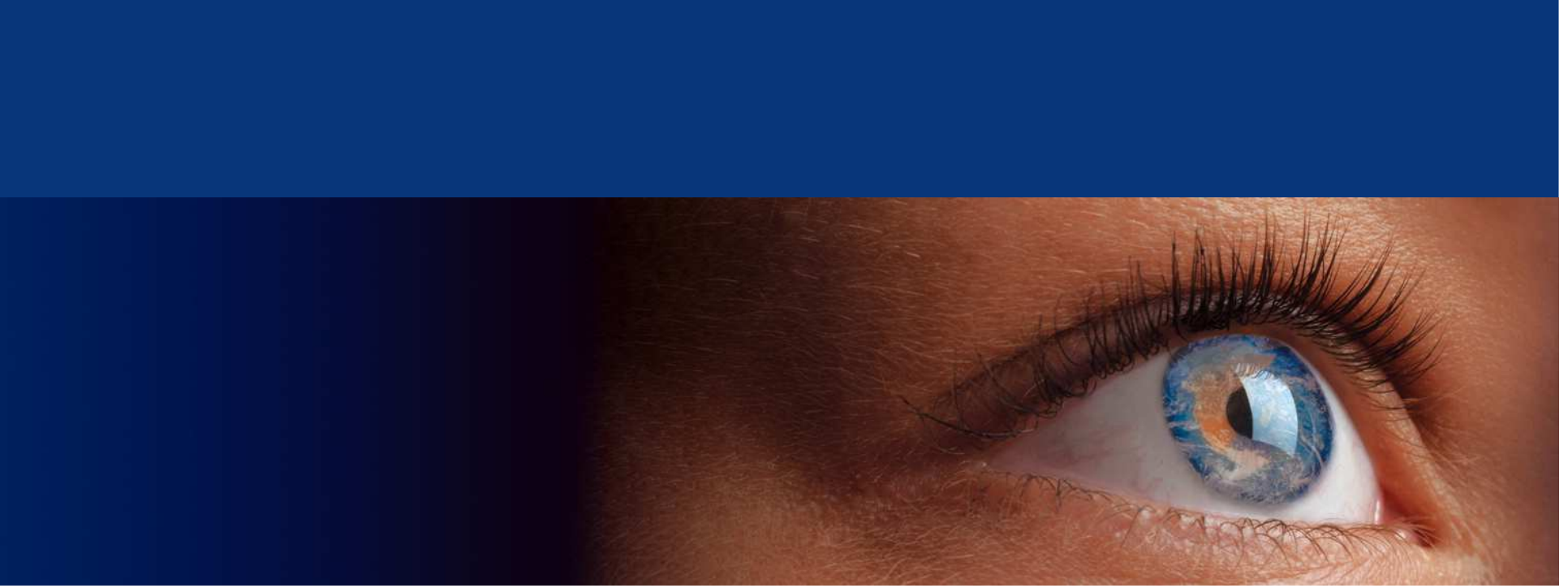

GMP compliant cleaning in the Pharmaceutical Industry

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06. November 2012

Belimed
Infection Control

Topics

- Why GMP Cleaning?
- Prevention of Cross Contamination in Automated GMP Washer
- About Belimed

Why cleaning?

- Prevention of Cross Contamination
  - between batches
  - between products within the same factory / facility
- Prevention of drug contamination during manufacturing cycle
- Constant Guarantee of drug quality

Where is GMP cleaning necessary?

- General Production steps:

Filtration / Grinding

↓

Weighing

↓

Preparation / Mixing

↓

Filling / Dosing

↓

Packing

- Goods to be washed:

Shovels / Filters / Containers

↓

Containers / Funnels / Glassflasks

↓

Hoses / Vessels / Bins

↓

Valves / Pumps / Trays

↓

Packing

Cleaning Methods in GMP Facilities

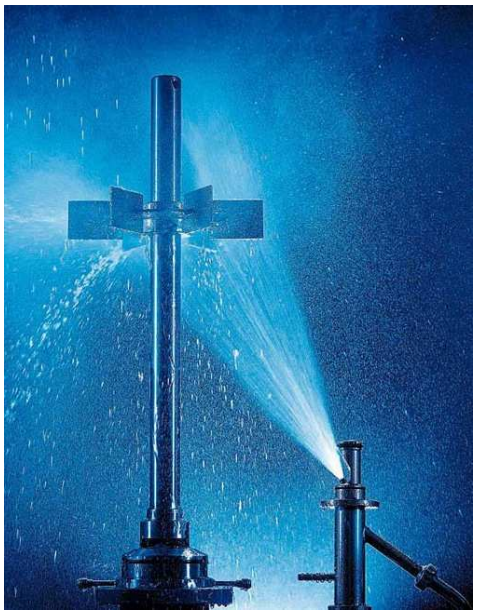
- Manual Cleaning
- Clean-in-Place (CIP)
- Automated GMP Cleaning

Manual Cleaning

- Advantage
  - Very large pieces
  - Very small pieces
  - Fragile pieces
- Disadvantage
  - Water consumption
  - Difficult to validate
  - Difficult repeatability
  - Long cleaning time

