Biostream International BV
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Technical Specifications

Model BioTwin 7.5 & 30 Liter (Double vessel)

All pictures in this document can differ from the final system offered

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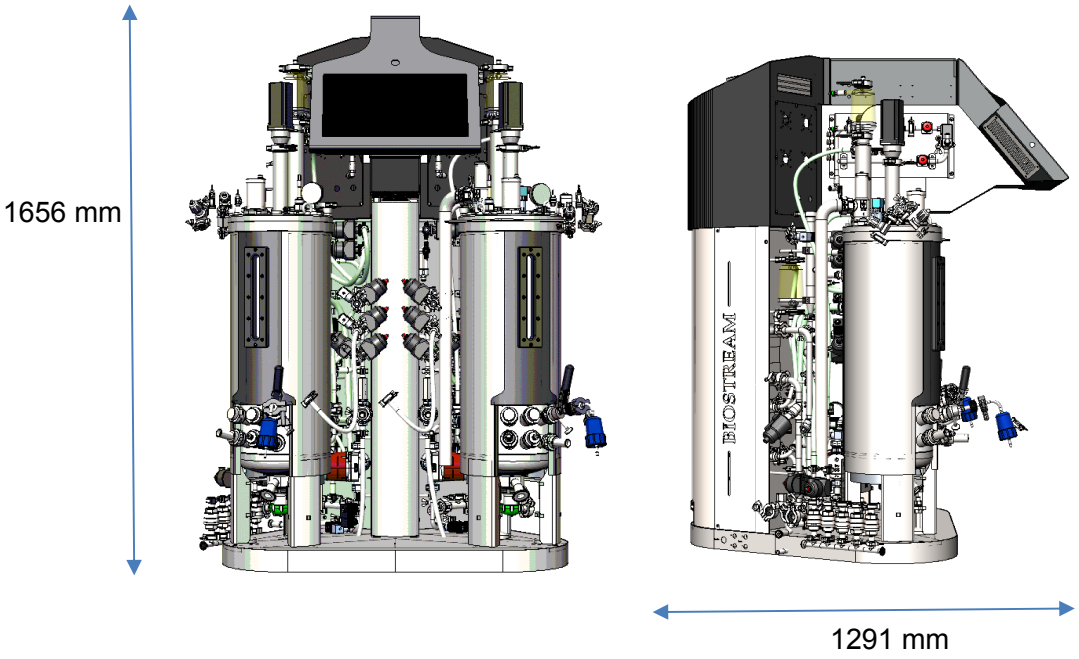
Technical Description of the BioTwin 1x7.5 L and 1x30L total volume

- It consists of two vessels of 7.5 and 30 L Total volume vessels, controller cabinet with a control unit and a two piping frames.
- The design of the vessel, parts and accessories, is studied and manufactured for easy use and easy access for service or maintenance.
- The proposed system meets or exceeds the specified performance requirements.
- The 100% stainless steel construction of the vessel and the piping is a guarantee of the high quality and long life of this system. The complete piping assembly is mounted on one frame.
- Vessel is completely self-draining by gravity.

Supporting

- Vessel supported by three legs.
- Material: stainless steel 1.4301, AISI 304.

Dimensions :



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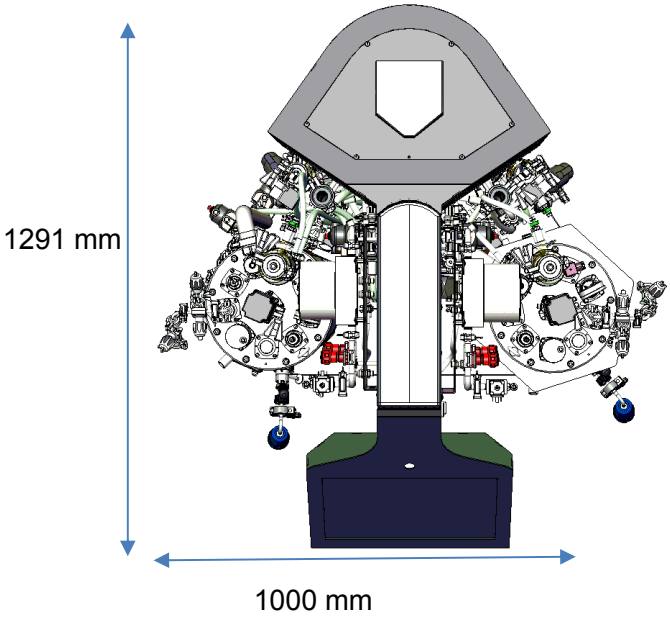

(the pictures are not presented with the vessel offered)

Piping:

To work in total security and sterility over long periods this fermenter has particular features as:

- Process piping made with standard and/or orbital welding which guarantee to work on absolute sterile conditions even after several years of use.
- Biological membrane valves on the circuits in contact with the culture medium.
- Two steam circuits, one for the service and one for the process, allow to use, if necessary, two different qualities of steam.
- Two separate condensates drain respond to the legal rules for contaminated effluent treatment.
- All the inlet and outlet connections are in stainless steel and grouped on the back of the frame.
- The open frame design, made in stainless steel and mounted on 3 feet allows easy access to all the parts and guarantee an unlimited life of the bioreactor.

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Material.

- Vessel and accessories in contact with the medium: stainless steel 1.4404 (316 L)
- Parts and accessories not in contact with the medium or the process are minimum stainless steel 1.4301 (304)
- O-rings: EPDM.
- Membranes of the valves in process circuits are in EPDM according to the international recommendations cGMP.

Finishing.

Process lines.

- Internal finishing Ra ≤ 0.4 micron, electro polished
- External finishing Ra ≤ 1.2 micron
- Other lines Ra ≤ 1.2 micron

Membranes valves.

