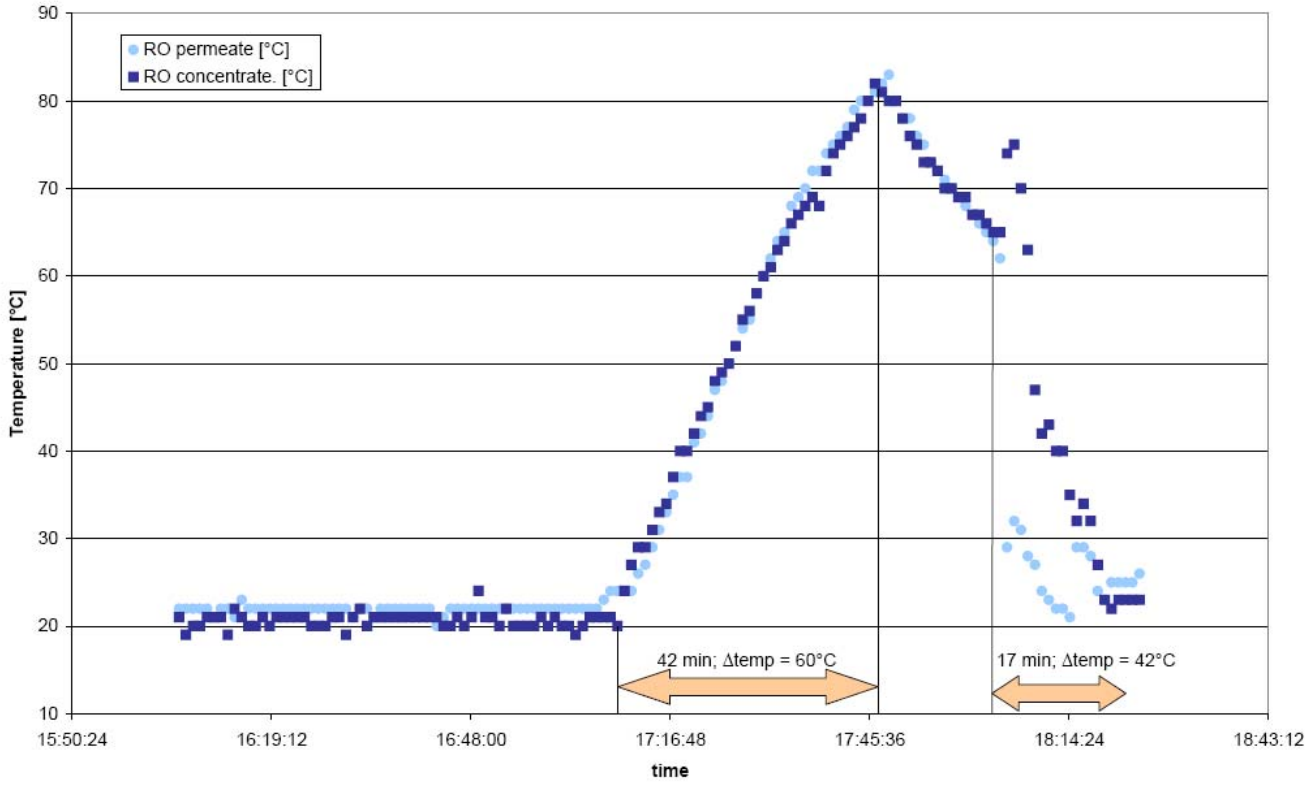
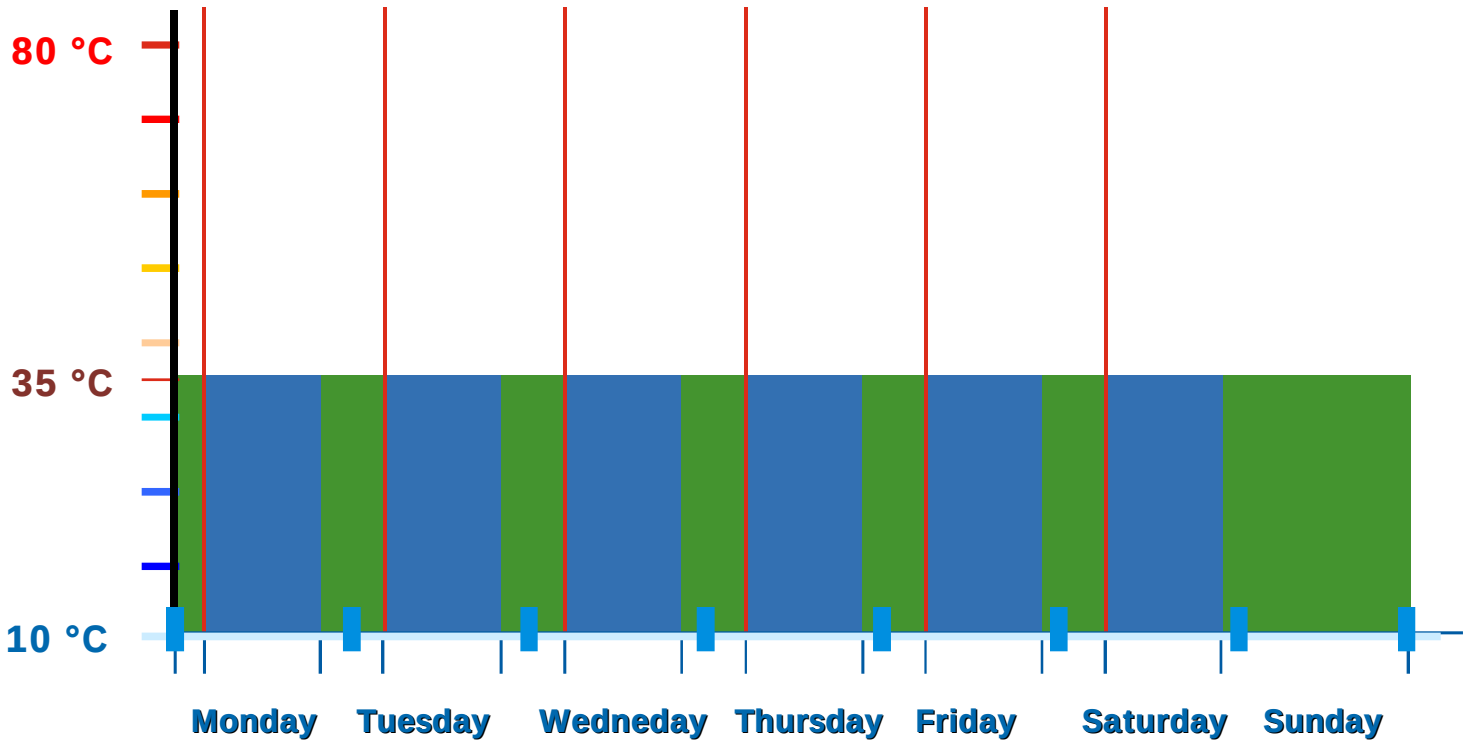
File
System no.: 1 EcoRO Dia I/IIC
Aquaboss vision
Operating phase
Hot Disinfection
Hard water operation
Eco
Operating phase
heating
Error/Alarm display
Digital OUT
K3 Disinfection ON
K4 Dialysis operation OFF
K5 Standby ON
K6 Alarm OFF
Test Relay OFF
Digital IN
Remote Control OFF
Hardness Alarm OFF
HWD1 ON
HWD2 OFF
Battery low OFF
Protective Switch I ON
Protective Switch II ON
Emergency ON
Loop Return
K7
PH2
PSAL 4
OK
(Y30)
ÜV1
VL
Y10
from ÜV2
LS 2
LS 1
FI
Y2
M1
K4
Y9
Y6
NV4
CISAH 2[µS/cm]
500
0
6000
CIS1 [µS/cm]
382
0
2500
VF
5um 20"
PH3
TICSAH 1 [°C]
69
0 25 50 85
K1
Y5.1
PSAL 2
OK
K6
DG
Loop-Feed
CISAHH 3 [µS/cm]
0
100
16
ÜV2
To break tank
PSAH 1
OK
PH1
Y5
TISAH 2 [°C]
67
0 50 90
Y7
NV2
NV3
M2
Y90
Y8

