Operating Manual

Techfors-S

In Situ Sterilisable Pilot Scale Bioreactor

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1 General Information

1.1 About this Manual

This manual enables the safe and efficient handling of the device.

All the information and instructions in this operating manual comply with the current standards, legal regulations, the latest technological and scientific developments and the knowledge gained from the manufacturer's many years of experience in this field.

This operating manual is a component part of the device. It must be kept near to the device and must be accessible to the operators at all times.

The users must read the operating manual thoroughly and fully understand its contents before beginning any work.

Adhering to all the safety and operating instructions in this manual is essential to ensure that work is carried out safely.

The scope of delivery may differ from the explanations, descriptions and figures in this operating manual due to special designs, additional options specified on ordering and the latest technical/mechanical modifications.

This manual contains illustrations to aid general understanding. These may differ from the actual device as supplied.

1.2 Explanation of Special Notices

1.2.1 Warning Notices

Warning notices in this manual are indicated by a coloured bar and begin with a signal word that signifies the degree of the hazard.

⚠ WARNING

The signal word "WARNING" indicates a potentially dangerous situation that may result in severe or even fatal injuries if not avoided.

⚠ CAUTION

The signal word "CAUTION" indicates a potentially dangerous situation that may result in minor injuries if not avoided.

1.2.2 Other Notices

ATTENTION

The word “ATTENTION” on a blue bar indicates a situation that may result in significant damage to property if not avoided.

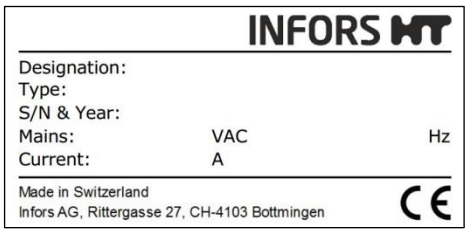
INFORMATION

Texts located below a grey bar bearing the notice “INFORMATION” provide useful tips and recommendations for ensuring efficient, fault-free operation of the device.

1.3 Device Identification

1.3.1 Identification Plate

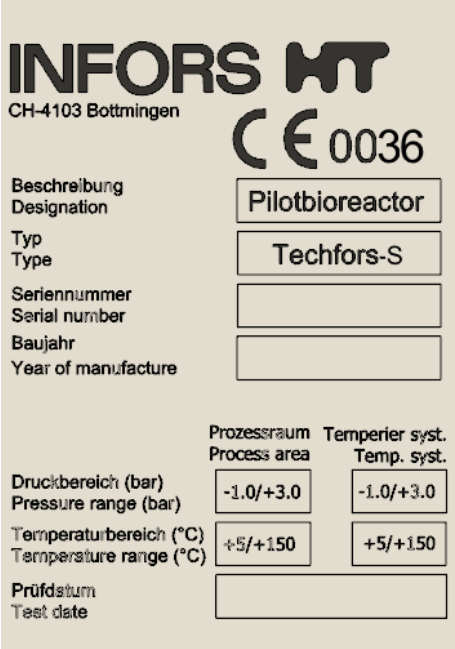
The identification plate is designed to allow clear identification of the device. It contains the following information:



- Manufacturer name
- Designation = Category of device
- Type = Device type (name)
- S/N = Serial number
- Year = Year of manufacture
- Mains = Nominal voltage and frequency
- Current = Current consumption
- Manufacturer address
- CE marking

One identification plate can be found on the instrumentation cabinet and one on the support of the basic unit.

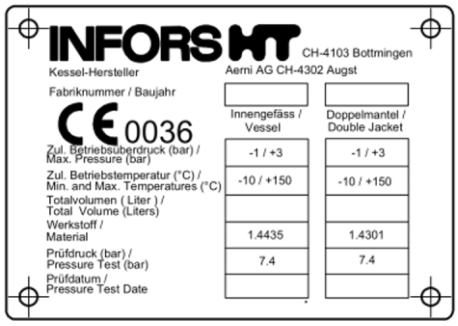
1.3.2 Plant Identification Plate



The plant identification plate is located on the central pillar of the basic unit and contains the following information:

- Manufacturer name with address
- Designation of plant
- Device type (Name)
- Serial number
- Year of manufacture
- CE marking
- Process range (bar) in process area and temperature control system
- Temperature range (°C) in process area and temperature control system
- Test date

1.3.3 Vessel Identification Plate



The vessel identification plate is welded onto the outside of the vessel. It contains the following data:

- Manufacturer of the device with address
- Manufacturer of the vessel with address
- Number of manufacture / Year of manufacture

Values for vessel and vessel jacket

- Max. operating pressure
- Max. operating temperature
- Total volume (litres)
- Material
- Pressure test
- Pressure test date

1.4 Declaration of Conformity

The device is in compliance with the essential requirements of the following Directives:

- Directive 2006/42/EC on Machinery
- EMC Directive 2014/30/EU
- Pressure Equipment Directive 2014/68/EU

The declarations of conformity in accordance with the Directive on Machinery and the Pressure Equipment Directive are included in the overall documentation supplied with the device.

1.5 Customer Service and Services

Our Customer Service is at your disposal for technical advice and specialist enquiries. For contact information, see page 2.

Due to their familiarity with the potential applications of the device, the Customer Service team is able to provide information on whether the device can be used for a specific application or modified to handle the planned process.

Furthermore, our colleagues are always interested in new information and experiences resulting from user's applications for the device that may be valuable for the continued development of our products.

2 Safety and Responsibility

This section describes general considerations relating to user safety that must be taken into account when working with the device.

In the remaining sections, warning notices are used only to highlight particular hazards directly arising from the actions being described in the section in question.

It is essential to read the operating manual carefully – especially this section and the warning notices in the text – and to follow the instructions therein.

This section also refers to areas that are the responsibility of the provider due to certain risks arising from particular applications for which the device is used deliberately and with full awareness of the associated risks.

2.1 Intended Use, Incorrect Use and Misuse

The in situ sterilisable pilot scale bioreactor Techfors-S from INFORS HT is designed especially for cultivation of microorganisms for research and development in a biotechnology laboratory and exclusively for the use of Group 2 fluids in accordance with Article 13 of the Pressure Equipment Directive 2014/68/EU.

The device is designed and constructed exclusively for the intended use described above.

Intended use also includes following all the instructions in this operating manual, especially those relating to:

- The installation site
- User qualifications
- Correct operation and maintenance
- The use of undamaged hoses and glass vessels

Any failure to observe the requirements specified in this manual shall be deemed incorrect use.

Any use of the device outside the scope of the intended use as described above shall be deemed misuse.

This also applies to applications for which the device is not designed, such as the use or production of explosive gases, which is not permitted because the device is not explosion-proof.

For use for special applications not covered by conventional, intended use, the device must be modified and certified accordingly by the manufacturer.

Any use of the device outside of a biotechnology laboratory, i.e. in any environment in which the conditions required for the safety of the users cannot be fulfilled or cannot be fulfilled to their full extent, shall also be deemed misuse.

2.2 Qualified Personnel

Due to the complexity of the device and the potential risks arising from its operation, the device may only be used by qualified, specialist personnel.

2.2.1 Provider

The term “provider” applies to all persons who are responsible for making the device and the necessary infrastructure available. These persons may also be included in the group of people known as “users”, though this is not always the case.

Irrespective of whether a provider is a member of the company’s board of management or a supervisor, they bear a special level of responsibility with regard to the processes and the qualification and safety of the users.

2.2.2 User

General

The term “user” applies to all persons who come into contact with the device in any way and perform work on or with it. This primarily applies to the following activities, which can be performed by the manufacturer’s own specialists or a variety of other persons (it is not always possible to distinguish clearly between the different types of person):

- Assembly, installation and commissioning
- Definition and preparation of the process
- Operation
- Troubleshooting and remedying of faults
- Maintenance and cleaning (autoclaving, if necessary)
- Service work and repairs

- Disassembly, disposal and recycling

Qualified personnel

On account of their specific education, training and – in many cases – experience, the qualified personnel required for this work are able to recognise risks and respond accordingly to potential hazards.

The qualified personnel (either internal or external) who cannot be categorised under the separate “operators” group are made up of the following groups of persons:

- Electricians (electrical engineers)
- Decontamination specialists
- Repair specialists
- Specialists in disassembly and (environmentally friendly) disposal
- Recycling specialists

2.2.3 Operator

The “operators” are a specific sub-group of users distinguished by the fact that they work with the device. They are the true target audience for this operating manual.

Qualified technicians

Only technicians who have been trained for working in a biotechnology laboratory can be considered for the role of operator. These include:

- Process technicians in the fields of biotechnology and chemistry
- Biotechnologists (biotechnicians)
- Chemists with a specialisation in biochemistry; chemists in the field of organic chemistry or biochemistry
- Life scientists (biologists) with special education in cytology, bacteriology, molecular biology, genetics, etc.
- Lab assistants (lab technicians) from various fields

In order to be classed as a “sufficiently qualified technician” for the operation of the device, the persons in question must have received thorough training and have read and understood the operating manual.

The operator must be informed in a training session provided by the provider of the tasks delegated to the operator and the

potential risks of improper conduct. Tasks that go beyond the scope of operation under normal conditions may only be performed by the operator if this is specified in the manual and the provider has explicitly entrusted said tasks to the operator.

Technicians in training

Persons in this group who are undergoing training or apprenticeships are only permitted to use the device under supervision and in accordance with the instructions of a trained and qualified technician.

2.3 Unauthorised Persons

The term “unauthorised persons” applies to all persons who can access the work area but are not qualified to use the device in accordance with the aforementioned requirements.

Unauthorised persons are not permitted to operate the device or use it in any other way.

2.4 Responsibility of the Provider

The device is used for industrial and scientific purposes. As such, the provider of the device is individually liable with regard to the legal requirements relating to occupational health and safety in a biotechnology laboratory. In particular:

- The provider is responsible for ensuring that the work and environmental regulations applicable in a biotechnology laboratory are observed.
- The provider must ensure that the device remains in safe and proper working condition throughout its entire term of use.
- The provider must ensure that all safety equipment is fully functional and is not disabled.
- The provider must ensure that the device is only worked on by qualified users, and that said users receive sufficient training.
- The provider must ensure that the protective equipment required for working with the device is provided and worn.
- The provider must ensure that this operating manual remains in the immediate vicinity of the device throughout its entire term of use.

2.5 General Hazards

This section covers general hazards and residual risks that are always present when using the device in accordance with normal, intended use.

The following notices are general in nature. As such, with a few exceptions they are not repeated in the remaining sections.

2.5.1 Electrical Current

The device runs on electrical power. There is an immediate risk of fatal injury if contact is made with live parts.

The following points must be observed in order to avoid the risk of fatal injury:

- In case of damage to insulation, disconnect the device from the power supply immediately and arrange for it to be repaired.
- Disconnect the device from the power supply before commencing any work on the electrical system.
- Always use qualified electricians for any work on the electrical system.
- Keep moisture away from live parts. It may lead to a short circuit.

2.5.2 Unauthorised Spare Parts and Accessories

Incorrect or imitated spare parts and accessories as well as spare parts or accessories that have not been authorised by the manufacturer represent a significant safety risk. As such, we recommend procuring all spare parts and accessories from an authorised dealer or directly from the manufacturer. For the contact details of the manufacturer's representatives, see page 2.

2.6 Particular Hazards

This section covers particular hazards and residual risks that may arise when using the device for special applications in accordance with normal, intended use.

Since the use of the device for such applications is deliberate, it is the responsibility of the operators and the provider to ensure that all personnel are protected from potential damage to health. The

provider is responsible for ensuring that the appropriate protective equipment for such applications is provided, and that the necessary infrastructure is in place.

2.6.1 Hot Surfaces

In operational state with active tempering, there is a danger of burns on hot surfaces.
Since applications at high temperatures are intentional, it is the responsibility of the users to ensure that they have sufficient protection.

The motor gets hot during operation. There is a risk of burns if it is touched.

2.6.2 Dangerous Gases

The use or production of dangerous gases i.e. toxic or asphyxiant gases entails a significant health risk, especially in enclosed spaces.

In order to prevent high emissions of dangerous gases, the following measures must be taken:

- The gas connections on the device must be checked before any cultivation processes using dangerous gases are initiated.
- The gaskets on the device must be checked at regular intervals and replaced if necessary.
- Siphon off exit gas safely.

2.6.3 Flammable or Explosive Substances

The use or production of flammable or explosive substances is not covered under “intended use” of the device, as the device is not explosion-proof.

If the provider intends to use the device for such purposes, he must check its suitability for the planned application with the responsible local authorities.

2.6.4 Corrosive or Toxic Substances

The use or production of corrosive or toxic substances entails a significant health risk. As such, special measures must be taken to protect the users for such applications.

Since the device is used deliberately for such applications, it is the responsibility of the users to ensure that they have sufficient protection.

2.6.5 Bioactive Substances or Pathogenic Organisms

The use or production of bioactive substances, pathogenic organisms or genetically modified cultures entails a significant health risk. As such, special measures must be taken to protect the users for such applications.

Since the device is used deliberately for such applications, it is the responsibility of the users to ensure that they have sufficient protection.

2.6.6 Overpressure or Vacuum

The operating pressure range specified on the vessel identification plate must be adhered to.

When carrying out manipulations on the vessel, it has to be considered that the vessel may be under pressure or vacuum.