- Internal finishing Ra ≤ 0.4 micron, electro polished
- External finishing Ra ≤ 1.2 micron

Utilities

Electrical power supply 400 VAC 50Hz 16A

- Clean steam 1,5 bar for medium contact
- Service steam 1.5 - 2,5 bar for heating and sterilization
- Cooled water in ≥ 2,0 bar
- Cooled water return without pressure and vacuum
- Air instrumentation 6 to 7 bar
- Compressed air and other gases ≥ 2,5 bar
- Contaminated condensates without pressure and vacuum
- Double jacket drain without pressure and vacuum

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Control cabinet

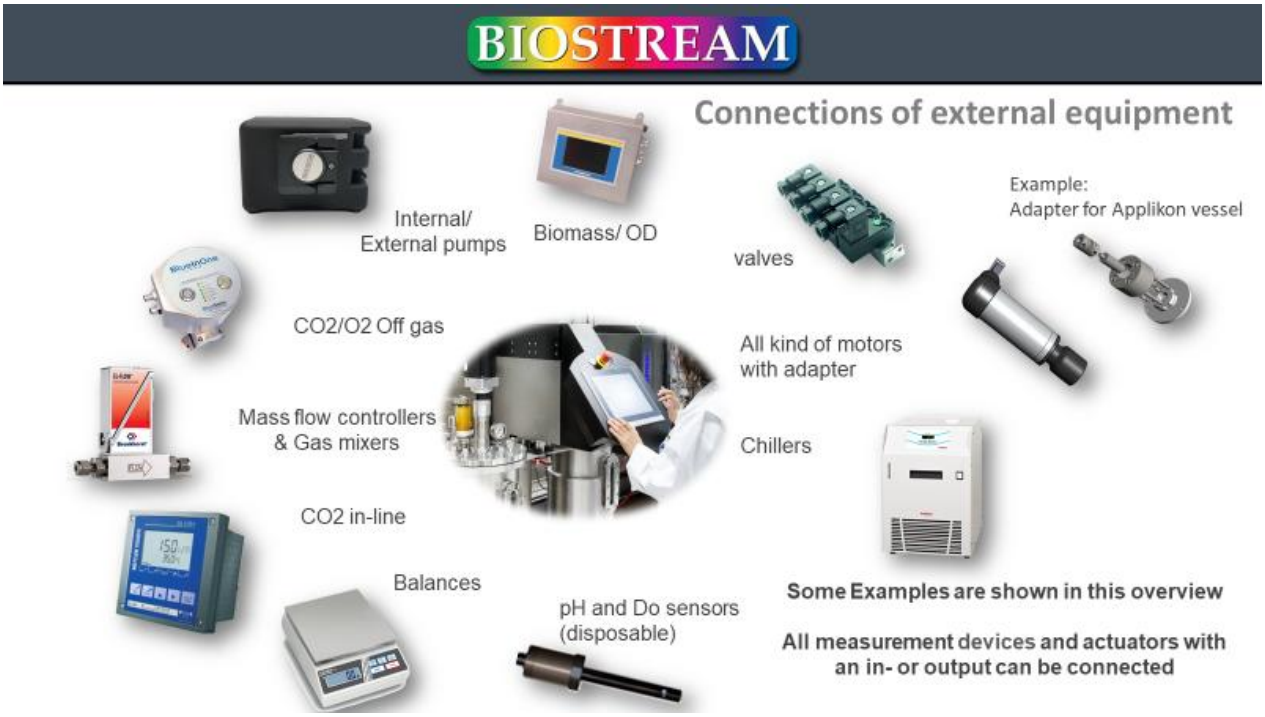
The bioreactor control is achieved by a modern and reliable Touch screen control system. It is composed of main sensor transmitters agitation, Temperature, pH, pO2, Antifoam, Mass Flow, Pressure, level, Redox, Biomass, current loop, voltage input) for a total of 20 analog and 10 digital (on/off) inputs. Also, the analog (12x) and digital (24x) outputs allow to drive and control all the devices mounted on the bioreactor or are available for future extensions. Easy upgradable with more input of output channels via extension boards or **OPC.**

Connection via OPC to external logging & controlling software or to your own SCADA software.

Minimum sixteen control loops are managed simultaneously.

Every control loop is independent, modular and flexible to allow the user to modify the parameters for fine tuning of the control strategy.

Parameters can be configured individually for measurement (range, calibration), control (set-point, alarm limits, regulation, output Active, PID, digital and direct analogue outputs) and remote set point control.



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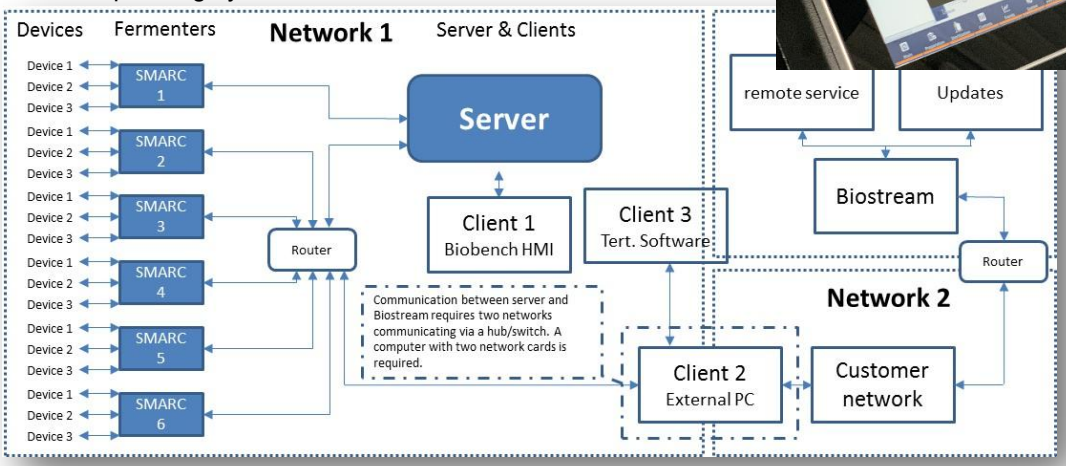
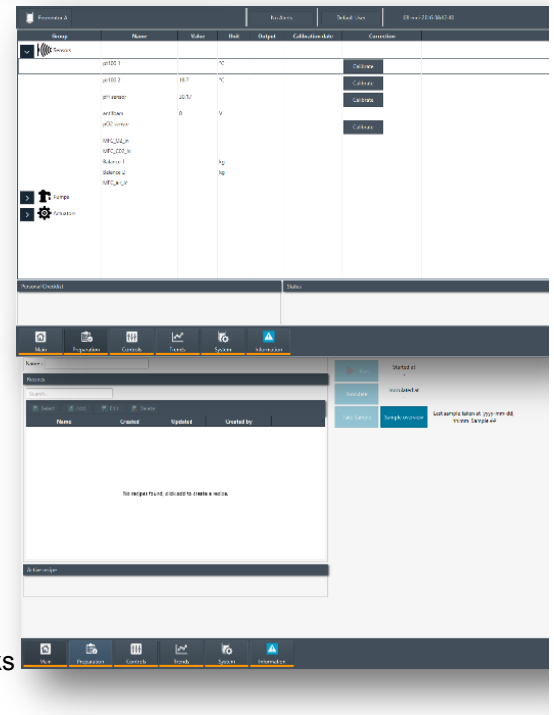
Touch screen

aluminium housing with glass front
all connectors at the bottom of the rear side
PC to be opened from the back side
all components easily accessible
protection class front side IP 44, rear side IP 20 (higher IP rating possible)
19 inch touch screen computer
2Ghz processor
1333 Mhz DDR3, 4 or 8 Gb internal memory
Linux operating system



Control board overview

Software on touch screen



- Color display with tabs for selection of different options.
- Schematic with key valve status & parameter values shown
- Trend graph with selectable time-base for display of actual values
- Full configuration for parameters, operation, sterilization and general properties of the control system.
- Allow safe cleaning of the touch screen.
- Standard cascade possibilities.
- Different levels of password for validation

The tabbed options are:
Main - a synoptic screen with access to control of parameters.