Temperature profile of RO heating cycle

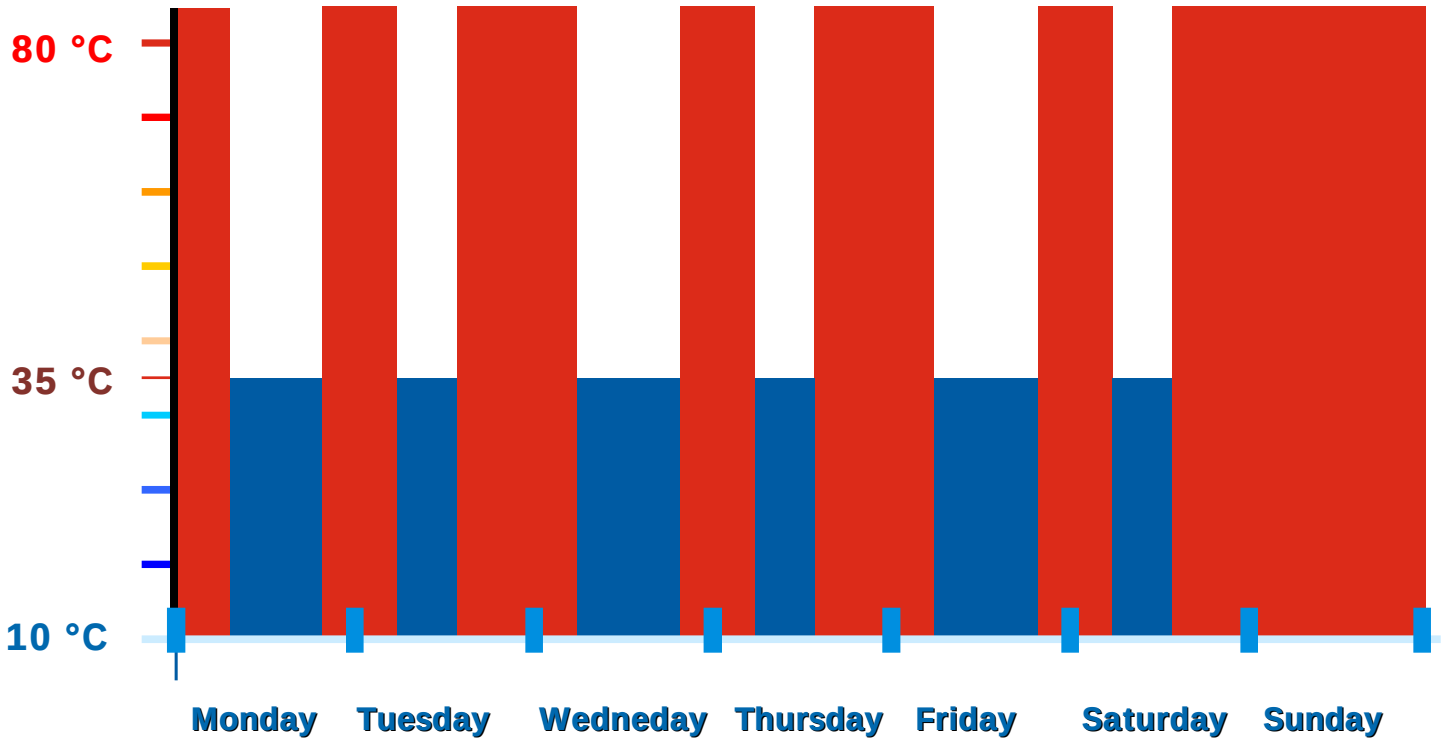


Flown-through inline heater

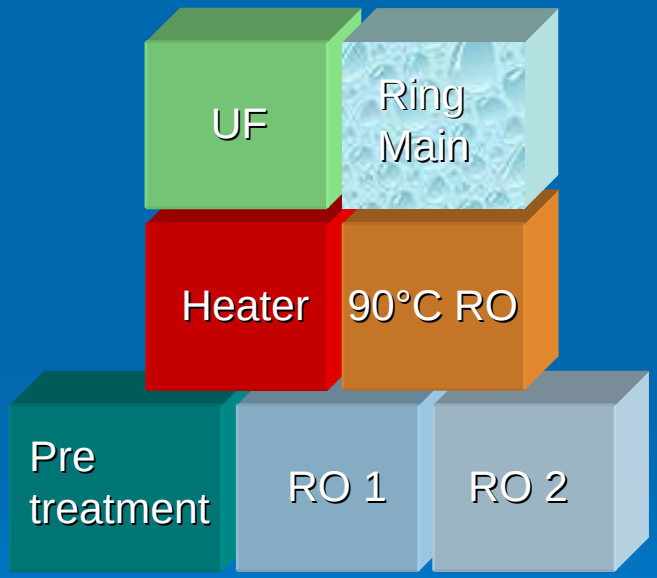
Permanent Hot Disinfection (PHD)



Permanent Hot Disinfection (PHD)