The correct inlet pressures and the correct pressure settings of the pressure reducing valves must be ensured at all times.

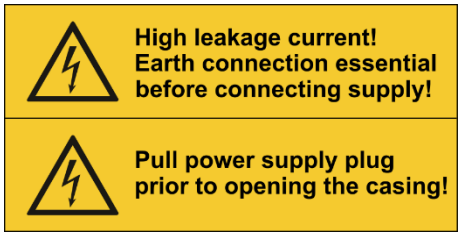
2.6.7 Steam

The escape of steam can lead to severe scalding and burns!

All steam-carrying components must be checked for signs of damage and for correct position before use.

2.7 Warning Symbols on the Device

The following warning symbols (stickers) are attached to the device:



Position

Instrumentation cabinet

Meaning

- Danger of high leakage current. It is mandatory to establish earth connection before connecting the device to the power supply!
- Danger of electrical current. Switch off the device and pull the power supply plug before opening the cabinet.

Position

- Vessel
- Heating element (temperature control system)

Meaning

Caution, risk of being burned due to hot surfaces!

WARNING

Illegible or missing warning symbols on the device will lead to the user being exposed to risks that the warning symbols in question were designed to make him or her aware of.

It is the provider's responsibility to ensure that all the stickers with warning symbols on the device are always intact.

2.8 Declaration of Decontamination

When returning the device for repair, disassembly or disposal, it is required for the safety of all parties involved and because of legal provisions that a lawful declaration of decontamination is present.

The following must be observed if this is the case:

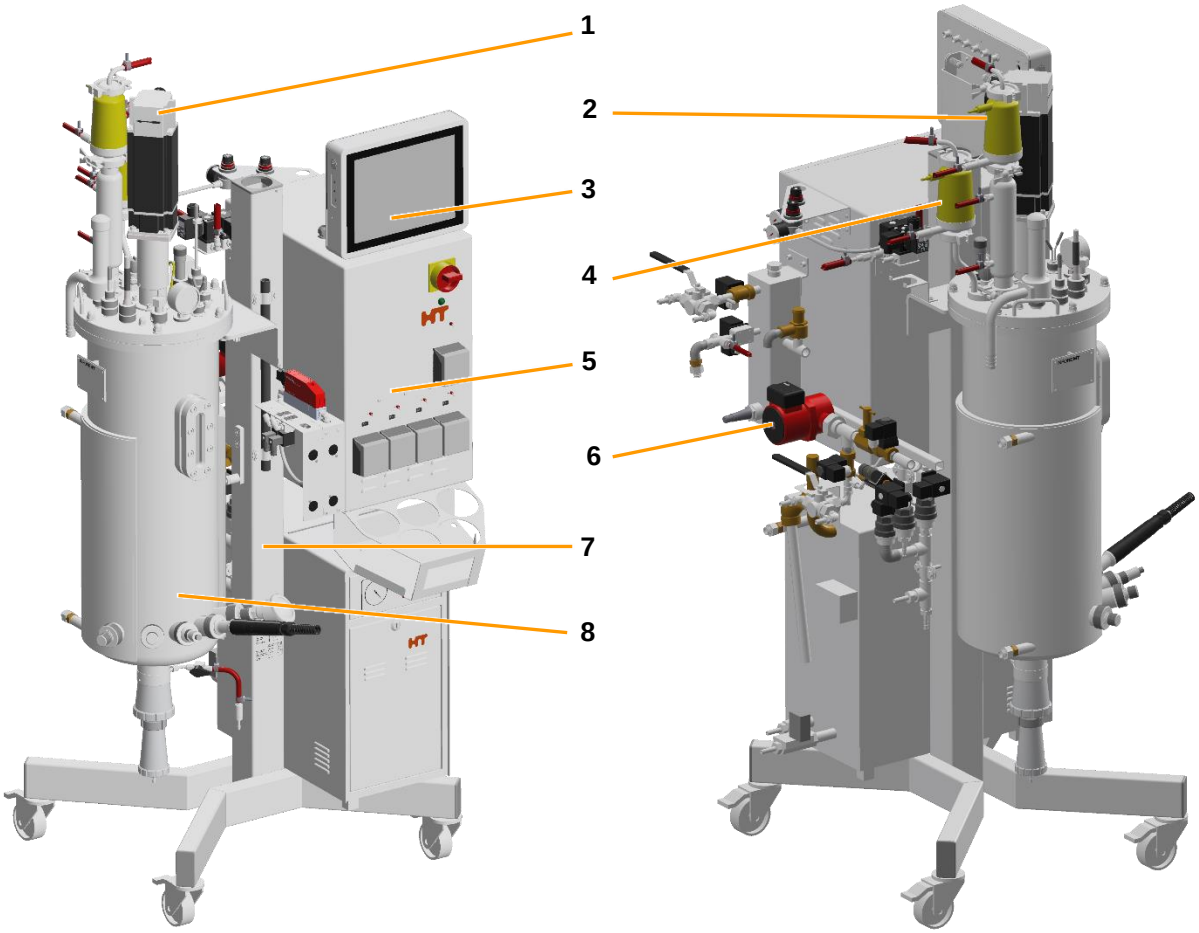
- The device, the component part or accessory must be entirely decontaminated before sending to the manufacturer
- The provider is therefore required to completely and truthfully fill out a declaration of decontamination, and have it signed by the person responsible.
- **The declaration of decontamination must be affixed on the outer packaging in which the device is sent back.**
- These forms can be obtained from the licensed dealer or the manufacturer. See address on page 2.

Important notice

If the return shipment is not accompanied by a signed and complete declaration of decontamination or it is not affixed to the outer packaging, the shipment will be returned unopened to the sender at their expense (see also T&C).

3 Setup and Function

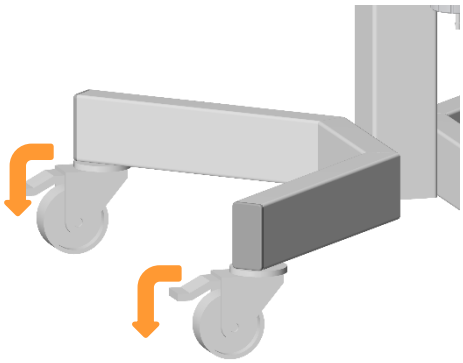
3.1 Basic Unit



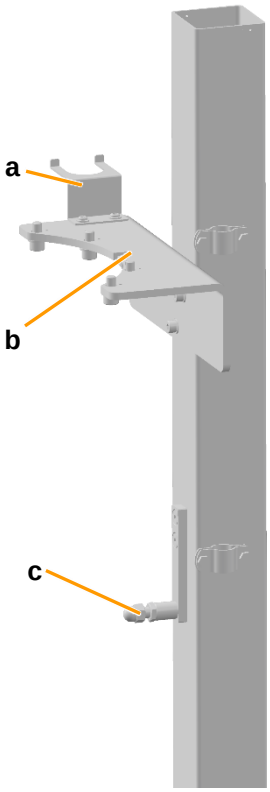
1	Motor (stirrer)	5	Instrumentation cabinet
2	Exit gas filter (exit gas system)	6	Circulation pump (temperature control system)
3	Operating panel	7	Central column
4	Inlet air filter (gassing system)	8	Vessel

The basic unit consists of the central column with support, instrumentation cabinet and operating panel, vessel, temperature control system, stirrer and gassing/exit gas system. Measurement and control systems for pH and pO_2 as well as antifoam are also included as standard.

Setup and Function



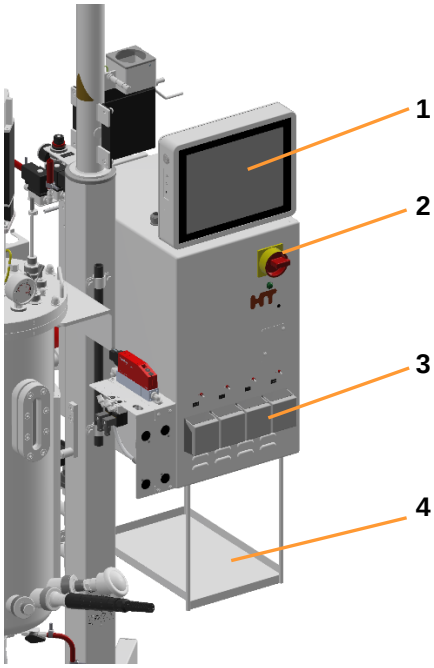
The support features four swivel castors with brakes. The brakes must be locked.



The vessel mounting (b) is installed on the central column. It contains a holder (a) for hanging the exit gas cooler, e.g. when performing preparatory work on the vessel. A spacer (c) for the vessel is also provided on the central column.

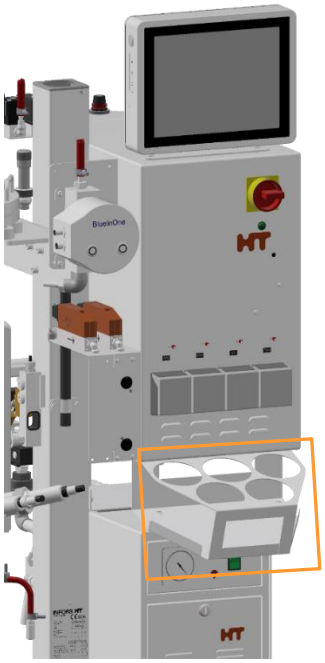
On devices with weighing system for the vessel, the vessel mounting and the holder for the exit gas cooler are integrated into the frame of the weighing system. For details about the weighing system refer to main chapter “Options”, chapter “Weight Measurement – Weighing System”.

3.2 Instrumentation Cabinet



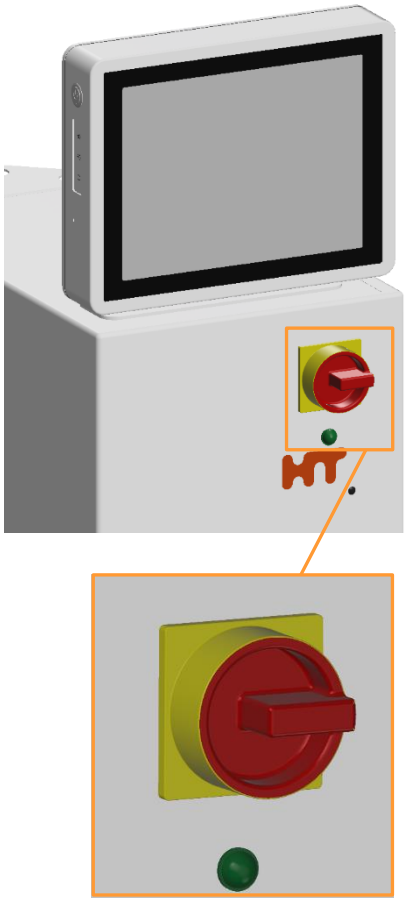
1 Operating panel
2 Main switch
3 Peristaltic pumps
4 Shelf for reagent bottles

The instrumentation cabinet is attached to the right-hand side of the central column. It contains the entire measurement and control system. A shelf for the reagent bottles is attached to the underside of the instrumentation cabinet.



For devices with integrated steam generator, a holder for the reagent bottles is attached to the instrumentation cabinet.

3.2.1 Main Switch



The red main switch is located at the top right of the front panel of the instrumentation cabinet.

TO SWITCH ON

Turn the main switch clockwise (quarter turn) in position **I/ON** and the green power indicatior light is illuminated.
The device is switched on and in the idle state.

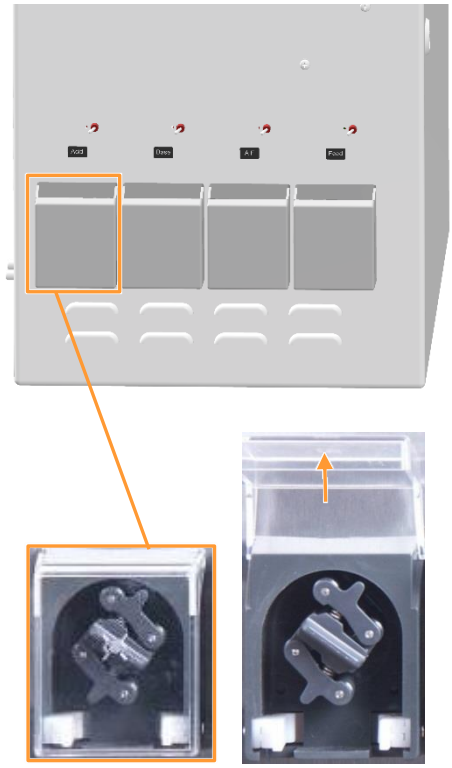
TO SWITCH OFF

Turn the main switch counter-clockwise (quarter turn) in position **0/OFF.**
The device is disconnected from the power supply. Only the mains supply feed is still electrified.
If necessary, secure the main switch against re-starting using a lock (not provided) and additionally unplug the power cable when starting maintenance work.

ATTENTION

Switching the device off at the main switch without previously stopping the bioreactor and shutting down the system on the operating panel may lead to damage of the operating panel!

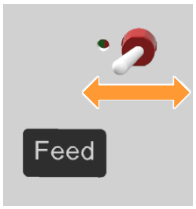
3.2.2 Pumps



Four peristaltic pumps with hinged cover are located as standard in the lower area of the instrumentation cabinet. The pumps are driven by stepper motors and direction of rotation is clockwise in automatic running mode.
The pumps are labelled according their function:

- Acid
- Base
- Antifoam
- Feed

Optionally, two further feed pumps can be integrated.