Clean-in-Place

- Advantage
  - Large pieces of equipment directly cleaned in place without disassembling
  - Time saving (often directly ready to use)
- Disadvantage
  - Difficult installation
  - Difficult validation
  - Big amount of water needed
  - Cost of cleaning device



Automated GMP Cleaning

- Advantage
  - Reproducibility
  - Possibility to validate the washer
  - Possibility to record the cycles
  - Different cycles for different wash exercises
  - Different racks for different wash goods
  - Water saving

- Disadvantage
  - Space requirements
  - Investment cost

Elements of Automated Cleaning

Parts to Clean

Load Carrier (rack)

Cleaning Process

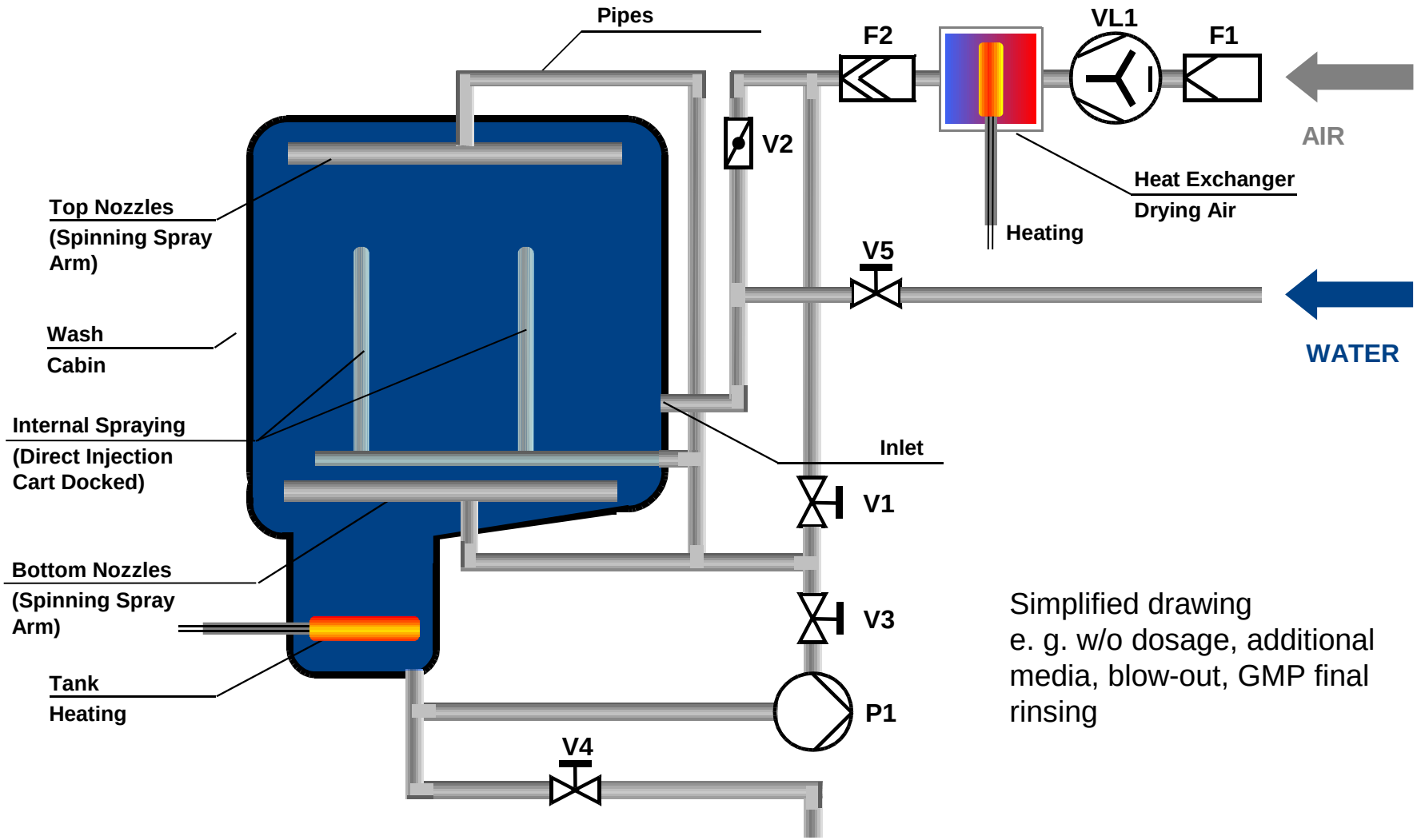
Washer

Example of a Washing machine Belimed PH840

- Usable cabin dimensions (mm)