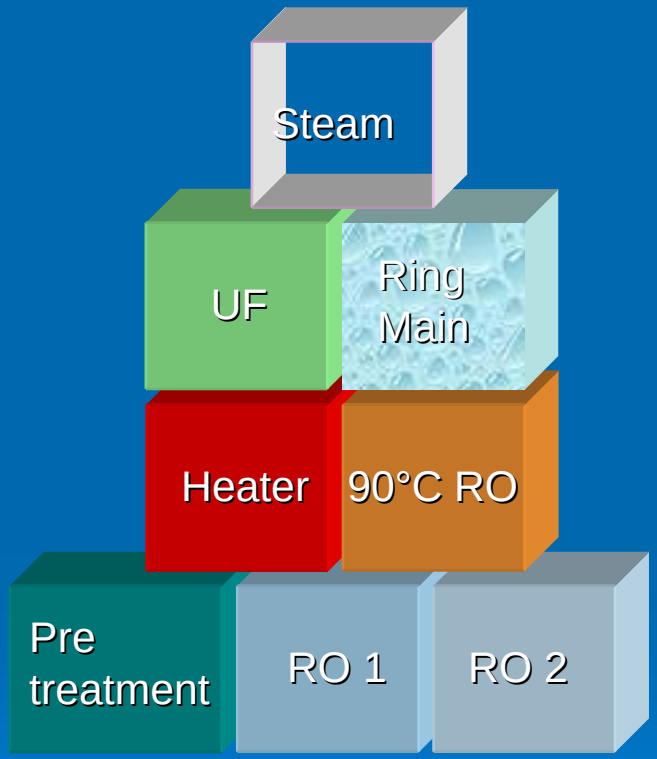
Sterile Filtration



Sterile Filtration

- Pharmaceutical grade sterile filtration.
- Loop integrated. Heat and steam resistant
- Pharmaceutical grade sampling valve.
- Sterile clamps.

10 min @121°C ?