The pumps can be manually operated (forward and reverse flow) using the rocker switches above each pump head, provided that the device is switched on.

- Push and hold the rocker switch to the right: the pump drive shafts turns clockwise.
- Push and hold the rocker switch to the left: the pump drive shaft turns counter-clockwise.

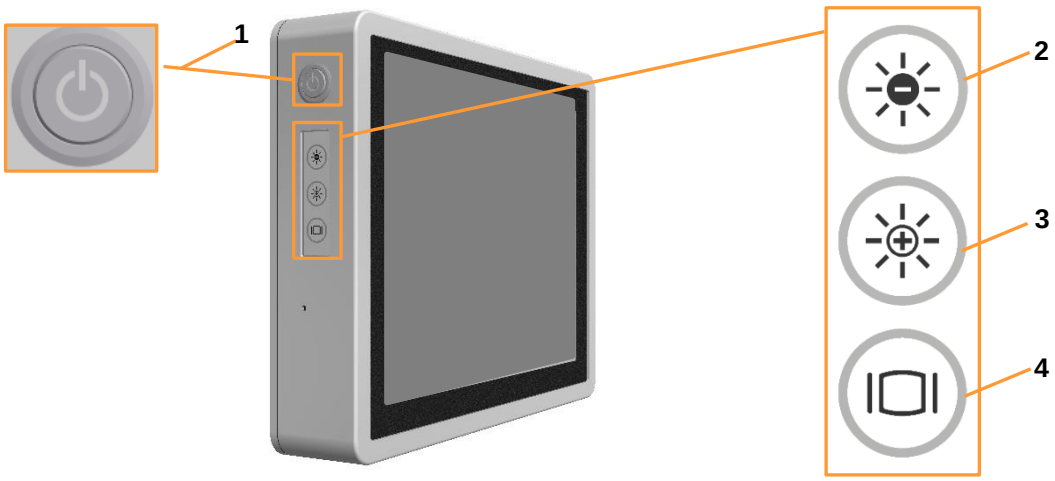
Filling and emptying the pump hoses is also possible via touch screen software. For details see main chapter “Operation Touch Screen Software”, chapter “Filling and Emptying Pump Hoses”.

3.3 Operating Panel

The operating panel is mounted on the instrumentation cabinet with a vertically swivelling bracket. It has a 12" colour-touch screen with protection IP66. The operating panel is switched on at the main switch.

3.3.1 Monitor Keys

Four monitor keys are situated on the upper left side of the touch screen operating panel.



1 **ON/OFF** key

2 **DECREASE** brightness key: to set the display illumination darker

3 **INCREASE** brightness key: to set the display illumination brighter

4 **DISPLAY** key: to switch the display on/off

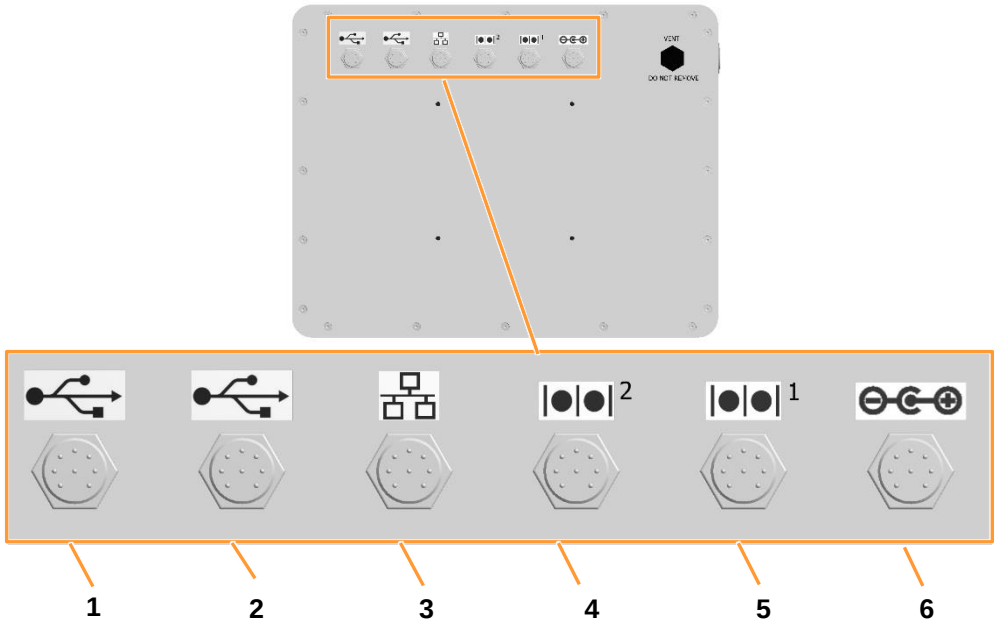
Special details about the ON/OFF key

The touch screen operating panel is switched on and off at the main switch on the instrumentation cabinet. Therefore, separate switching on at the **ON/OFF** key is not necessary. The symbol on the key is illuminated when the operating panel is switched on.

Switching the operating panel off during a running process is the equivalent to a power failure!

3.3.2 Operating Panel Connections

Six connectors labelled with different symbols are situated on the rear side of the operating panel.



1 USB2.0 x 2: for backups and service purposes [1)]

2 USB2.0 x 2: (Reserve)

3 Ethernet: for Ethernet cable [1)] to connect with a network

4 COM2 (Reserve)

5 COM1: for iDDC bus cable [1)] (display cable), connector is labelled with RS485 additionally

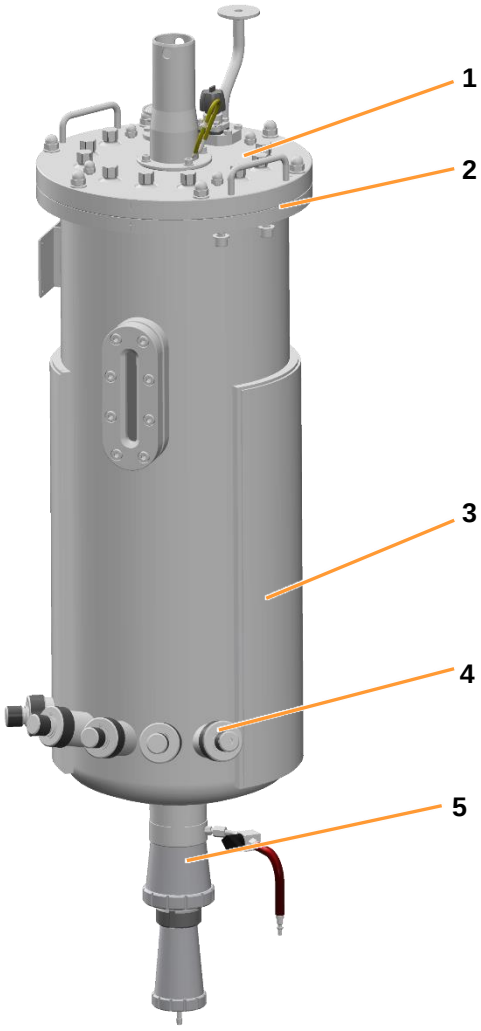
6 DC: for power supply cable [1)]

[1)] *Cable supplied with device*

3.4 Vessel

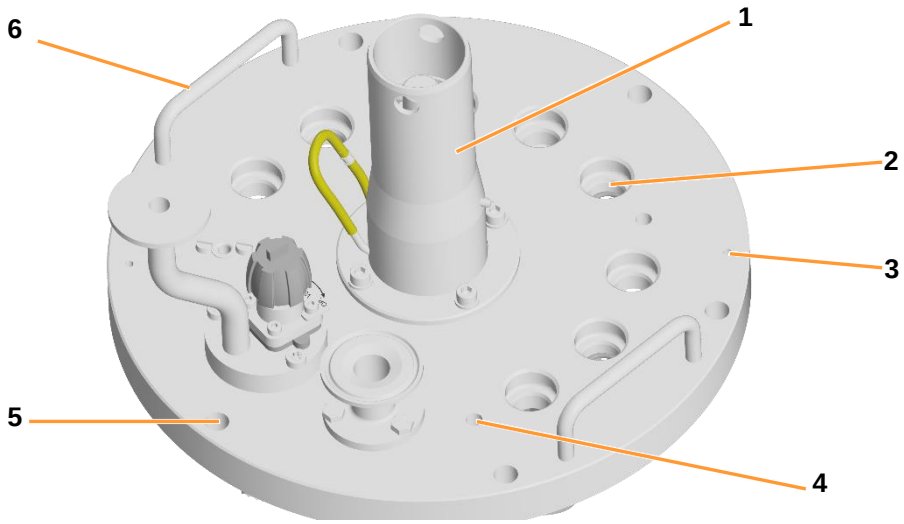
The pilot scale bioreactor Techfors-S is available in three vessel sizes: 15, 30 and 42 litre total volume. The only difference between the vessels is the number of ports and the tpye of harvest/sample valve (bottom valve)

1 Vessel top plate
2 Vessel flange
3 Vessel jacket
4 Ingold nozzle
5 Harvest/sample valve (bottom valve)



The vessel and all components in contact with medium are made of stainless steel 316L. The standard features of the three vessel sizes is described in the following chapters.

3.4.1 Vessel Top Plate



1 Drive hub for motor

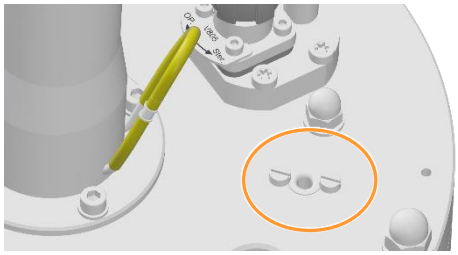
2 19 mm port (8 or 9 pc.) for built-in-parts/accessories such as safety valve, antifoam sensor, manometer, vessel light, inoculation needle(s), push valve(s) etc.

3 4 mm drill hole (2 pc.) for ground connection of antifoam sensor

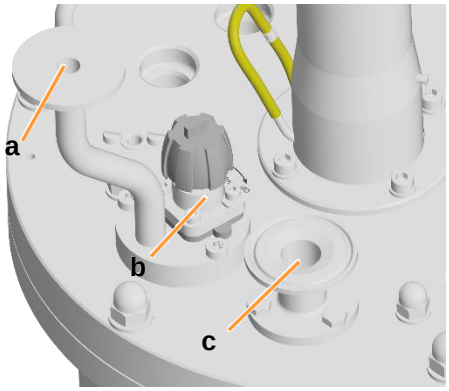
4 Threaded holes (4 pc.) for baffles

5 Threaded holes (6 pc.) for affixing the top plate

6 Handle (2 pc.)



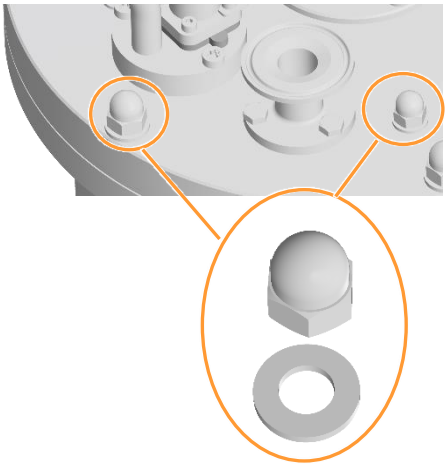
Immersion pocket for temperature sensor (Pt100)
15 L TV and 30 L TV: these feature an additional 10 mm port with immersion pocket for the temperature sensor (Pt100).



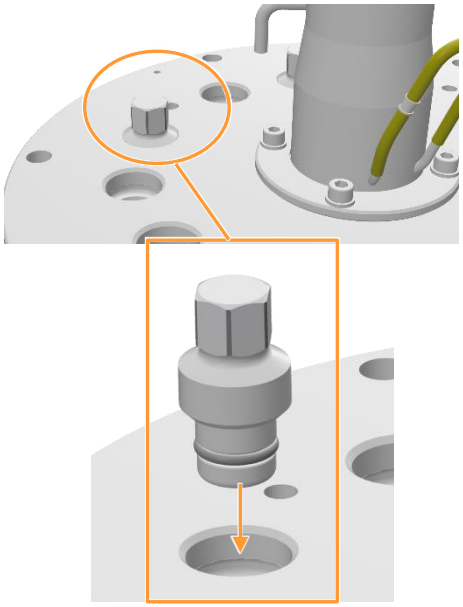
Connection flange (Tri-Clamp) inlet air and exit gas
Connection flanges for inlet air (a) with diaphragm valve **02.16.01** (b) and for exit gas (c) are located on the vessel top plate.