Preparation	- Short cut to calibration of sensors
Controls	- Parameter set point, controller output, PID etc.
Trends	- On-line graphical display of actual values
System	- Change general setting
	- Alarm display and acknowledgement
Information	- Multimedia integration like movies, SOPs

Each tabbed section will lead to a screen with selectable options or links to other choices via buttons or tabs.

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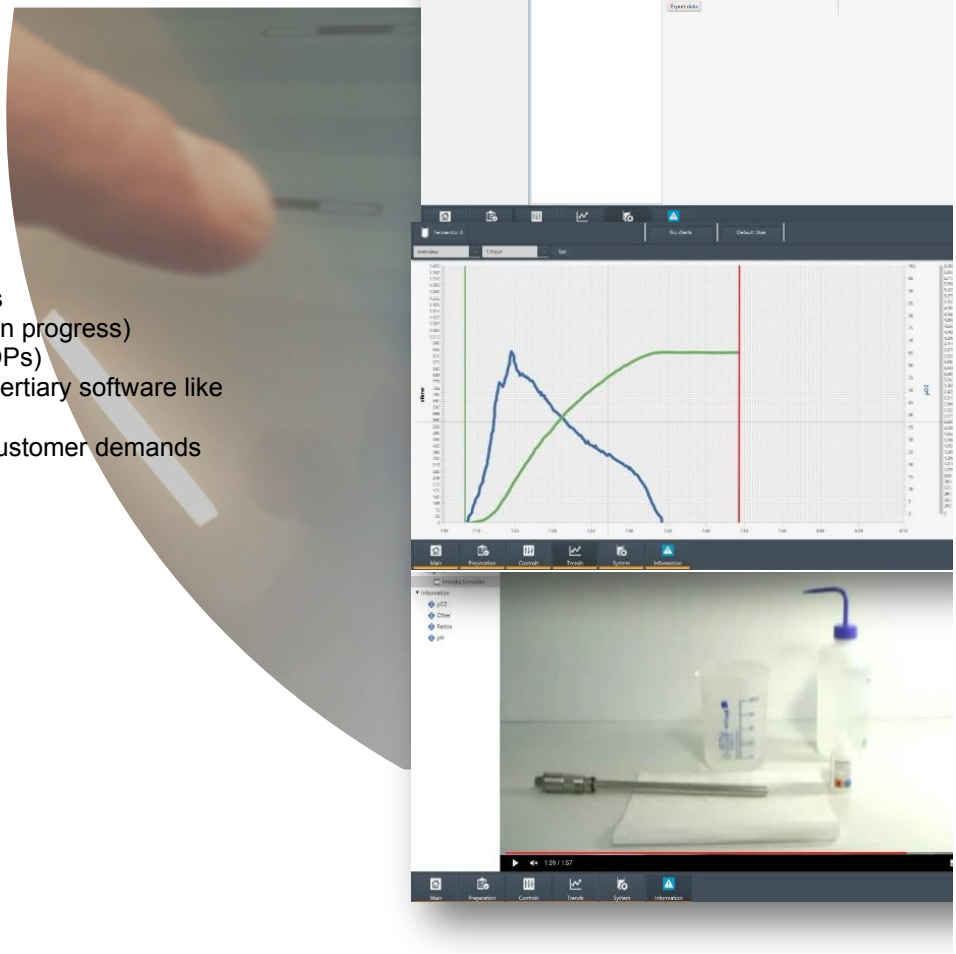
Other features:

- Easy and free installation of the same software on a PC
- Simple and intuitive use
- All kind of sophisticated programming via recipes
- Cascade possibilities
- Sample tracking
- Alarming with confirmation
- Easy one, two-point calibration with graphical view and accuracy
- Adding external devices yourself.
- Exporting functions to Excel or other programs
- Volume corrected feeding.
- Automatic reactor filling.



- Own defined on-line graphs
- Comparison with old data (in progress)
- Integration of protocols (SOPs)
- Communication with other tertiary software like matlab and flatfile
- Specific programming for customer demands

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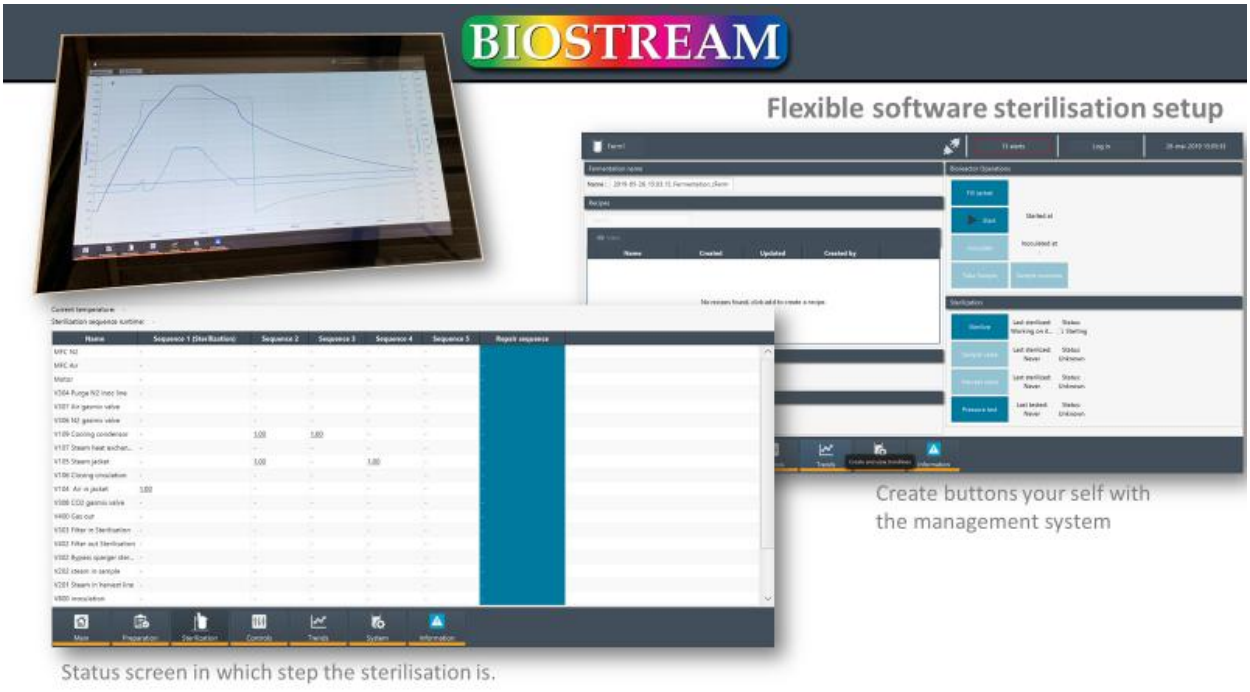