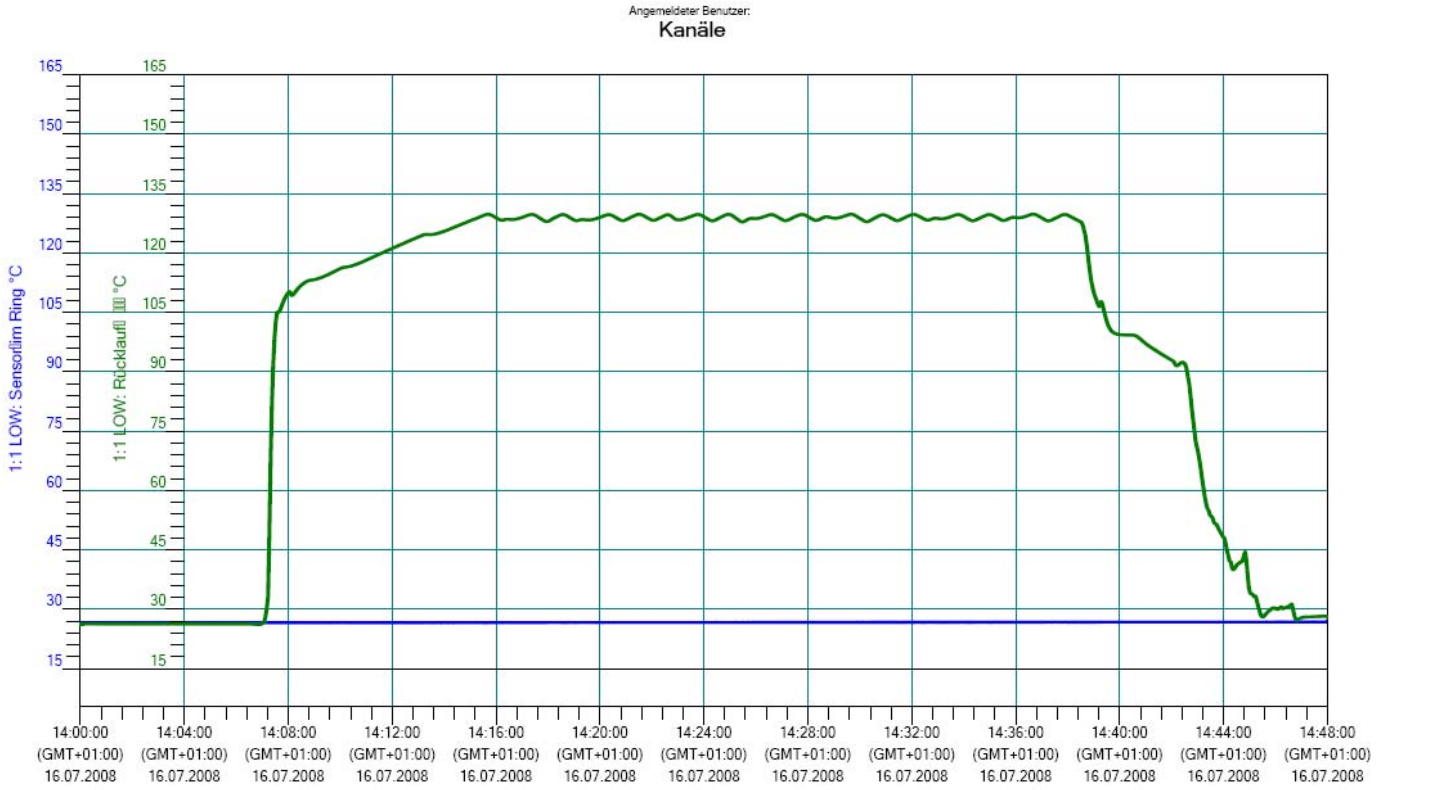
10 min @121°C!

- Only DSF / stainless steel ring mains are qualified for steam sterilization (121°C; 10 min).
- Ring main installations must comply with EC Directive 97/23/EC (*Pressure Equipment Directive (PED)* or other applicable national standards.

Steam sterilization of ring main

- Upon installation stainless steel ring mains can be equipped with additional steam traps and drain fittings.
- Installation must comply with pharmaceutical GMP standards for steam sterilization.