Setup and Function

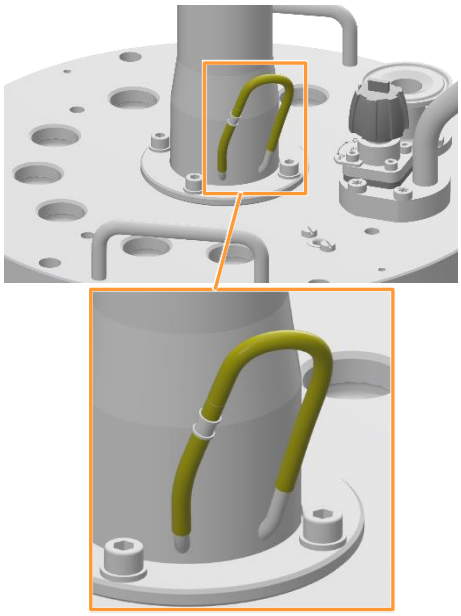
The vessel top plate also features:



- 4 cap nuts M8 with metal washers for affixing the baffles
- 6 cap nuts M10 with metal washers for affixing the top plate

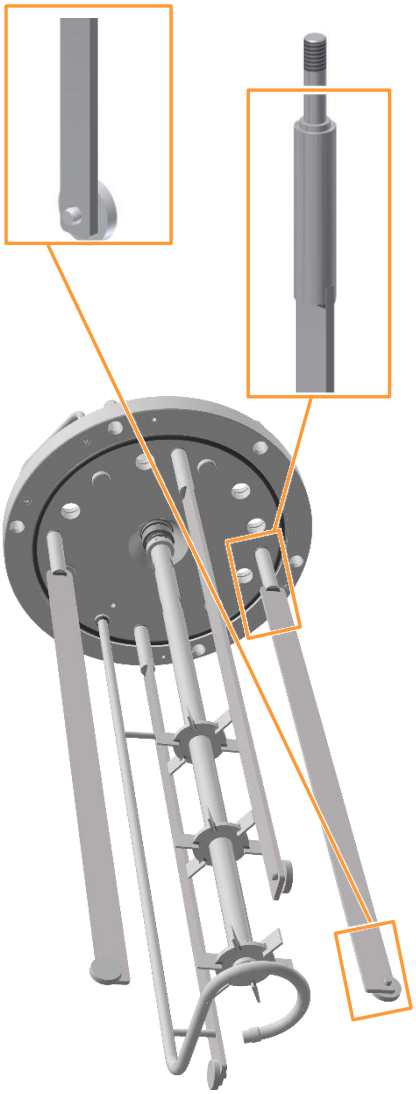


- Blanking plug with fixed O-rings for 19 mm ports



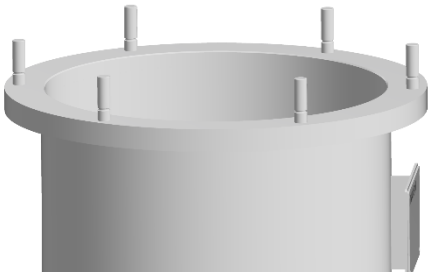
- Connection nozzle and silicone hose for lubricating the mechanical seal

- O-ring (top plate seal)



- Stirrer shaft and 2 or 3 Rushton impellers; see the chapter “Stirrer” for details.
- Ring sparger and 4 baffles with holder and spacers. A baffle is permanently connected to the sparger; for details, see the chapter “Gassing System, Gas Entry”.

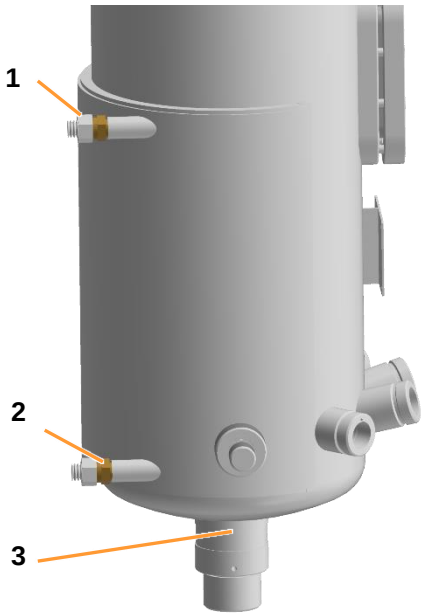
3.4.2 Vessel Flange



The vessel flange has six flat studs for affixing the vessel top plate.

3.4.3 Vessel Jacket and Bottom

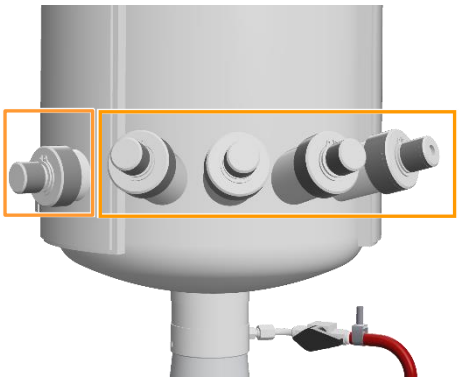
The medium in the vessel is tempered using the water circulating in the vessel jacket. Depending on the temperature control system, the water is heated electrically or with steam. For details, see the chapter “Temperature Control System and Sterilisation”.



1 Water outlet
2 Water inlet
3 Connection nozzle for harvest/sample valve

The harvest/sample valve (bottom valve) **05.12.01**) as well as the pressure hoses for the water inlet and water outlet of the vessel jacket are pre-installed ex-factory. A manometer permanently installed ex-factory at the water outlet of the vessel jacket indicates the pressure in the temperature control system.

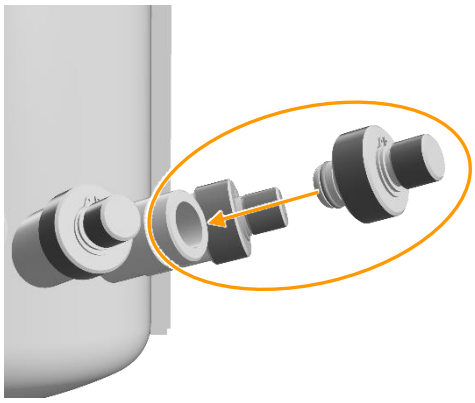
3.4.4 Ingold Nozzles



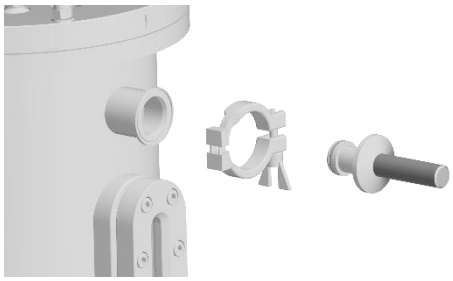
The Ingold nozzles are readily accessible on the lower part of the front side of the vessel. The number of Ingold nozzles varies depending on the vessel size, see table below.

Vessel TV (total volume)	Number of Ingold nozzles, iD = 25 mm, G G1-1/4"	
	horizontal	angled (15°)
15 L	1	2
30 L	1	3
42 L (picture)	1	4

The angled nozzles are used for pH and pO_2 sensors by default. The temperature sensor for 42 L vessels is also mounted in one of these nozzles. The horizontal nozzle serves as reserve or is used for the (optional) sample valve **17.13.01**.



Each Ingold nozzle has a blanking plug with fixed O-ring.

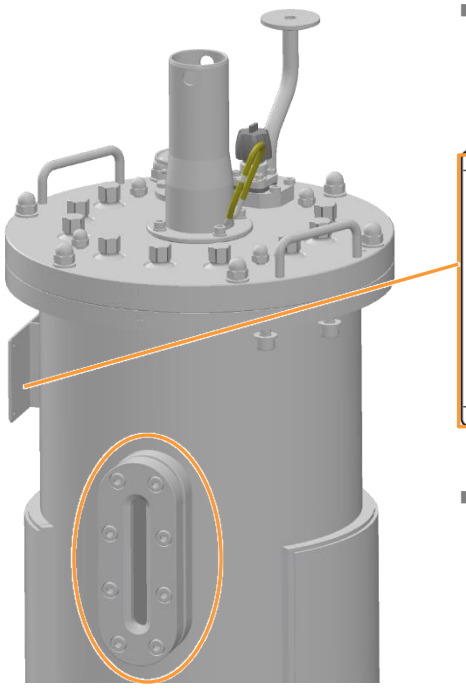


INFORMATION

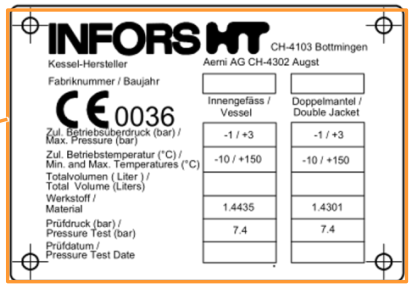
If the device is to be used together with the (optional) mobile CIP unit of the device manufacturer, an adapted vessel design is required for this. In this case, the vessel has two additional Tri-clamp ports with blanking plugs in the upper vessel section

3.4.5 Vessel Identification Plate and Sight Glass

Each vessel has:



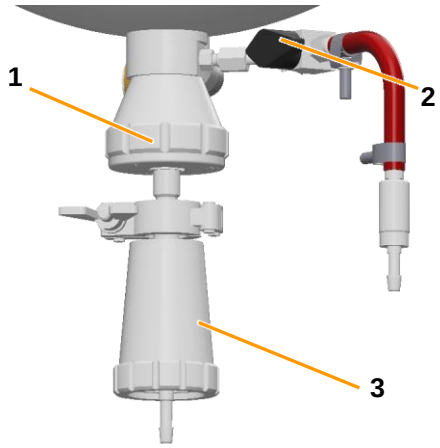
- Vessel identification plate, its content is described in main chapter “General Information”, chapter “Vessel Identification Plate”.



- Sight glass (middle of the sight glass = working volume)

3.5 Harvest/Sample Valve (Bottom Valve)

The combined harvest/sample valve (bottom valve) **05.12.01** is pre-installed ex-factory in the connection nozzle on the vessel bottom. The steam trap and clean steam line (pressure hose) are also pre-installed with manual valve **05.10.01**. The type of valve varies depending on the vessel size.

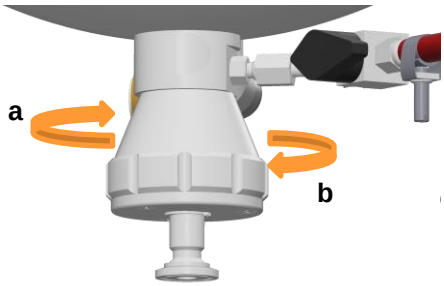


Valve type for 15 L and 30 L TV

1 Harvest/sample valve**05.12.01**

2 Clean steam valve (valve **05.10.01**) with steam line (pressure hose)

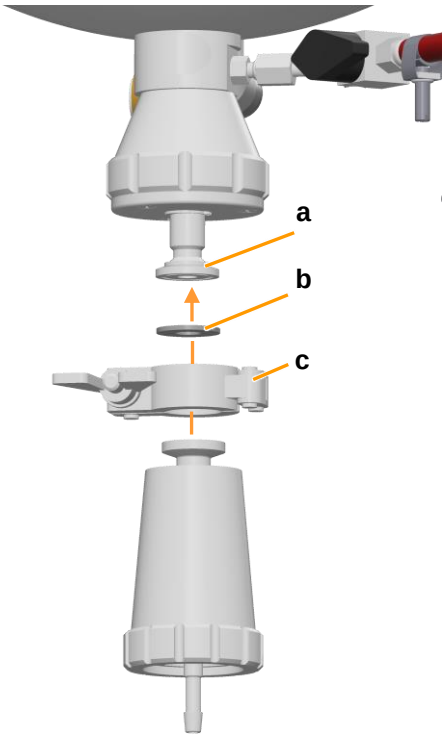
3 Steam trap



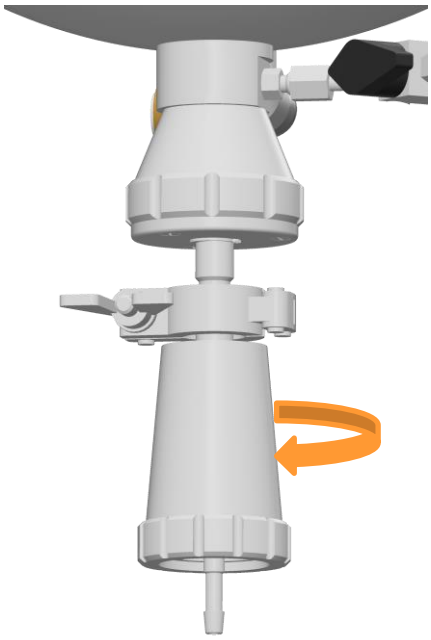
The harvest/sample valve is opened and closed manually:

- Open the valve: turn clockwise (a).
- Close the valve: turn counter-clockwise (b).

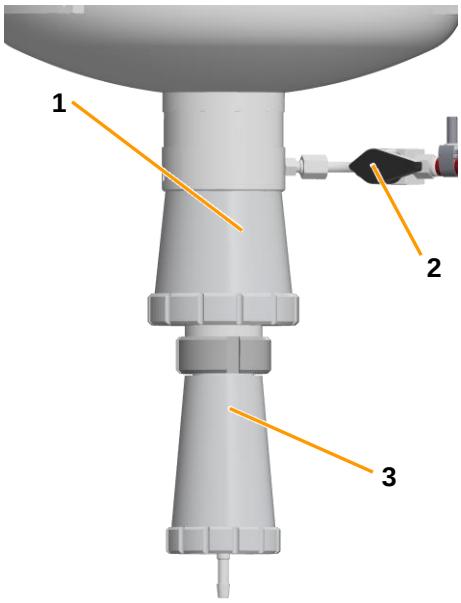
Setup and Function



The steam trap for sterilisation is affixed to the connection flange (a) of the harvest/sample valve with a clamp (c) and a flat gasket (b).