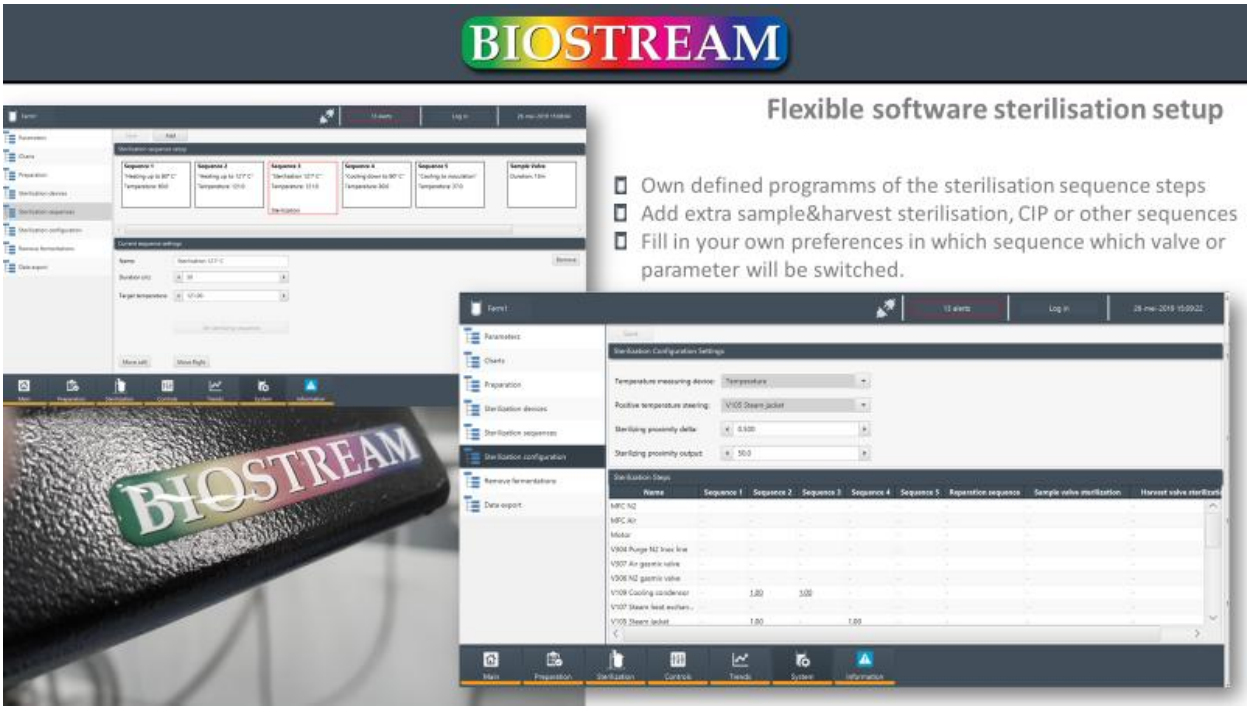

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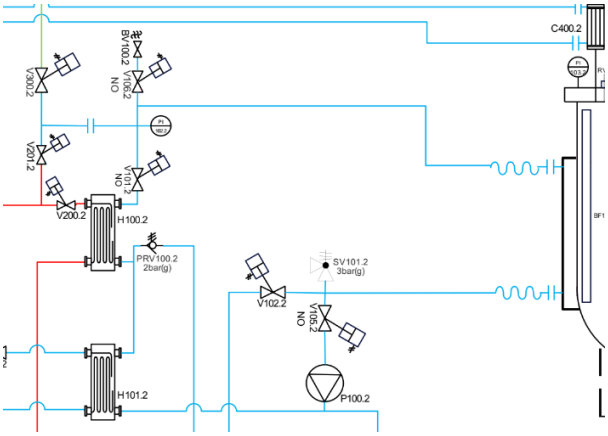
Water loop construction

Fully automatic cooling/heating/sterilization system. Temperature control through feeding tap water directly into the double jacket or chilled water (via heat exchanger) and heating through feed of steam into a heat exchanger. Safety is ensured through the use of a safety valve which has been tested by a specialist manufacturer. Condensate leaves via steam traps and a separate line with circulation system. Water entry into the exit gas cooler is via an in-line pressure regulator and solenoid valve. Switching either on or off is controlled.



LED status light

Three different integrated light green/orange/red

Green – Unit is ready to use, Safety is released
Blue – Unit is running
Red – Sterilization