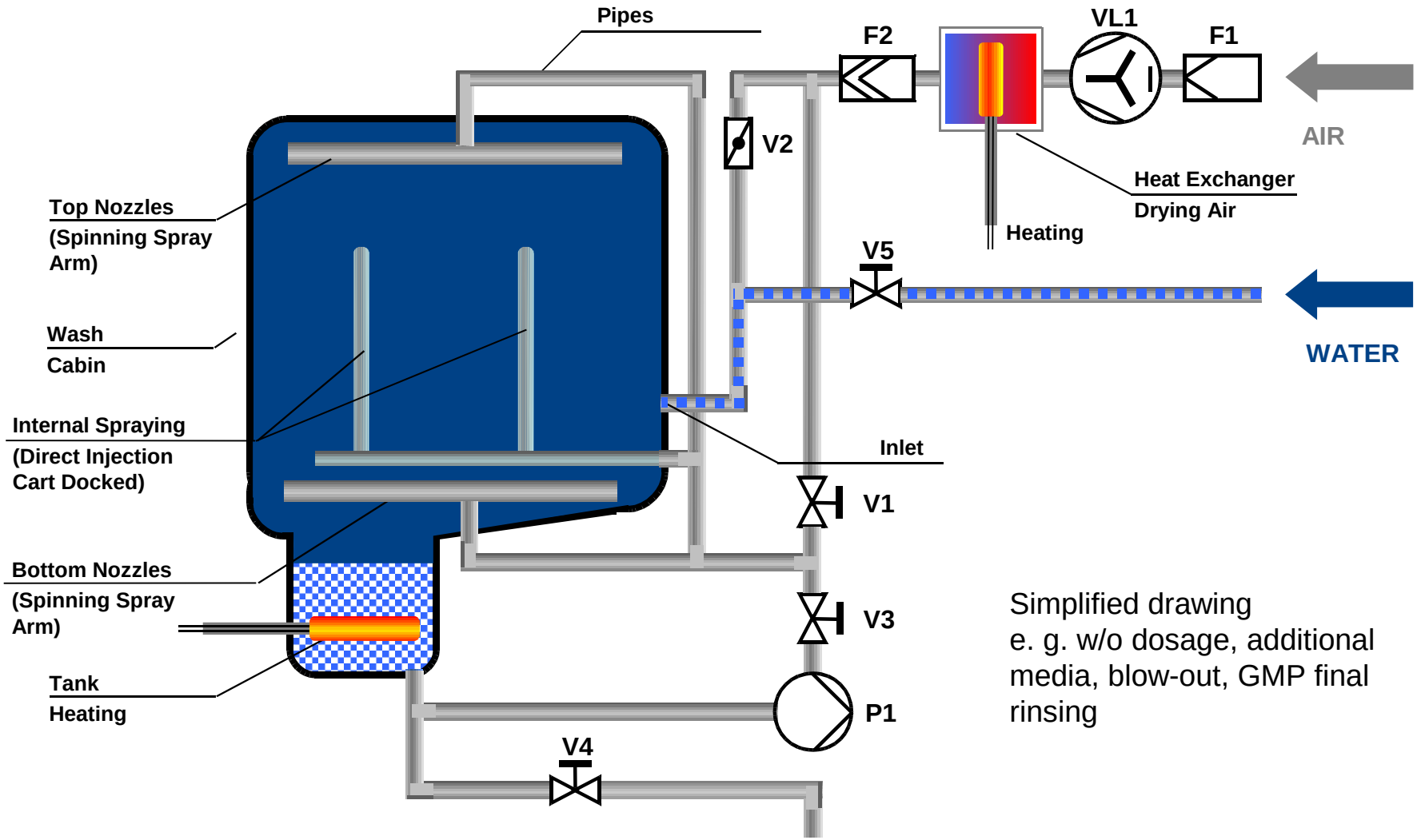
  H 990 x W 830 x D 830
- Cabin volume 682 L, Tank volume 60 L
- Easy to clean exterior Design
- Stainless steel cabinet,
  in Pharma No. 4 brush finish Ra ≤ 1,0 µm