For sampling, the steam trap is unscrewed from the needle by turning it counter-clockwise.

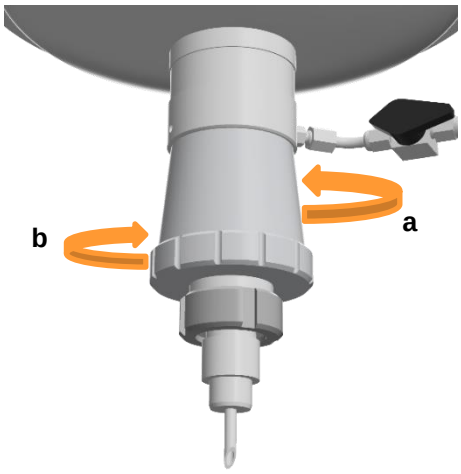


Valve type for 42 L TV

1 Harvest/sample valve **05.12.01**

2 Clean steam valve (valve **05.10.01**) with steam line (pressure hose)

3 Steam trap

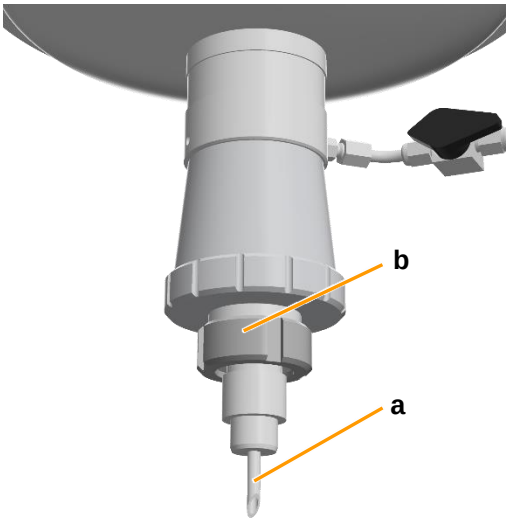


The harvest/sample valve is opened and closed manually:

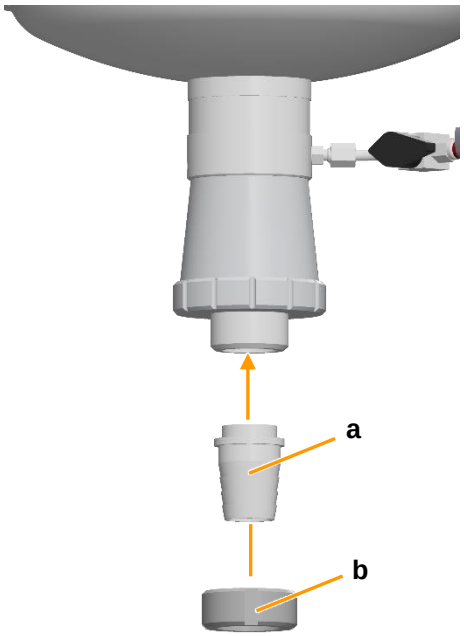
- Open the valve: turn counter-clockwise (a).
- Close the valve: turn clockwise (b).

Setup and Function

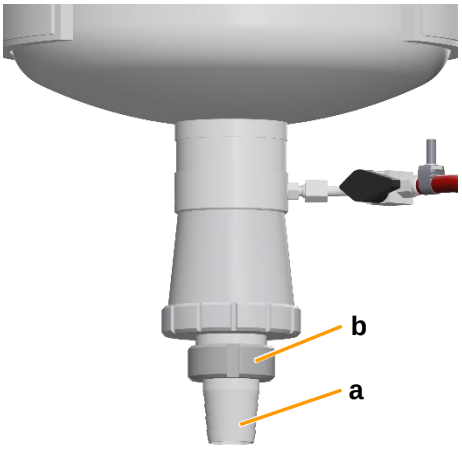
This valve type has a valve insert with a needle (a) for sampling. The valve insert is placed in the harvest/sample valve and affixed using a groove nut (b).



The steam trap for sterilisation is screwed clockwise onto the valve insert.



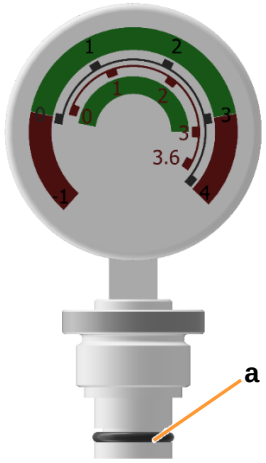
To harvest/drain, a valve insert with a nozzle (a) is used to connect the hose line provided by the operator. This is also affixed using the groove nut (b).



The sterilisation of the harvest/sample valve is started via the touch screen software on the operating panel. For details, see the main chapter “Operation Touch Screen Software”.

Sampling and harvest/emptying are described in the chapters “Sampling” and “Harvest/Emptying” of the main chapter “Cultivation”.

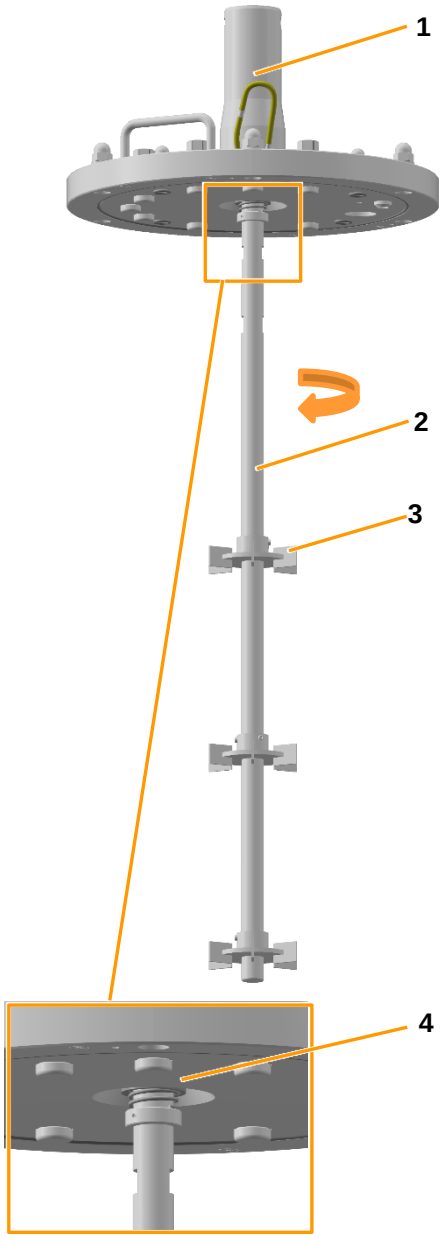
3.6 Vessel Pressure Display (Manometer)



The maximum permissible vessel pressure is 3.0 bar. Manometer **08.30.01** indicates the pressure in the vessel in a range from 0 – 4.0 bar. The manometer has two different measuring scales. The outer scale corresponds to the pressure at a vessel temperature of 25 °C. The inner scale corresponds to the pressure at a vessel temperature of 121 °C. Two red markings indicate the non-permissible pressure range of the vessel.

The manometer comes with an O-ring (a) and is mounted in a 19 mm port in the top plate. For details, see the chapter “Mounting the Manometer” in the main chapter “Before Cultivation”.

3.7 Stirrer



1 Drive hub
2 Stirrer shaft
3 Impeller
4 Mechanical seal

The stirrer shaft is driven from above and turns clockwise (right / top view). The stirrer shaft is screwed onto the drive hub in the top plate and sealed using a simple mechanical seal.

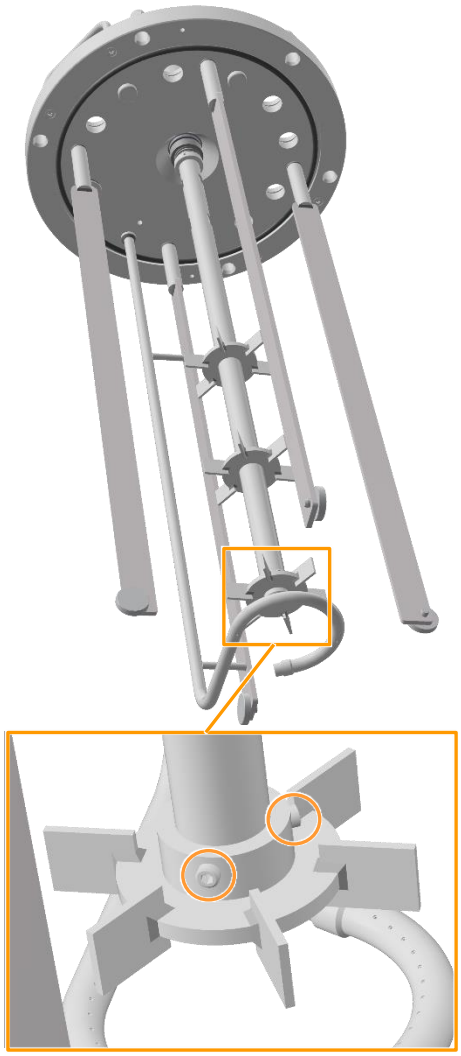
ATTENTION

Manipulations on the mechanical seal can damage it.

The mechanical seal must always be lubricated. For this purpose, there are two connection nozzles with a silicone hose on the drive hub.

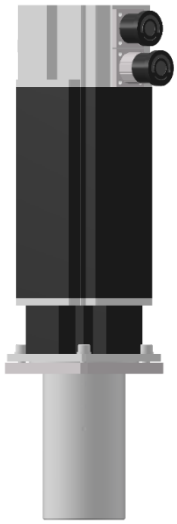
For details on lubrication, see the chapter “Lubricating a Mechanical Seal” in the main chapter “Cleaning and Maintenance”.

3.7.1 Impellers

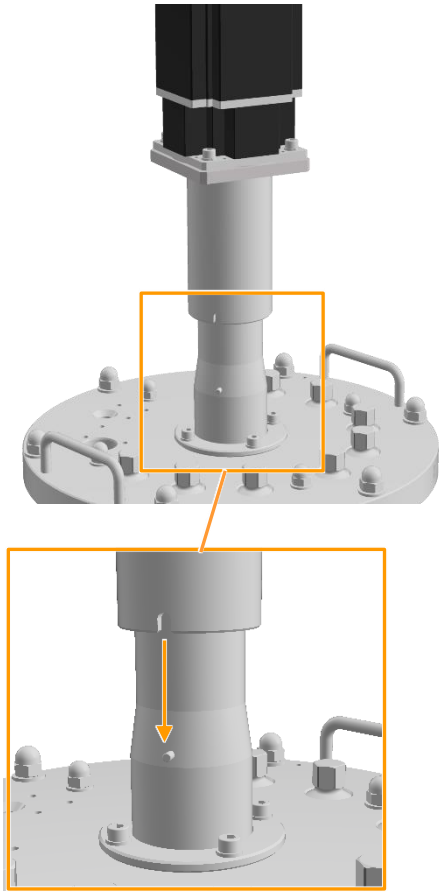


Depending on the vessel size, two (15 l TV) or three (30 l and 42 l TV) Rushton impellers are fixed to the stirrer shaft by means of grub screws.

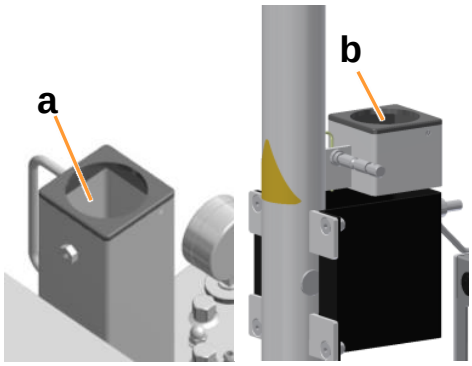
3.7.2 Motor



An air-cooled servo motor is used as the motor.



It is coupled by plugging it on the drive hub on the vessel top plate. For this, the groove on the motor must be aligned with the pin on the drive hub. This locks the motor into its position.

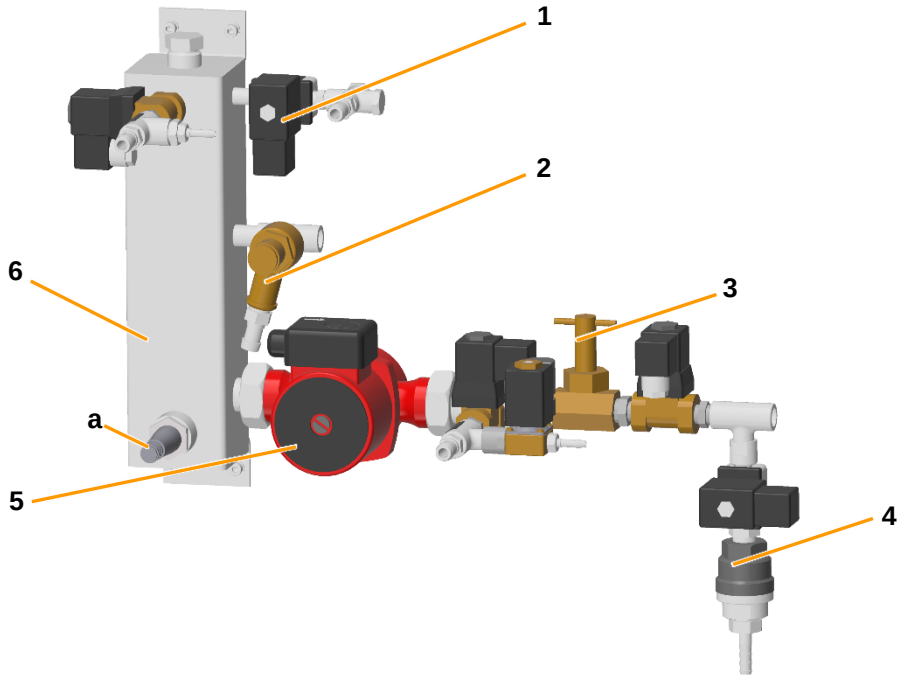


After uncoupling, the motor can be placed into the designated opening at the top of the central column (a).