Different options possible

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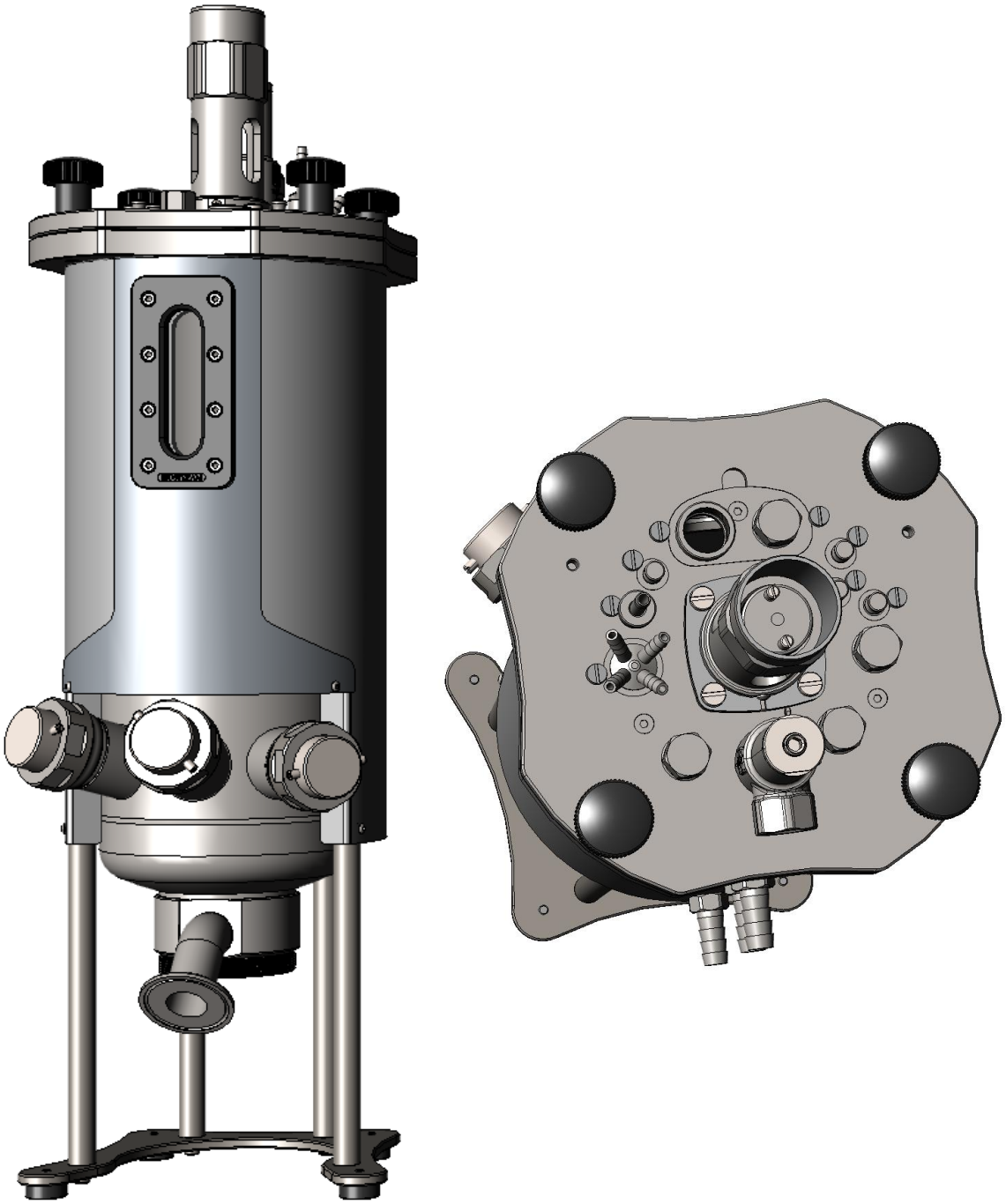
Top and side view of the 7.5 L vessel



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Vessel

- Cylindrical wall, with counter flange welded on it
- Dished round bottom
- Double jacket on cylindrical wall and bottom.
- **Insulated jacket**
- **Is produced under PED regulation based on an ASME design.**

Vessel Characteristics

- Useful volume L 5 L
- Total volume L 7.5 L
- Minimum volume L Around 1 L. Useful volume is depending on the usage of the process.
- RATIO H/D 3/1

Internal vessel Dimensions

- Height vessel 588 mm
- Diameter (inner) 195 mm

Vessel specifications

- Working pressure vessel -1 to 3 bar G
- Working pressure double jacket -1 to 4 bar G
- Working temperature vessel / double jacket -10 to 145°C

Material:

- In media contact Stainless steel 1.4404 or 1.4435 = AISI 316L
- Not in media contact Stainless steel 1.4301 = AISI 304

Surface

- Inner surface Ra ≤0.4µm electro polished
- Outer surface Ra ≤1.0µm electro polished

Vessel top plate

- Stirrer drive - Top; motor drive
- 5 x 10 mm ports - inoculation needle; Anti-foam sensor; Level sensor;
- 5 x 12 mm (PG13,5) - Exit gas cooler, sensors, Manometer
- 1 x 28 mm - Four way needle

Vessel side wall

- 2 x Tri-Clamp (DIN20) - Inlet for sparger; inlet head space gassing
- Air tube - Ring sparger
- Baffles - 3 baffles

Double Jacket

- 2 x Ingold DN25 - Angled 15°; pH; pO2;
- 1 x Ingold DN25 - Straight; Sample valve

Vessel bottom

- Bottom valve - Novaseptic

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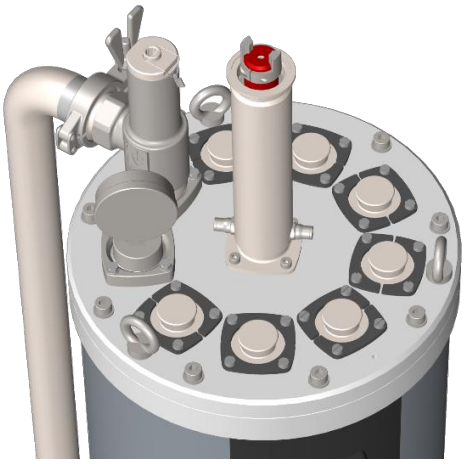
Top and side view of the 30 L vessel



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Vessel

- Cylindrical wall, with counter flange welded on it
- Dished round bottom
- Double jacket on cylindrical wall and bottom.
- **Insulated jacket**
- **Is produced under PED regulation based on an ASME design.**

Vessel Characteristics

- Useful volume L 20-25 L
- Total volume L 30 L
- Minimum volume L Around 5 L. Useful volume is depending on the usage of the process.
- RATIO H/D 3/1

Internal vessel Dimensions

- Height vessel 727 mm
- Diameter (inner) 243 mm

Vessel specifications

- Working pressure vessel -1 to 3bar
- Working pressure double jacket -1 to 4bar
- Working temperature vessel / double jacket -10 to 145°C

Material:

- In media contact Stainless steel 1.4404 or 1.4435 = AISI 316L
- Not in media contact Stainless steel 1.4301 = AISI 304

Surface

- Inner surface Ra ≤0.4µm electro polished
- Outer surface Ra ≤1.0µm electro polished

Vessel top plate

- Stirrer drive - Top; motor drive
- 9 x 40 mm ports - Anti-foam needle; Anti-foam sensor; Level sensor; Inoculation; Manometer, Acid / Base; Spare
- 1 x Tri-Clamp 1-1/2” - Exit gas cooler
- 1 x Tri-Clamp 1-1/2” - Automatic pressure release valve

Vessel side wall

- 2 x Tri-Clamp (DIN20) - Inlet for sparger; inlet head space gassing
- Air tube - Ring sparger
- Baffles - 3 baffles