Flow Scheme of Cleaning System



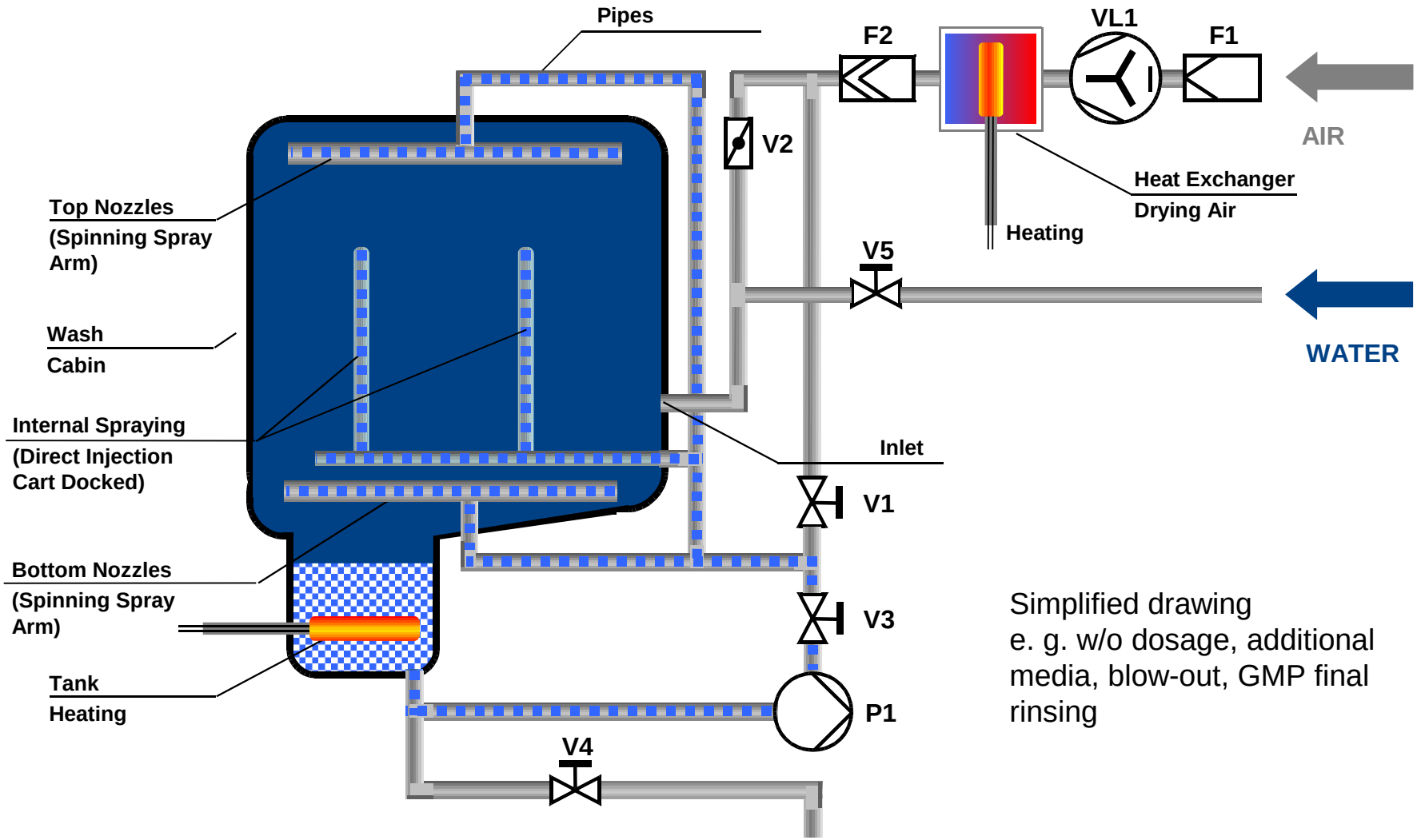
Simplified drawing
e. g. w/o dosage, additional media, blow-out, GMP final rinsing

Flow Scheme of Cleaning System – Filling of Tank



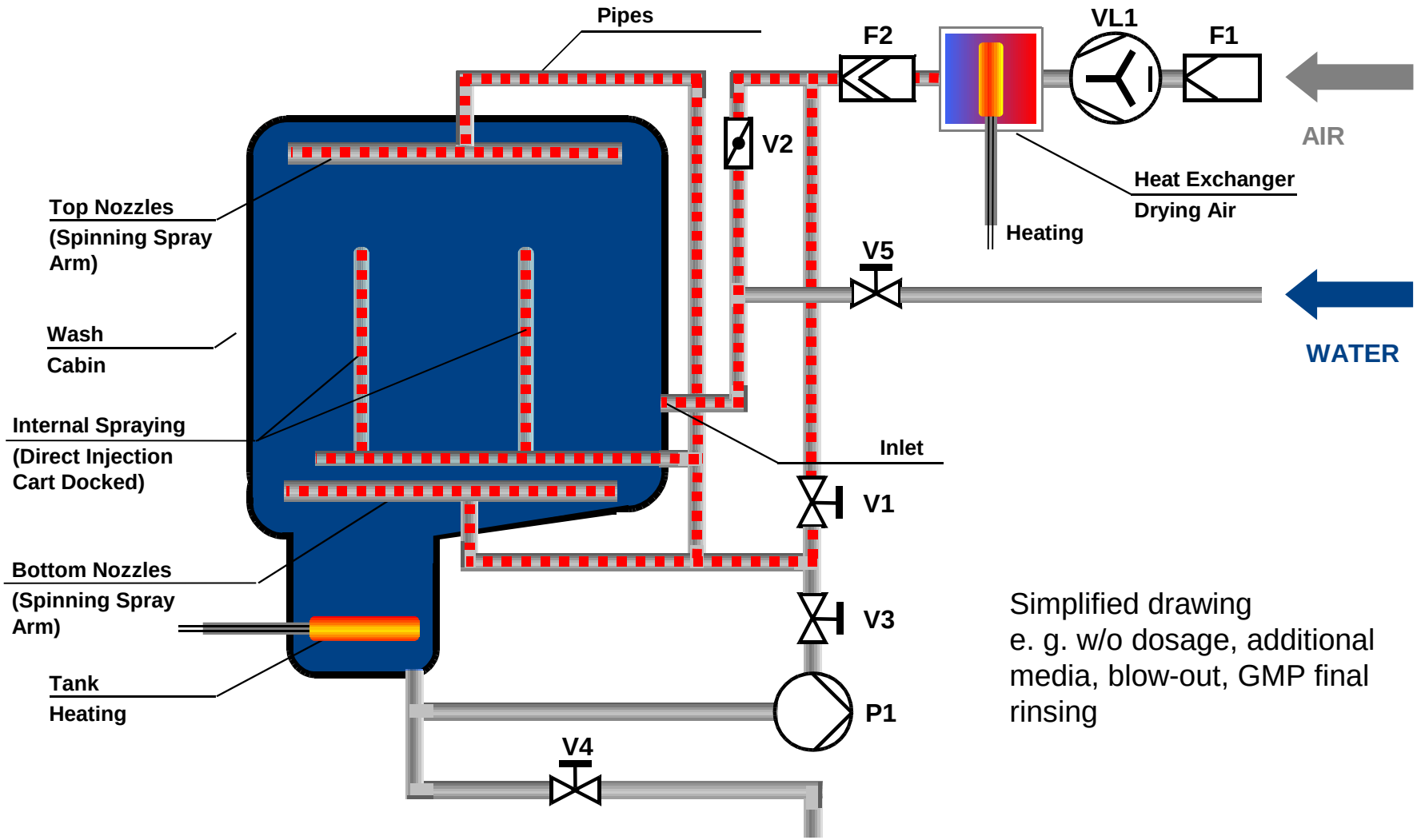
Simplified drawing
e. g. w/o dosage, additional media, blow-out, GMP final rinsing