When using the (optional) lifting device for the vessel top plate, the motor is inserted into the holder (b) on the lifting device.

3.8 Temperature Control System and Sterilisation

The temperature control system consists of a heating element and a circulation pump, which ensures circulation of the heating/cooling liquid in the vessel jacket. The figure below shows the temperature control system with electric heating as an example.



1 Solenoid valve (**01.06.03**)
2 Safety valve (**01.08.01**) with hose nozzle (Ø 13 mm)
3 Flow monitor (**01.43.01**)
4 Steam trap (**01.20.01**)
5 Circulation pump (**01.22.01**)
6 Heating element with heating cartridge (a)

Setup and Function

Heating

Depending on the chosen variant of the temperature control system, the heating element either has an electronic heating cartridge or an injection nozzle for direct steam injection.

Cooling

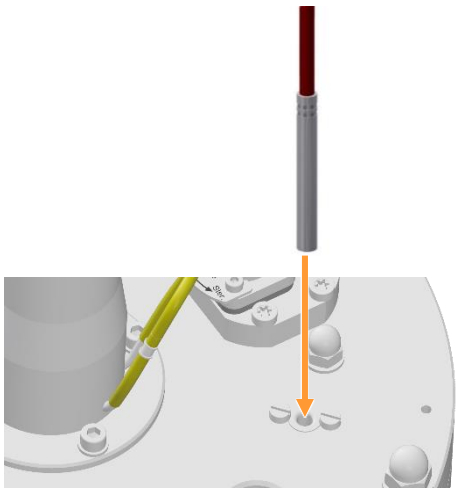
Cooling is effected via tap water or a chilled water system provided by the operator. The water is fed directly into the vessel jacket, or the temperature control circuit.

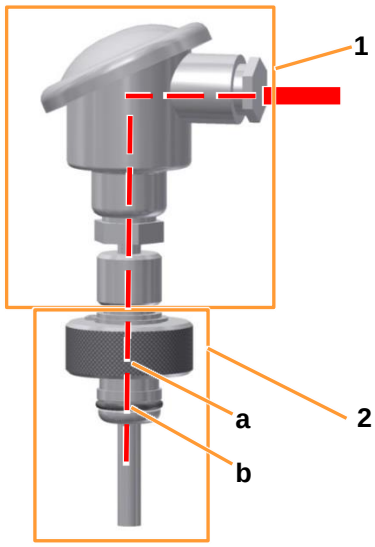
Optional 3-way ball valves on the water inlet and water outlet facilitate manual switching between tap water and chilled water. The ball valves are marked accordingly.

Temperature measurement

The temperature in the vessel is measured using a resistance thermometer (Pt100 sensor).

15 L and 30 L TV: Here, the temperature sensor is inserted into an immersion pocket in the vessel top plate.





42 L TV: Here, the resistance thermometer has a connecting head and screw-in socket for installation in an angled Ingold nozzle on the vessel.

1 Connecting head

2 Screw-in socket with:

a) coupling nut
b) O-ring

An O-ring on the screw-in socket is used as the seal. By screwing the coupling nut onto the screw-in socket, the temperature sensor is affixed in the Ingold nozzle.

Temperature control

Temperature control is effected via solenoid valves in the temperature control circuit. A CE-certified safety valve is used to protect the temperature control circuit from excess overpressure (>3 bar).

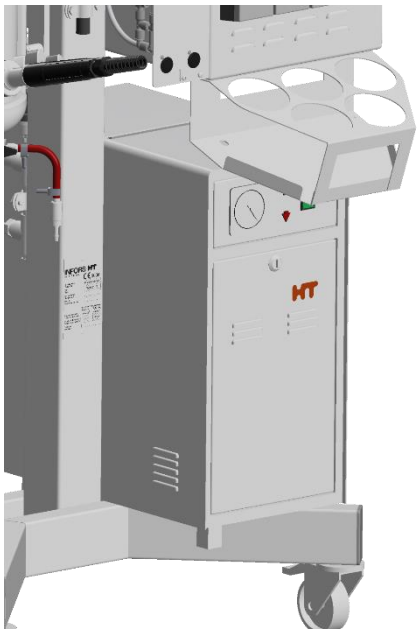
Circuit description: Vessel jacket – heating element – circulation pump – vessel jacket.

Pressure indication

The max. allowed pressure in the temperature control system is 3.0 bar The manometer **01.30.01** indicates the pressure in a range from -1.0 to +4.0 bar. The manometer is permanently pre-installed ex-factory and is located at the water outlet of the vessel jacket.

Sterilisation

The medium to be sterilised in the vessel is heated up and sterilised by feeding steam into the vessel jacket. The steam generated by the liquid in the vessel sterilises the inlet air and exit gas filters at the same time. The entire process is automatic and controlled using the touch screen software.



Steam is fed in either by steam supply provided by the operator or by an optional, integrated steam generator (example in picture on the left).

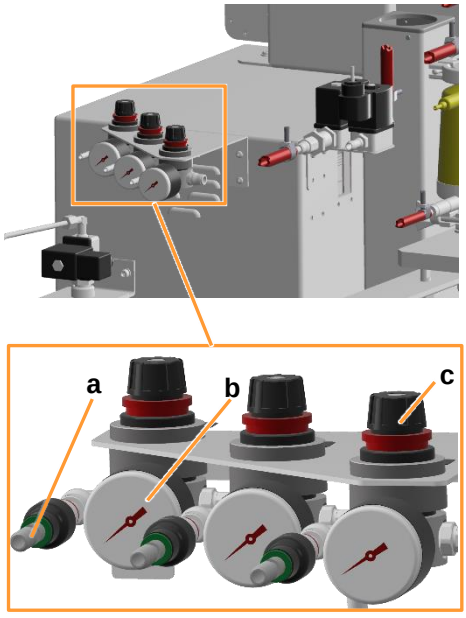
The harvest/sample valve (bottom valve **05.12.01**) is sterilised with clean steam via a separate line from the same steam supply. The same applies to the optional sample valve **17.13.01** and the optional resterilisable feed line.

For details on all sterilisation processes, see main chapter “Operation Touch Screen Software”, chapter “SIP - in Situ Sterilisation” including its subchapters.

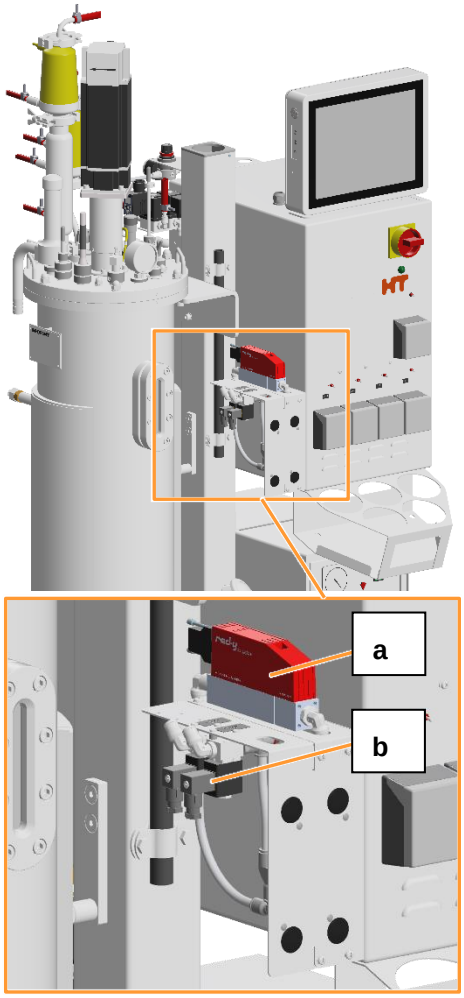
3.9 Gassing System

The following gases can be used:

- Air
- Oxygen (O_2)
- Nitrogen (N_2)

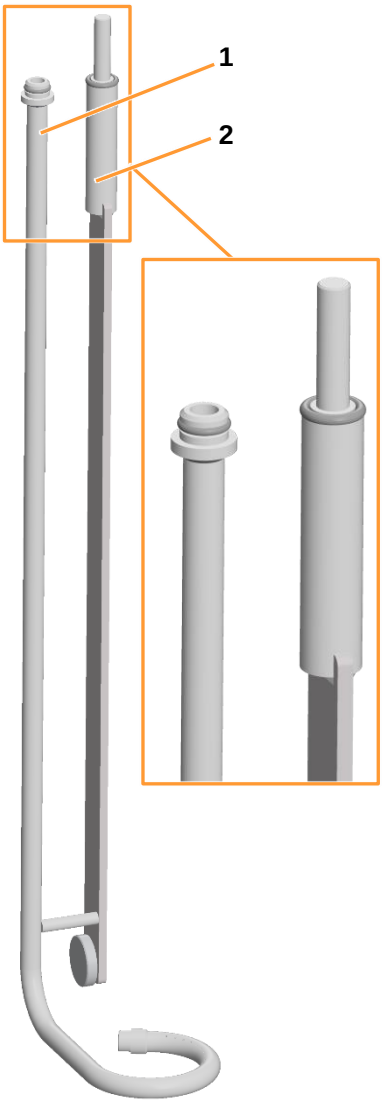


The gas connections are located on the rear of the device and are labelled with the corresponding gas. Each gas connection has a check valve (a), manometer (b) and a pressure reducing valve (c). The number of connections varies depending on the configuration.



Depending on the chosen gassing strategy, the device is fitted and configured with the corresponding gassing units, that is, rotameter, solenoid valve and mass flow controller. The example on the left shows a mass flow controller (a) and two solenoid valves (b).

3.9.1 Gas Entry

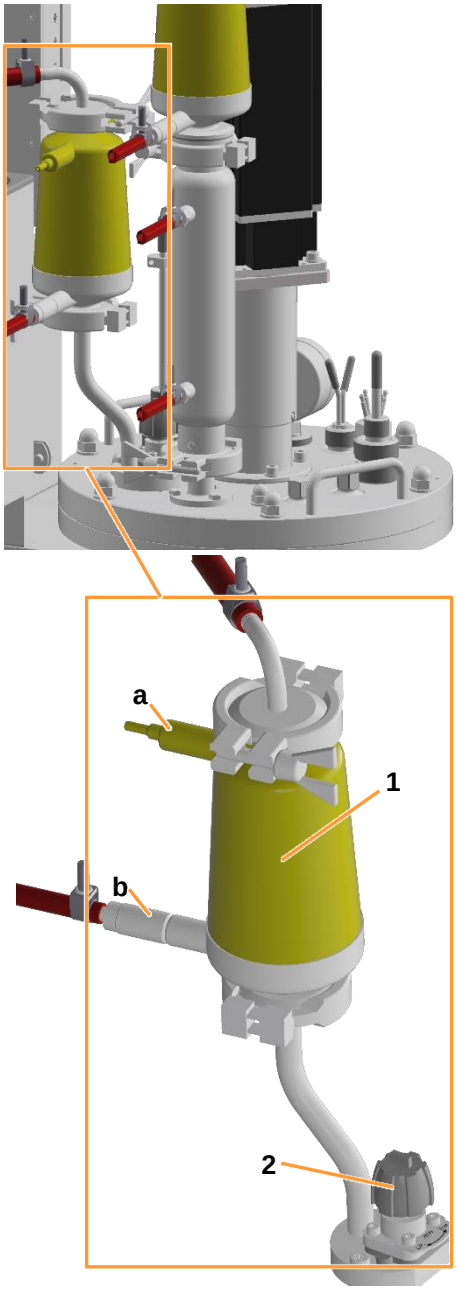


1 Ring sparger

2 Baffle (deflector plate)

Gas enters the vessel via a ring sparger. To stabilise the sparger in the vessel, this is welded to one of the four baffles.
The sparger is fitted with an O-ring at the top end and is installed in the port, where the diaphragm valve **02.16.01** (see next section) is located. The baffle is screwed into the corresponding threaded hole in the vessel top plate and is affixed to the vessel top plate with metal washers and hexagon nuts (M8), like the other three baffles.