Double Jacket

- 5 x Ingold DN25 - Angled 15°; Temperature sensor; pH; pO2;
- 1 x Ingold DN25 - Straight; Sample valve

Vessel bottom

- Bottom valve - Novaseptic

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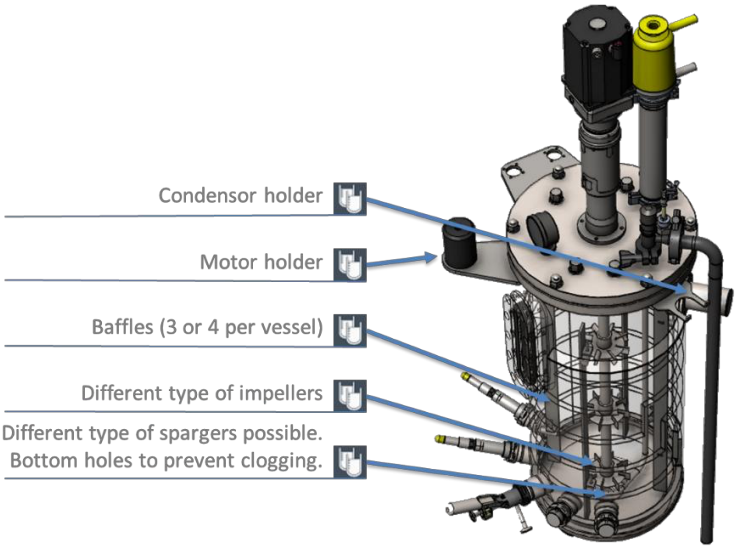


Drive system

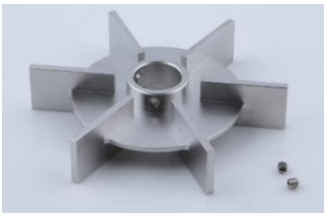
Speed regulation with air cooled drive motor controlled by frequency exchanger centrally mounted on the top of the vessel.

Motor AC servo motor
Power drive motor: Depends on the vessel

Double mechanical seal with gas/liquid seal with EPDM.

Driving ax, material Stainless steel AISI 316 L, Working length around 655 mm

Material : 316L
Surface : Ra ≤ 0.4µm
O-Ring : EPDM



Re-changeable stirrer (3 pcs):

Type : 6-blade-impeller type “Rushton”
Material : 316L
Surface : Ra ≤ 0.4µm
O-Ring : EPDM
Dimension : 0.33 x ID vessel

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Agitation

Stirrer speed:	**Speed is adjustable between up 700 RPM**. Speed can depends on the vessel And applications. Torque measurement is an option for indirect viscosity measurement

Temperature

Range	from around 5°C above room temp to 130°C. with chiller there is a possibility to go 2 °C with glycol Isolation for condensation with low temperature is not offered
Sensor	Pt-100 sensor, 25 mm adapter.
Material body	316L
Element	Pt100
Accuracy	Class A
Max. temperature	-50 – 200°C
Accuracy	+/- 0.1°C in range +10° to +50°C in fluids. Above 50°C is +/- 0,3°C in fluids.
Control	Water-jacket vessel: PID control with cooling valve and water jacket heater.

Sterilization/Pasteurization

Mode:	Completely automatic, but easy adaptable behind a password level Independent sample and harvest valve sterilization

pH

Range	2 - 14
Control	PID. Base and Acid Setting of dead band
Sensor	Intelligent pH probe with calibration data, runs and more. See data downstairs

DO

Range	0 – 150 %
Control	Different options integrated of cascades are possible eg flow, gasmix and speed
Sensor	Intelligent DO probe with calibration data, runs and more.

Auxiliary equipment	All kinds of external measurements can be integrated in the touch screen.
Warranty	2 years

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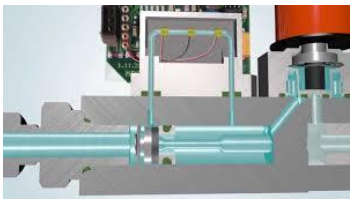
Gas inlet and control

Inlet gas control (sparger) with calibrated mass flow controller. Gas enters via separate pressure regulation valves incl. manometer. Fully automatic sterilization of the inlet filter and associated pipework. Gassing via sparger. Steam inlet to the filter housing. Condensate will leave via a stainless steel condensate line integrated into the common condensate collection system.



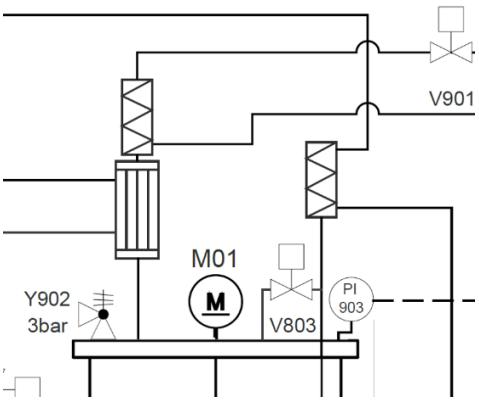
Mass flow controller Air:
Measurement range : See offer
Accuracy : 1% of full scale + 0,5% of reading
First 20 % of the scale has lower accuracy then the
Above mentioned specifications

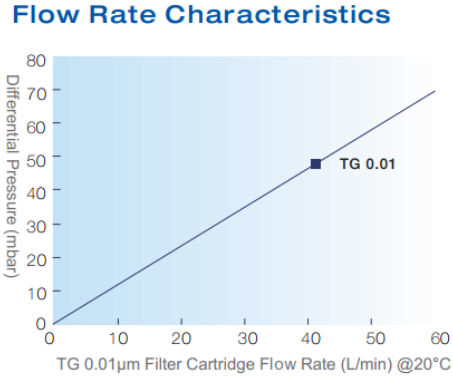
Filter assembly sparger & head space

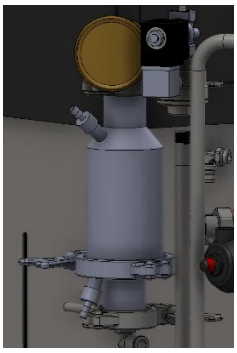
Hydrophobic PTFE Cartridge Filter Pore Size:
0.2 Micron/ Length: 5" (EFA 0.3 m2) Adaptor:
O-Seal/ Ring: Silicone

Inline steam sterilization: 100 Cycles for 30 min at 145 °C
Forward (differential pressure < 30 kPa) + 50 cycles reverse (differential pressure <10 kPa)

Maximum operating pressure: 6,9 bar at 25 °C







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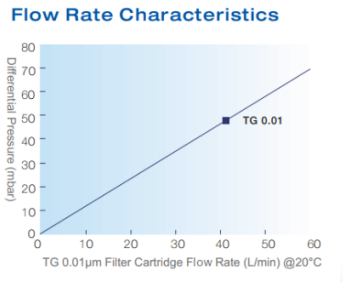
Gas outlet

Outlet via a thermodynamic exit gas cooler with top mounted membrane filter. Fully automatic sterilization with removal of condensate via a stainless-steel line and return to common condensate collection pipework.