Flow Scheme of Cleaning System – Cleaning



Simplified drawing
e. g. w/o dosage, additional media, blow-out, GMP final rinsing

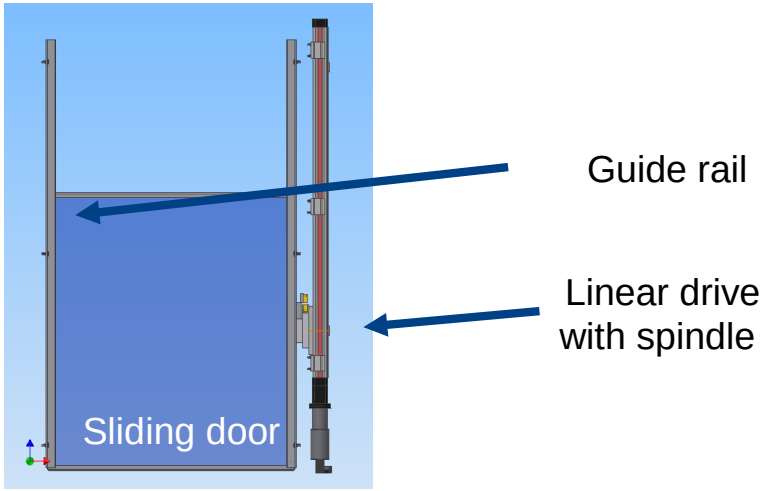
Flow Scheme of Cleaning System – Drying

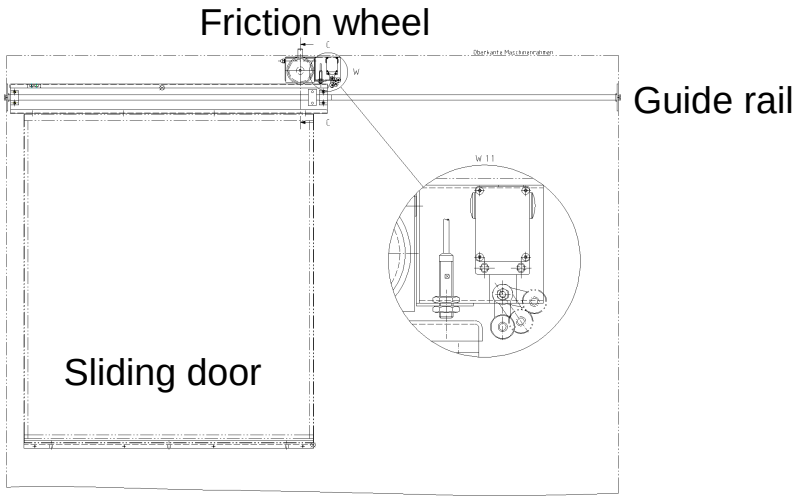


Simplified drawing
e. g. w/o dosage, additional media, blow-out, GMP final rinsing

GMP Compliant Design – Automatic Full-Glass Door

- **Automatic, sliding glass door for easy visual inspection**
- Pneumatic door seal with lateral seal valve
- Vertical or Horizontal door opening Door actuation with friction wheel
- Force in case of failures < 150 N according to legal requirements (ZH1 / 494)





GMP Compliant Design – Piping / Valves

- **Single pipe system for washing, rinsing, drying to prevent cross contamination**
- **Completely self draining, installation with 2-4% slope**
- **No dead ends**
- Pneumatic actuated aseptic diaphragm valves self drainable inbuilt