3.9.2 Inlet Air Filter and Valve 02.16.01



1 Inlet air filter

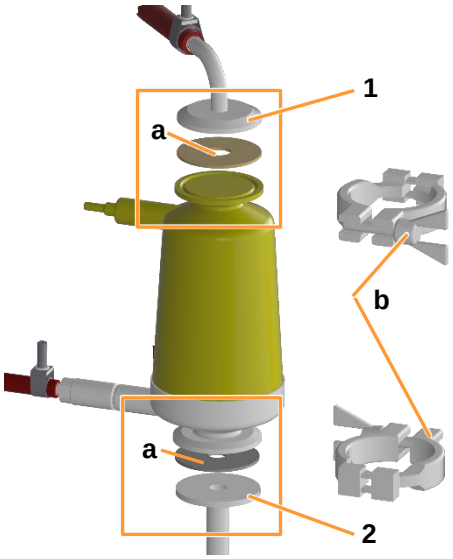
2 Valve **02.16.01**

A membrane filter that can be sterilised using steam is placed in the gassing line. Valve **02.16.01** on the vessel top plate directs the process gas/gas mixture into the sparger during the bioprocess, and air into the head space during the cool-down phase of full sterilisation. The valve is operated manually:

- Position **STER:** Valve position during sterilisation.
- Position **OP:** After finishing the sterilisation and reaching the pre-selected inoculation temperature for the bioprocess, the valve must be returned to position **OP**.

The corresponding instructions are also shown in the respective process sequence in the touch screen software.

The filter has two manual twist valves. The condensate hose is connected to the lower twist valve (b). This valve must be open. The upper twist valve (a) is not used and must be closed.



1 Gassing hose flange

2 Vessel top plate flange

The inlet air filter is connected to the flange on the vessel top plate with a clamp (b) and a flat gasket (a). The same applies to the connection of the gassing hose to the inlet air filter.

3.9.3 Gassing Strategy

The following variants can be selected as the gassing strategy:

Basic

- Manual flow control via rotameter.
- Gasmix via solenoid valves.

Standard

- Flow control via an electronic mass flow controller.
- Gasmix via solenoid valves.

High End

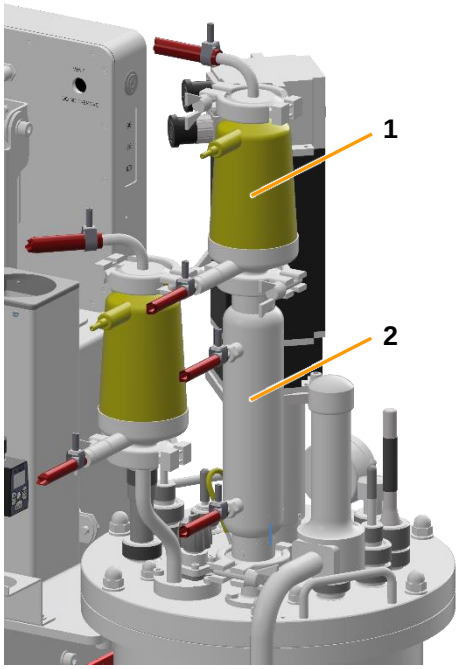
Flow control and Gasmix via electronic mass flow controllers, 1 unit per gas.

3.9.4 Gas Mix System

Several gases are mixed before they are fed into the vessel. The composition of the gas mix is set and controlled using the touch screen software.

A detailed description of the touch screen software is available in the main chapter “Operation Touch Screen Software”.

3.10 Exit Gas



Any cultivation can increase the pressure inside the vessel through heating or gas production, even without active gassing. Hence, an exit gas line must be available for all cultivation processes in a bioreactor.

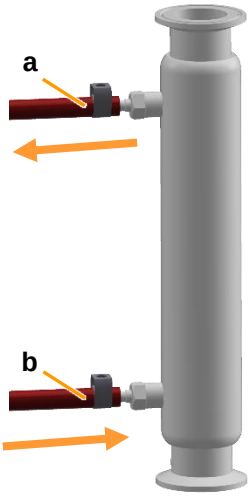
1 Exit gas filter

2 Exit gas cooler

Exit gas streams over the exit gas cooler, exit gas filter and a solenoid valve (**03.06.02**, not pictured) into the atmosphere or into the operator's exit gas line or an appropriate ventilation system.

The pressure in the vessel can be controlled optionally via a pressure control valve (**03.41.01**) in the exit gas line and a pressure sensor on the vessel. For details, see the chapter "Pressure Control" of the main chapter "Options".
It is also possible to analyse the exit gas while the bioprocess is running. For more details, see the chapter "Exit Gas Analysis" of the main chapter "Options".

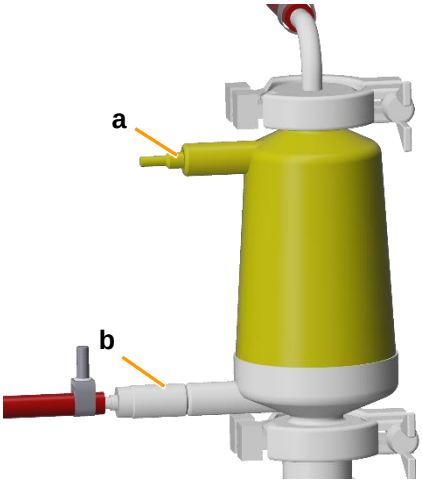
3.10.1 Exit Gas Cooler



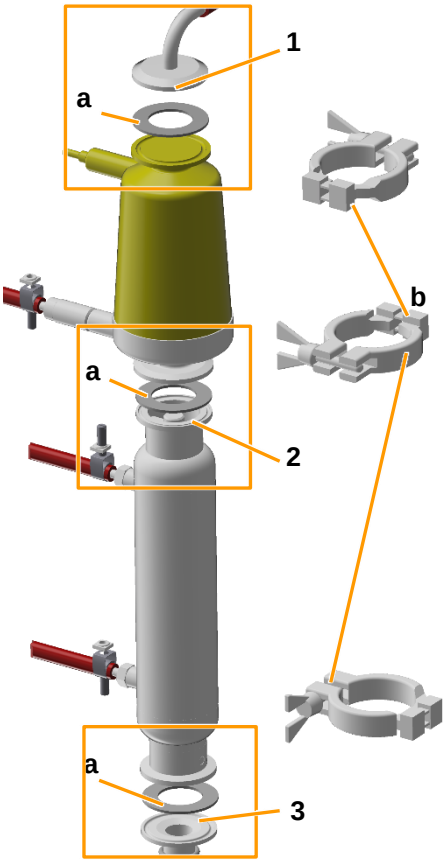
The exit gas cooler dries the exit gas through condensation, thus preventing the exit gas filter from becoming clogged with moisture. At the same time, it also prevents water loss in the culture medium.

The exit gas cooler has pressure hoses for the water inlet (b) and outlet (a). Water is fed in from the supply for the temperature control system; this is done automatically during the bioprocess and the full sterilisation in accordance with the appropriately programmed process sequences.

3.10.2 Exit Gas Filter



A hydrophobic steam sterilisable membrane filter of the type Novasip is used as the exit gas filter. The filter has two manual twist valves. The condensate hose is connected to the lower twist valve (b). This valve must be open. The upper twist valve (a) is not used and must be closed.



1 Exit gas flange

2 Upper exit gas cooler flange

3 Vessel top plate flange

The exit gas filter is connected to the upper flange on the exit gas cooler with a clamp (b) and a flat gasket (a). The same applies to the connection of the exit gas hose on the exit gas filter and the connection of the exit gas cooler to the flange on the vessel top plate.

3.11 pH Control

The pH value in the medium is measured by the pH sensor and controlled by addition of reagents (acid, base). Addition of acid and base takes place via the two peristaltic pumps *Acid* and *Base*.

Reagent bottles filled with acid and base are connected to the pumps and to e.g. resterilisable push valves or inoculation needles which are mounted in 19 mm ports of the vessel top plate.

3.11.1 Measurement System

Depending on the variant selected, the measurement system for pH is equipped and configured for analogue or digital sensors manufactured by METTLER or digital sensors manufactured by HAMILTON.

Variant: METTLER analogue

- Conventional pH sensor (potential measurement against reference)
- Type: 405-DPAS-SC-K8S/120

Variant: METTLER digital

- Conventional pH sensor (potential measurement against reference) with built-in electronics
- Type: InPro 3253i, ISM

Variant: HAMILTON digital

- Conventional pH sensor (potential measurement against reference) with built-in electronics
- Type: Easyferm Plus ARC

INFORMATION

pH sensors type Easyferm Plus ARC are preconfigured by the device manufacturer INFORS HT. Replacement sensors must be configured before use!

For details on the technical data, use, maintenance and storage of the pH sensors, see the separate documentation provided by the sensor manufacturer. Read and follow the instructions.

Calibration

As a general rule: calibration of a pH sensor must be carried out **BEFORE** sterilisation. For details refer to the main chapter “Operation Touch Screen Software”, chapter “pH Sensor Calibration”.

INFORMATION

If the pH sensor has already been calibrated externally, the bioreactor will use this data and there is no need for calibration on the operating panel. This only applies to digital pH sensors.

Mounting

The pH sensor is mounted in to an Ingold nozzle in the vessel. The suitable insertion housings from the sensor’s manufacturers are supplied with the sensors.

For details, see the chapter “Mounting and Connecting a pH Sensor” in the main chapter “Before Cultivation”.

3.12 pO_2 Control

The oxygen saturation of the (culture) medium is measured by the pO_2 sensor, and can be adjusted as follows:

Increasing the pO_2

The content of the oxygen dissolved in the medium (pO_2) can be increased using the following methods:

- Increasing the stirrer speed
- Increasing the gas volume flow rate (air and/or oxygen)
- Increasing the oxygen content in the Gasmix

  These approaches can also be combined

pO_2 reduction

In anaerobic processes, the vessel can be gassed using nitrogen. This displaces the oxygen dissolved in the medium.

For details about pO_2 control (cascades) refer to the main chapter “Operation Touch Screen Software”.

3.12.1 Measurement System

Depending on the variant selected, the measurement system for pO_2 is equipped and configured for analogue or digital sensors manufactured by METTLER or digital sensors manufactured by HAMILTON.

Variant: METTLER analogue

- Conventional, amperometric/polarographic pO_2 sensor
- Type: InPro 6820/25/080

Polarographic pO_2 sensors must be polarised for initial operation or after they have been disconnected from the power source.

Variant: METTLER digital

- pO_2 sensor with integrated opto-electronics
- Type: InPro6860i, ISM, choice of:
  - Classic, with Opto-Cap, straight
  - HD, with Opto-Cap angled, with “Anti-Bubble” technology low-noise measurement signal.

Variant: HAMILTON digital

- pO_2 sensor with integrated opto-electronics
- Type: Visiferm DO ARC, choice of:
  - ODO-Cap H0, straight, standard applications
  - ODO-Cap H2, convex, more robust, slightly longer response time.

INFORMATION

Digital pO_2 sensors are preconfigured by the device manufacturer INFORS HT. Replacement sensors must be configured before use.

For details on the technical data, maintenance and storage of the pO_2 sensors, see the separate documentation provided by the sensor manufacturer. Read and follow the instructions.

Measurement und calibration

Generally speaking, the following applies: Unlike measurements such as pH, which are calibrated to absolute measurement values, the oxygen measurement is always calibrated to a relative reference point. For this purpose, the calibration is set to 100 % relative oxygen saturation, usually with air at max. stirring speed and

maximum gas flow rate. The absolute concentration of dissolved oxygen in mmol/L may therefore vary at 100 % saturation, depending on the process.

INFORMATION

Depending on the specifications defined by the user, the pO_2 sensor will be calibrated either before the vessel is filled with medium or afterwards, in the prepared medium.

For details about calibration refer to the main chapter “Operation Touch Screen Software”, chapter “pO_2 Sensor Calibration”.

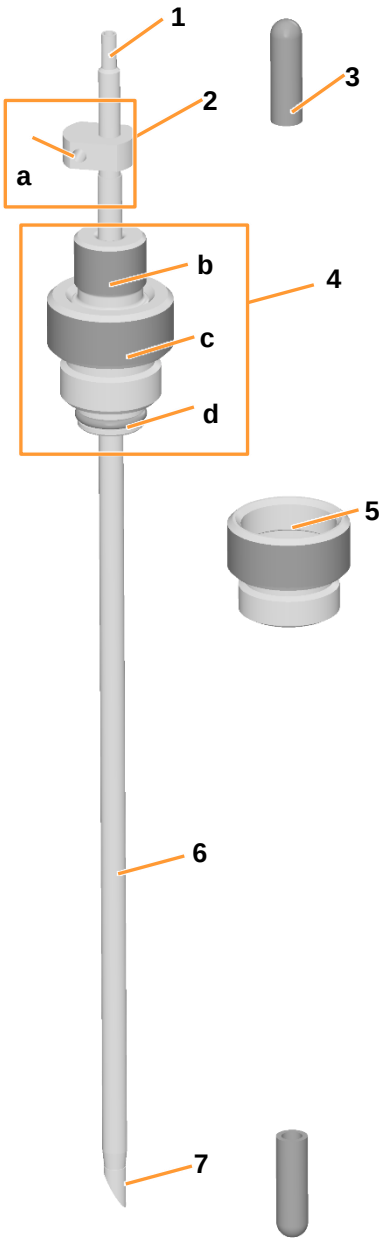
Mounting

The pO_2 sensor is mounted in an Ingold nozzle in the vessel. Analogue METTLER pO_2 sensors are designed in such a way that they can be mounted directly in the Ingold nozzles. Suitable insertion housings from the sensor manufacturers of the digital pO_2 sensors are included in the sensor delivery.

For details, see the chapter “Mounting and Connecting a pO_2 Sensor” in the main chapter “Before Cultivation”.