Hydrophobic PTFE Cartridge Filter Pore Size:
0.2 Micron/ Length: 5" (EFA 0.3 m2) Adaptor:
O-Seal/ Ring: Silicone

Inline steam sterilization: 100 Cycles for 30 min at 145 °C
Forward (differential pressure < 30 kPa) + 50 cycles reverse (differential pressure <10 kPa)

Maximum operating pressure: 6,9 bar at 25 °C



Pump(s)

New combined brushless DC motor, gearbox and integrated drive designed specifically for use with the pump heads

3 pieces on/off pumps
Manual forward/backward running of the pumps (Acid or Base, AF)
RPM : 8 to 408 rpm speed control with brake function
(extra pumps possible, not offered)

1 pieces analog pumps
Manual forward/backward running of the pumps (feed)
RPM : 8 to 408 rpm speed control with brake function

Pumps can be allocated to On/off and analog pumps.

Extra features:
Feedback if the pump is running
Left and right control motor
Colom 114 8-408 is in 'ml/min'

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Parts on the vessel

Pressure indicator, for port ø19 mm

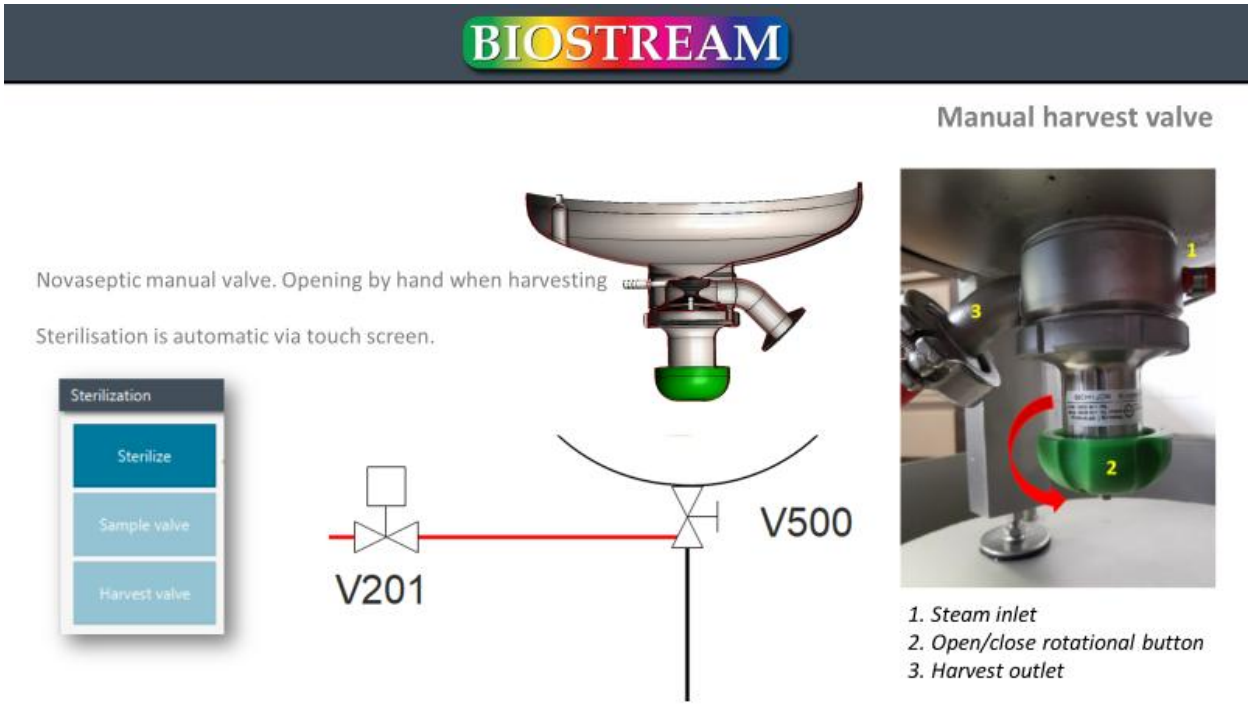
Connection 40 mm, with stop and gasket and with pressure indicator from WIKA. -1-3 bar

Safety valve, for port ø19 mm

Material product	316 L
O-ring	EPDM
Pressure	Max 2.5 bar

Harvest valve with tri-clamp

Material body	316L
Specs	Shut off 90º
Material diaphragm	EPDM



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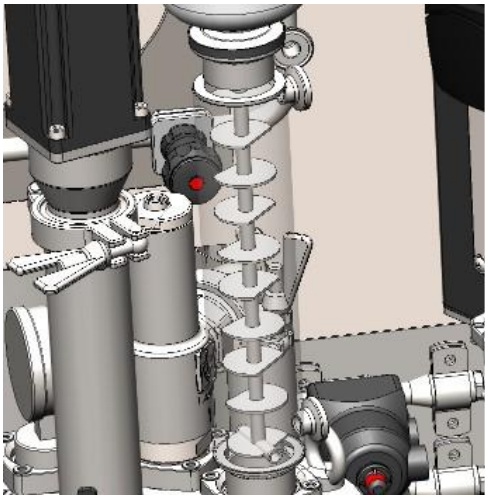
Temperature probe, 25 mm port adapter

Material body	316L
Element	Pt100
Accuracy	Class A
Max. temperature	-50 – 200°C

Condensor for cooling out going gas for Pilot bioreactors

- Water lock on the inlet to prevent water spill
- Dismantlable insert
- .Connection on a 40 mm
- All kind of fluids can be connected
- Manometer -1 to 3 bar



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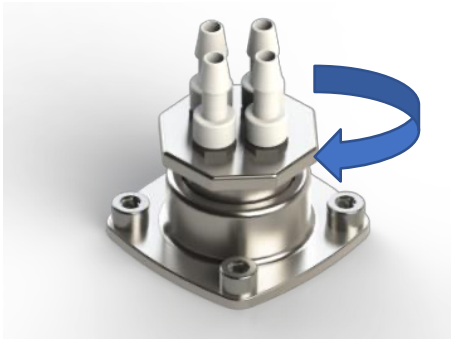
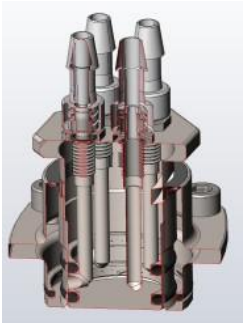
Push through valve with four needles

The sterilisable push valve allows the aseptic connection of a bottle with inoculum, feed solution or corrective reagent to a bioreactor in such a way that the valve components are sterilised first in an
autoclave and then with the vessel in-situ. Its method of use is simple:

- Connect the push valve to a feed bottle using flexible tubing
- Sterilise the whole assembly in an autoclave at 121 C or above
- Fit the sterilised push valve to the top plate of an unsterilized bioreactor
- Re-sterilise the bottom of the push valve with the vessel
- Open the push valve to allow flow of the liquid into the vessel.