Temperature profile sterilization

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Summary

- Whilst it is not possible to predict what the standard for dialysis-quality water will be in the future, it is likely that the maximum allowed levels of bacteria and endotoxin will be reduced.
- First international standards reference UP water quality.

Summary

- Regulatory Requirements for Medical Devices in Canada and Europe are similar.
- Different water treatment modules can be combined individually to match recent and future quality requirements for water for hemodialysis or ultrapure water.

CSA Z364.2.2 Water treatment equipment and water quality requirements for hemodialysis

- acute, chronic, and home-based hemodialysis;
- water for preparing dialyzing fluid and concentrate for hemodialysis;
- all water intended for contact with the dialyzing fluid pathway;
- the baseline quality of the feed water and any other input water;
- water treatment and monitoring equipment;
- water distribution systems; and
- product water used for flushing blood pathways before sterilization (but not afterwards).

European Pharmacopoeia 01/2009:1167

- Monograph is given for information.
- Analytical methods described and the limits proposed are intended to be used for validating the procedure for obtaining the water.

ERA/EDTA: Sect.IV Dialysis fluid purity

Nephrol. Dial. Transplant: 2002 17 [Suppl.7] 45-62

- IV.1 Water treatment system
- IV.2 Technical design of water treatment system
- IV.3 Monitoring and maintenance
- IV.4 Haemodialysis –proportioning machine
- IV.5 Electrolytic concentrates
- IV.6 Dialysis fluid purity: Implications in the haemocompatibility network system

EDTNA/ERCA Guidelines
Section 3 (Technical) Sept. 2001

Guidelines apply to the control and monitoring of:

- Water used for preparation of dialysis fluid in all settings, including patients' homes and acute care units
- Water used for in-house production of liquid concentrates
- Water used for reprocessing dialysers
- Water used for preparation of ultrapure dialysis fluid by equipment fitted with additional point-of-use filtration

ISO 26722: 2009 ***Water treatment equipment for haemodialysis and related therapies***

- ISO 26722:2009 is addressed to the manufacturer and/or provider of water treatment systems and/or devices used for the express purpose of providing water for haemodialysis or related therapies.

ISO 26722: 2009 ***Water treatment equipment for haemodialysis and related therapies***

- All devices, piping and fittings between the point at which potable water is delivered to the water treatment system and the point of use of the dialysis water.
- Examples of devices are water purification devices, online water quality monitors (such as conductivity monitors), and piping systems for the distribution of dialysis water.

ISO 13959: 2009 ***Water for haemodialyis and related therapies***

- Specifies minimum requirements for water to be used in the preparation of concentrates, dialysis fluids for haemodialysis, haemodiafiltration and haemofiltration and for the reprocessing of haemodialysers.
- Does not address the operation of water treatment equipment nor the final mixing of treated water with concentrates to produce the dialysis fluids used in such therapies. That operation is the sole responsibility of dialysis professionals.
- Does not apply to dialysis fluid regenerating systems.

ISO 23500 family of standards

- ISO 23500: Guidance for the preparation and quality management of fluids for hemodialysis and related therapies

ISO 11663: 2009 Quality of dialysis fluid for haemo-dialysis and related therapies	ISO 13958: 2009 Concentrates for haemo-dialysis and related therapies	ISO 13959: 2009 Water for haemodialysis and related thearapies	ISO 26722: 2009 Water treatment equipment for haemodialyis applications and related therapies

CD / ISO 23500

- Guidelines for the user / operator.
- Covers design, installation, operation and validation of water treatment for hemodialysis and related therapies

ISO 23500

- Microbiological parameters for dialysis fluids
- Microbiological parameters for ultrapure dialysis fluids and substitution solutions (ISO 11663)
- Validation of system performance
- Strategies for microbiological control
- Critical aspects of system design