GMP Compliant Design – Pipe Fittings

- Sterile Neumo BioConnect® flanges instead of conventional TriClamp connections

Neumo BioConnect®

TriClamp

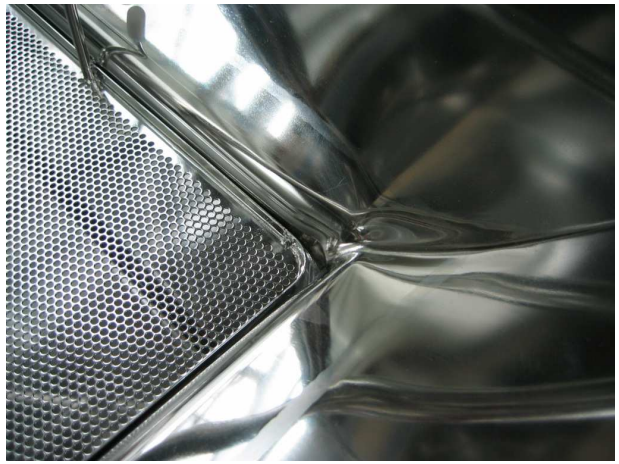
- Centric guiding prevents off-set of wetted areas
- Metal-to-metal-stop avoids stress or overcompression of gaskets (O-ring)
- Defined, symmetric compression of gasket

- Centric guiding of connection by gasket: off-set possible
- No metal-to-metal-stop
- Undefined, asymmetric compression of gasket

- **Wetted seal area 50% smaller**

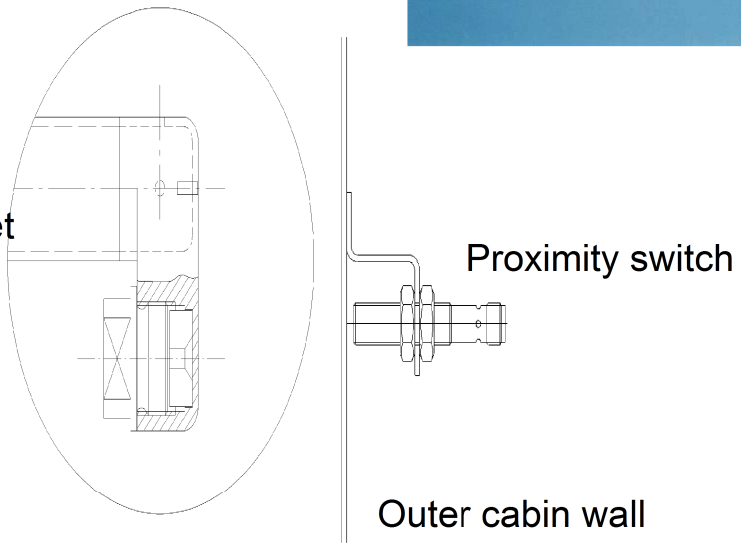
GMP Compliant Design – Wash Cabin and Tank

- **Cabin and tank interior in mirror sheet metal with round corners** (20 mm radius), no dead legs and crevice free
- **Inclined surfaces** (e. g. chamber floor and roof, piping)
- **No guard plates**
- No threaded fittings
- Weld seams smoothed and polished
- Surface roughness
  Cabin surface Ra ≤ 0.4 µm
  Weld seams Ra ≤ 0.8 µm



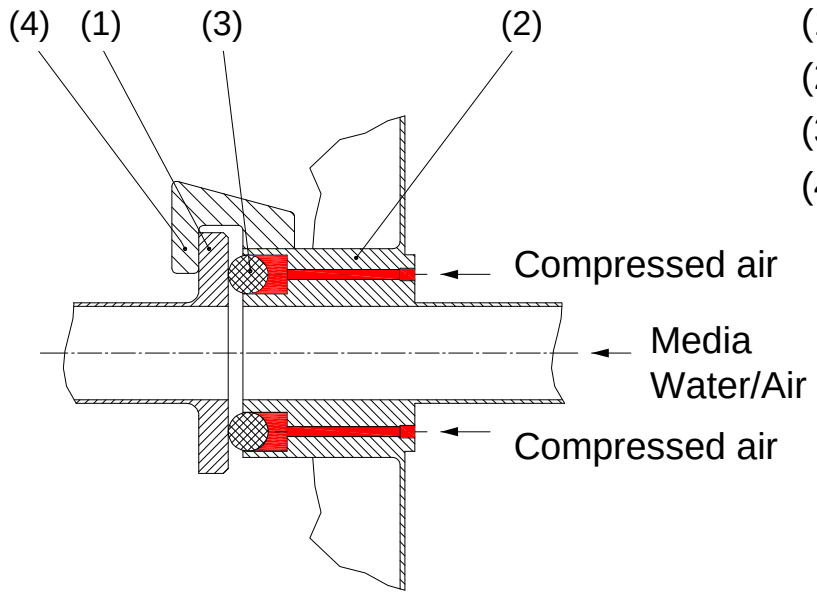
GMP Compliant Design – Rotating Spray Arm

- **No dead legs and slit free**
- **No screwed nozzles**
- Less weld seams
- Monitoring of spray arm rotation



GMP Compliant Design – Connection of Internal Spraying

- **Automatic docking of direct injection carts**
- **No dead legs, low surface roughness**
- **Pneumatic system for optimum sealing**
- **No pressure reduction, no loss off water**



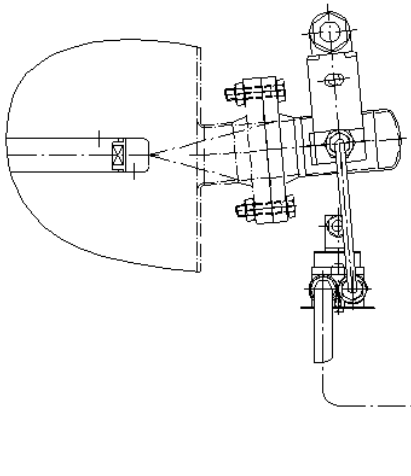
(1) Quick Coupling Connector (cart)
(2) Quick Coupling Connector (cabin)
(3) O-Seal with FDA approval
(4) Counter bearing (cabin)