Procedure
1. Ensure the push valve is in closed position:
The bottom section of the rotating piston is retracted. The upper section sticks out from the valve body. Turn the top section of the rotating piston anti-clock-wise to fully close the push valve as necessary.
2.Connect the reagent bottle equipped with silicone tubing and marprene section for the peristaltic pump to the push valve.
3.Sterilise the whole assembly in the autoclave.
When completely cool:
4.Fit the push valve into a free 19 mm port in the vessel top plate of the bioreactor.
5.Connect the tubing to the peristaltic pump
6.Sterilise the vessel in-situ as normal
This will also sterilise the only part of the push valve to be exposed since sterilisation in the autoclave
When the vessel has cooled down:
7.Turn the top section of the rotating piston clockwise the push valve opens; the bottom section of the rotating piston is pushed downwards into the vessel to expose the outlet for liquids. The gap between top section of the rotating piston and the valve body decreases.

Digital pH-sensor

The EasyFerm Plus sensors are designed to withstand demanding applications in pharmaceutical, biotechnology, and food & beverages industries. It is also suitable for harsh chemical processes. It withstands steam sterilization, autoclavation and cleaning in place (CIP). The electrolyte of the EasyFerm sensors is pre-pressurized to prevent the diffusion of sample into the sensor. The Everef-F reference cartridge ensures that the reference electrolyte remains free of silver and precipitation of proteins.
Advantages:

- Wide range of applications
- Ceramic diaphragm is an improved barrier of the electrode
- Highly reliable measurements after steam sterilization, autoclavation and CIP cleanings
- Drift-free measurement

EasyFerm Bio specifically designed for applications in Pharma and Biotechnology (EHEDG, Biocompatibility)
Pre-pressurized reference electrolyte ensures a clog-free diaphragm

Specifications	
Measuring range	0 – 14 pH
Process temperature	0 – 140 °C (Arc: analog 0 – 110 °C, digital 0 – 140 °C)
Pressure range (relative to ambient)	0 – 6 bar (pressurized)
Hygienic aspects	Autoclavable, SIP, CIP
pH glass	PHI
Electrolyte	Phermlyte
Reference system	Everef-F
Diaphragm	HP Coatramic
Temperature sensor	Pt100 in VP version Pt1000 in LEVP version

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pH/ORP Adapter

BIOSTREAM

Digital DO sensor

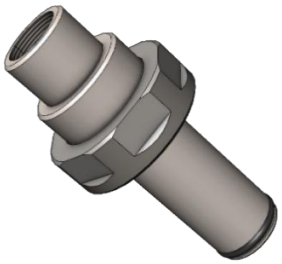
DO Arc-sensor 12 mm

The VisiFerm DO Arc is the first optical oxygen sensor with integrated opto-electronics, having the full functionality of a measuring device with selfdiagnostics. It is steam sterilizable, autoclavable and CIP compatible. The VisiFerm requires less maintenance than a classical oxygen sensor as it does not have a mechanically sensitive membrane or a corrosive electrolyte.

Advantages:
- No electrolyte or polarization is necessary.
- Quality of the sensor
- Calibration data available
- Re-calibration of the sensor during the run.
- Cascade possibilities with Stirrer, Flow, Gasmix and O2

a-length	120 mm
Accuracy at 25 °C	1 ± 0.05 %-vol: 21± 0.2 %-vol; 50 ± 0.5 %-vol
Analog Interface 1	4-20 mA for DO, programmable
Analog Interface 1 and 2	galvanically not isolated; pulse width modulation 3.5 kHz
ATEX Approval	No
Autoclavable	Yes
Baud Rate	4800, 9600, 19200, 38400, 57600,115200 bd
Certificate	Yes, with parameter settings and materials used
CIP	Yes
Diameter	12 mm
Digital RS485 Interface:	Modbus RTU, max 31 addresses
Drift at Room Temp. under Constant Conditions	< 1 % per week
Electrical Connector	VP 8
Electrolyte	None

DO Adapter



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Antifoam probe, for port ø19 mm

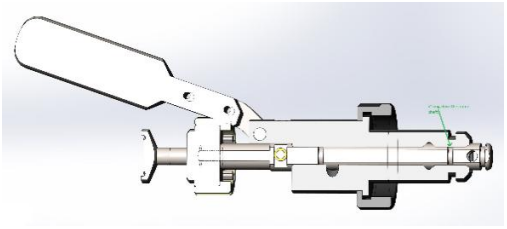
BIOSTREAM

Antifoam probe, for port ø19 mm

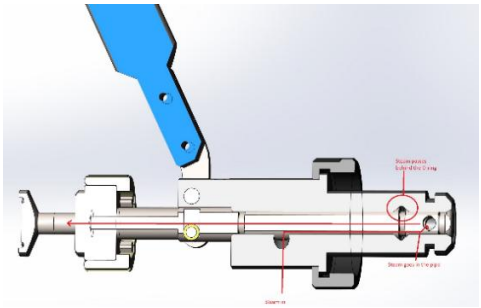
Sensor	Conductive with dosing needle
Control	Peristaltic pump (antifoam)
Range	0 / 100 % (ON/OFF)

Adjustable probe	Total length 550mm.
Material product wetted	316L, Ceramic
Surface product wetted	0.8µm electro polished
O-Rings	EPDM

Sampling valve 25 mm



Sampling system in open position



Sampling system closed (sterilization) position

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Vessel LED lamp

Material product	316 L
Protection class	IP65

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Lift system for head plate

Integrated motor for lifting head plate of vessel. Automatic controllable via touch screen. Security for minimum and maximum height.

Arm is swive-able and can be pulled out.