GMP Compliant Design – Wash Pump

- **Sterile pump (vertical installation)**
  - 3A2 sterile standard
  - Pump casing with no dead legs
  - Crevice-free seal surfaces
  - Sterile seals
  - Surface roughness Ra ≤ 0.8 µm
  - **Complete drainable**

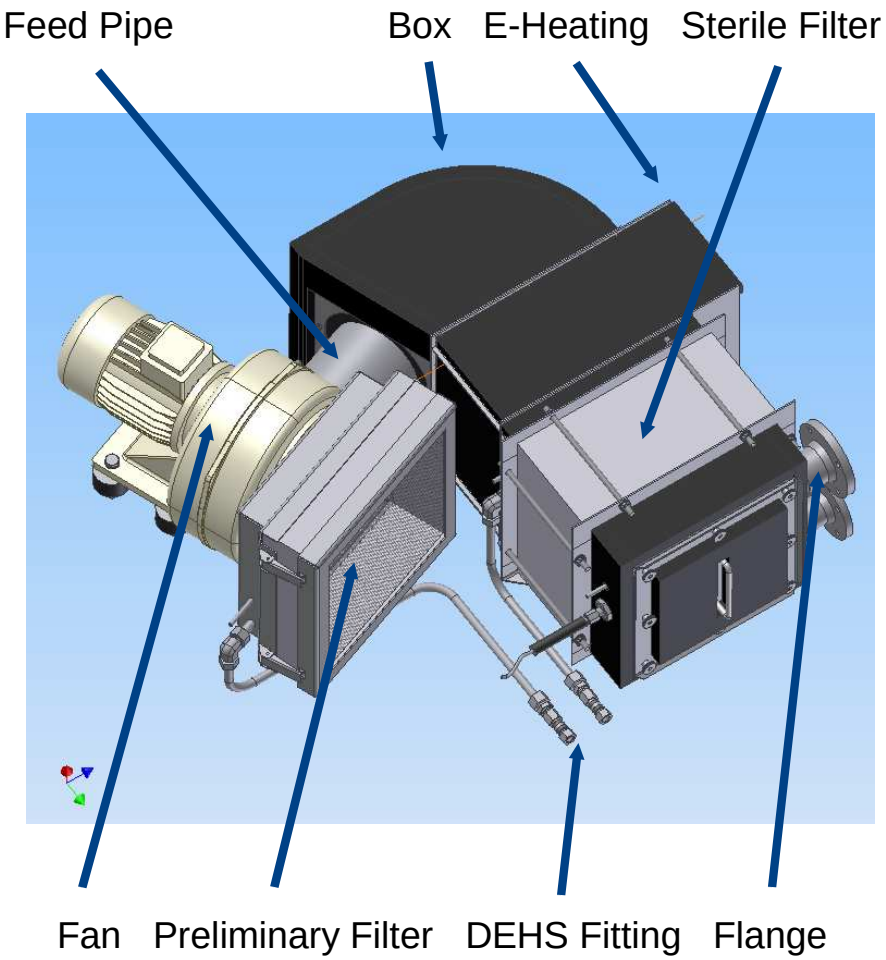
GMP Compliant Design – Dosing Unit

- **Precise dosing of detergent via dosing head**
- **Rotating spray arm rinses dosing head**
- Reduction of the number of openings in the cabin
- Use of diaphragm valves prevents dripping



GMP Compliant Design – Integrated Drying

- **Air duct into the cabin, into the carts and into the pipes**
- **Temperature control by PLC and PT 100 sensor class A**
- **Preliminary filter F9 and sterile filter H13/H14**
- Standardized filter test device with scan option via DEHS fitting
- Differential pressure measurement for monitoring of fan and filter function

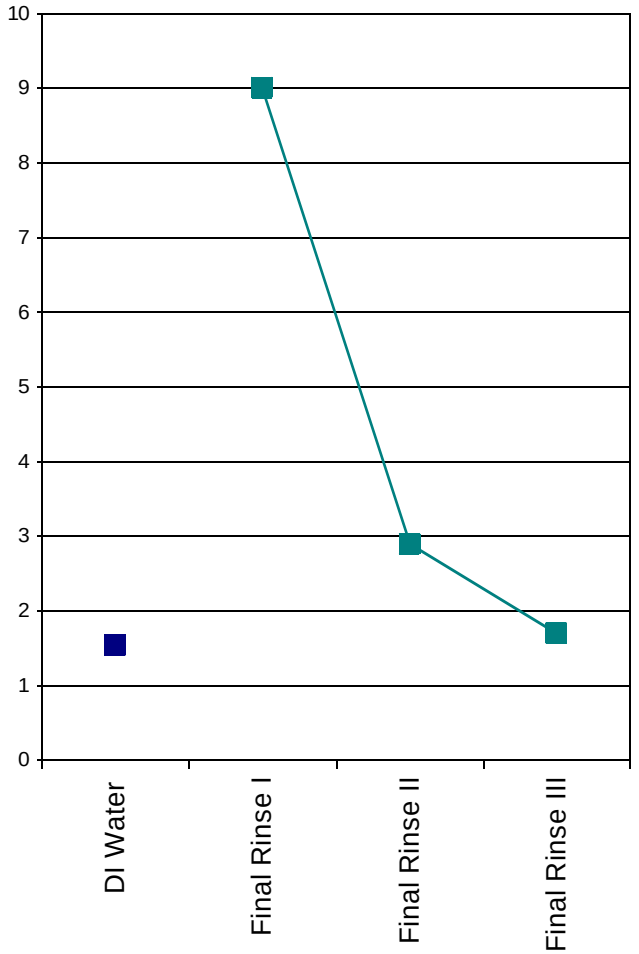


GMP Compliant Design – Self-Cleaning Performance

- Test cleaning process w/o neutralization:

3 min	Pre-rinsing with recirculation of cold purified water
10 min	Cleaning with recirculation 60°C of NaOH solution 2%
3 min	Rinsing I with recirculation of cold purified water (12µS)
3 min	Rinsing II with recirculation of cold purified water
3 min	Rinsing III with recirculation of cold purified water
3 min	Final rinsing I with recirculation of cold DI water (1,5µS)
3 min	Final rinsing II with recirculation of cold DI water
3 min	Final rinsing III with recirculation of hot DI water 80°C
15 min	Drying 110°C

- Conductivity (µS) of waste water

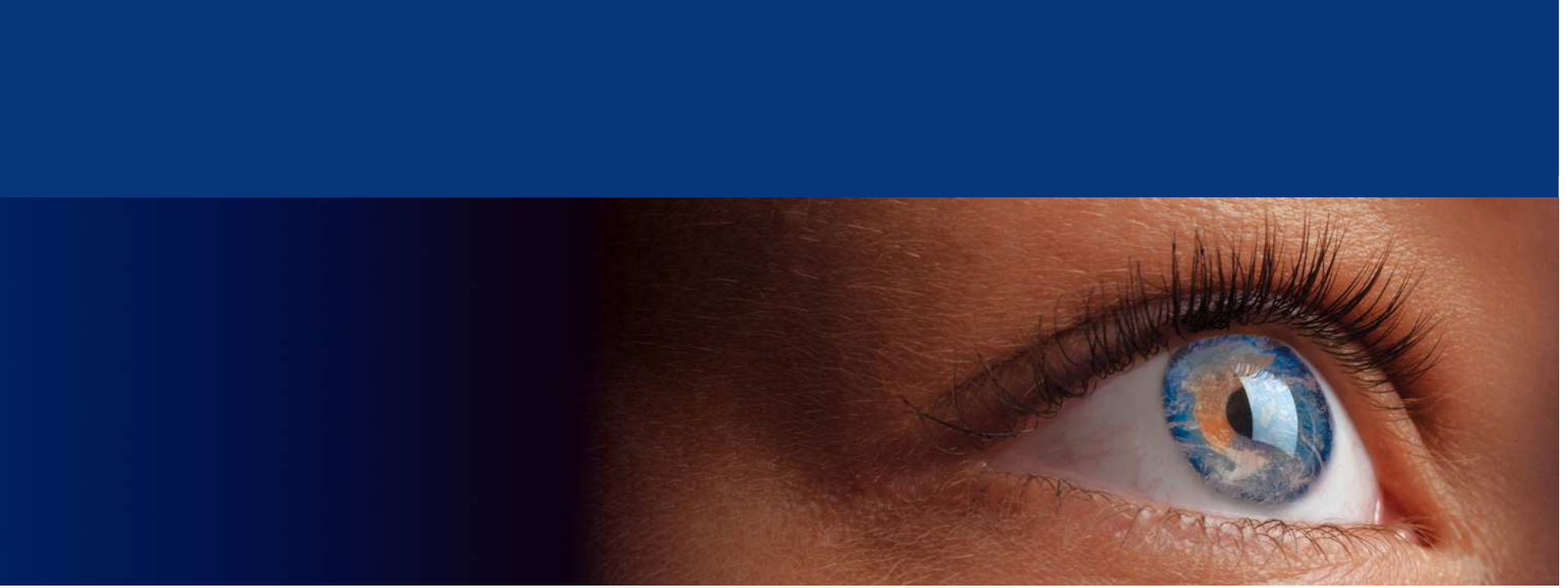


- Initial conductivity of fresh WFI water is achieved

Belimed Group – Infection Control

- 1 Group:
  - Belimed Group AG, Switzerland
  - 4 competence centers (CH, D, SI)
- Total number of employees: approx 990
- Total turnover 2011:195.0 Mio. CHF
- **GMP-compliant steam sterilizers** from 6-6-6 to 18-10-15 (350 - 4000L)
- **GMP-compliant cleaning systems** from PH820 – PH880 (300 – 6000L)
- Over **40 years** experience in cleaning and sterilization in the healthcare, pharmaceutical and laboratory sectors (15’000 installations)

Belimed Infection Control



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