3.13 Antifoam Control

Foam hinders the exchange of gas between the medium and the gas phase in the head space. The exit gas filter can become clogged with foam, which can cause a pressure build-up in the vessel. Several measures can be taken to prevent this. The most common method is to reduce the foam by adding antifoam agent. The antifoam agent is kept in a reagent bottle that is connected to the antifoam sensor and the antifoam pump via a hose. The antifoam sensor also acts as a dosing needle. When the sensor comes in contact with foam or liquid, the antifoam pump is activated and antifoam agent is added via the dosing needle.



Antifoam sensor

The antifoam sensor is supplied with a separate septum collar and two protective caps that cannot be sterilised. The mounting depth of the antifoam sensor can be adjusted when the hollow screw is loosened.

1 Hose connection
2 Sensor head with cable connection (a)
3 Protective cap
4 Clamping adapter with hollow screw (b) and threaded housing (c) with thread and O-ring (d)
5 Septum collar
6 Dosing needle with transparent insulation
7 Sensor/needle tip (sharp!)

INFORMATION

The antifoam sensor cannot be sterilised in situ and therefore has to be autoclaved separately.

Preparation and mounting of the antifoam sensor and connection of the sensor cable are described in the chapters “Preparing the Antifoam Sensor” and “Mounting the Antifoam Sensor and Connecting the Sensor Cable” in the main chapter “Before Cultivation”.

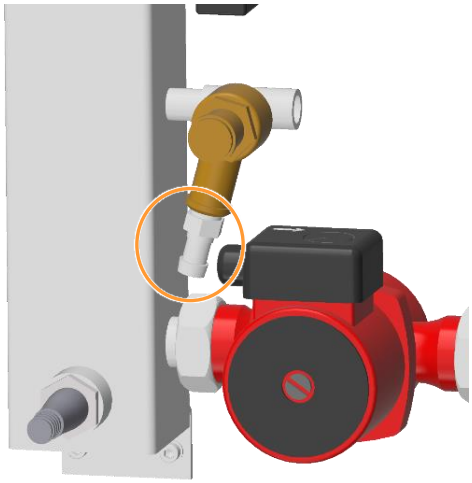
3.14 Safety Devices

3.14.1 Safety Valves

All used safety valves are TÜV approved component parts and must be integrated into the maintenance plan. Otherwise the operational safety cannot be guaranteed.

Furthermore, the provider is obliged to subject the safety valves to regular inspections in accordance with national regulations. More detailed information on the safety valves can be found in the corresponding documentation of the manufacturers.

3.14.1.1 Safety Valve Temperature Control Circuit



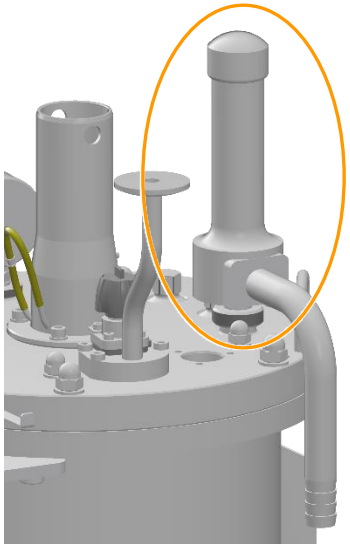
The safety valve in the temperature control circuit protects the vessel jacket against incorrect over pressure. It is fitted and adjusted by the device manufacturer and no attendance is required from the operator in normal operation.

INFORMATION

The safety valve is equipped with a hose nozzle (Ø 13 mm) to connect a hose or pipe line (operator's side) for safe drainage of any escaping steam or hot water, when the safety valve is triggered (opened).

For details refer to main chapter "Installation and Commissioning", chapter "Safety Valves".

3.14.1.2 Safety Valve Vessel



The safety valve with lifting device is mounted on the vessel top plate and protects the vessel (not the jacket!) against incorrect over pressure. It must always be mounted and intact.

Usually the safety valve remains closed. To ensure that the air in the safety valve can be completely removed and replaced by steam, it is possible to briefly vent the safety valve during the heating phase up to 103 °C.

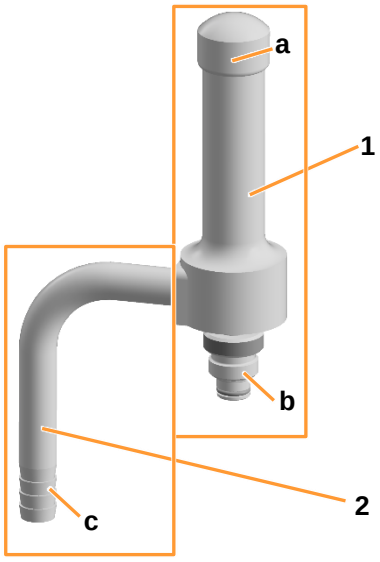
- Venting: turn the lifting device counter-clockwise (a) downwards, the engraving CLOSED disappears, the thread becomes visible at the top.
- Closing: turn the lifting device clockwise (b) up as far as it will go, the engraving CLOSED becomes visible, the thread disappears.

INFORMATION

With this method, sterilisation must be monitored and manual lifting of the hot valve involves a risk of injury. The risk of a not completely sterile safety valve, on the other hand, is hardly present with this type of valve.

Overpressure venting pipe

The safety valve has a connection thread for mounting into a 19 mm port in the vessel top plate. It is equipped with a short overpressure venting pipe.



1 Safety valve with lifting device (a) and connection thread (b) with fixed O-ring

2 Overpressure venting pipe with hose connection Ø = 21 mm (c)

INFORMATION

The open end of the overpressure venting pipe has a hose nozzle (Ø 21 mm) to connect a hose or pipe line (operator's side) for safe drainage of any escaping steam, hot and/or contaminated liquid or hazardous gases when the safety valve is triggered (opened).

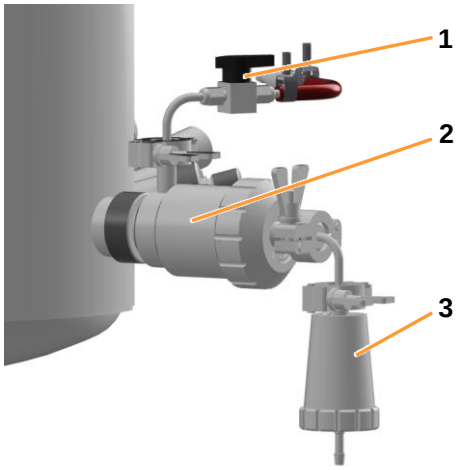
For details refer to main chapter „Installation and Commissioning “, chapter “Safety Valves”.

4 Options

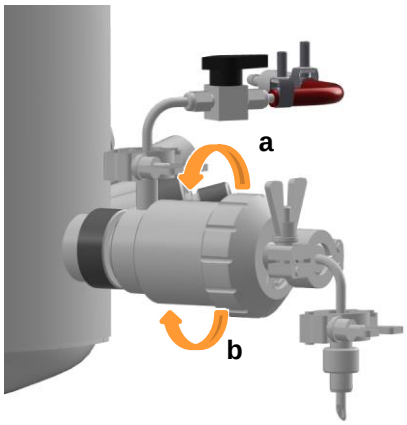
The following options are available in addition to the standard device.

4.1 Sample Valve

The sample valve **17.13.01** is pre-installed in the Ingold nozzle on the side of the vessel. In the same way, the steam trap is affixed to the valve using the condensate elbow and clamps, and the clean steam line (pressure hose) is pre-installed using manual valve **17.10.01**.



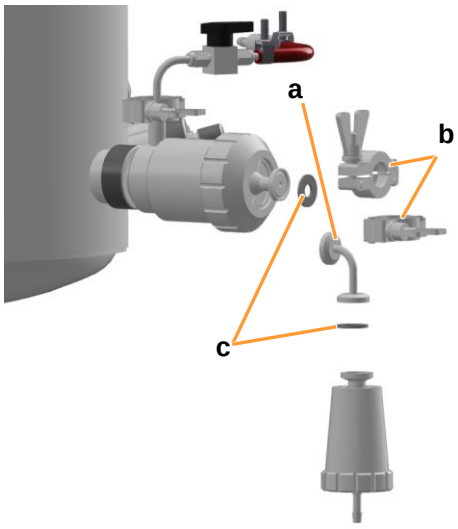
1 Clean steam valve (valve **17.10.01**) with steam line (pressure hose)
2 Sample valve **17.13.01**
3 Steam trap



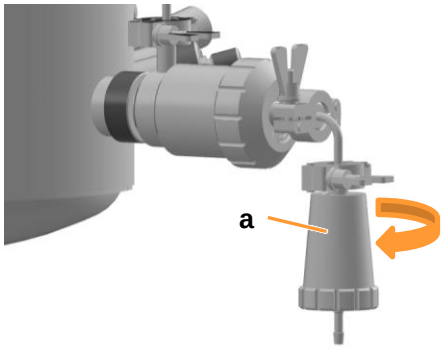
The sample valve is opened and closed manually:

- Open the valve: turn counter-clockwise (a).
- Close the valve: turn clockwise (b).

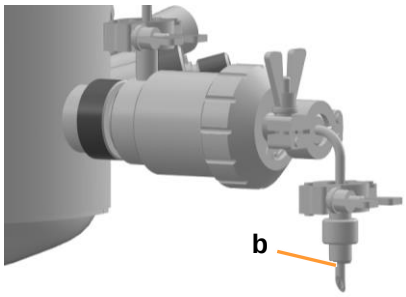
Options



The steam trap for sterilisation is affixed to the connection flange of the sample valve with a condensate elbow (a), two clamps (b) and flat gaskets (c).



For sampling, the steam trap (a) is unscrewed from the needle (b).

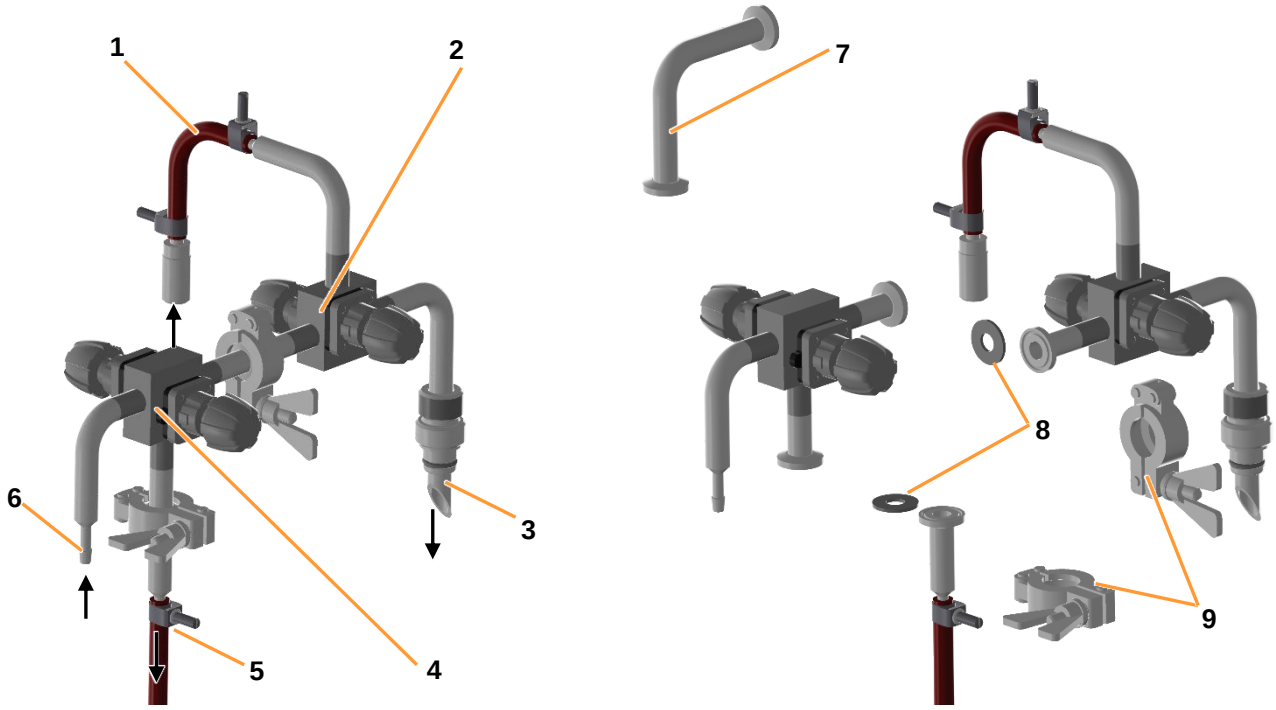


The sterilisation of the sample valve is started via the touch screen software on the operating panel. For details, see the main chapter “Operation Touch Screen Software”.

A general description of sampling is provided in the chapter “Sampling” of the main chapter “Cultivation”.

4.2 Resterilisable Feed Line

The resterilisable feed line allows an aseptic connection between the bioreactor and a container, e.g. a reagent bottle, for the sterile addition of liquids, e.g. feed solution etc.



1 Clean steam line (pressure hose with rapid coupling)

2 Block valve **13.16.01 / 13.16.03** (vessel feed line/steam feed line)

3 Connection nozzle for vessel top plate (19 mm port), with fixed O-ring.

4 Block valve **13.16.02 / 13.16.04** (condensate feed line/reagent bottle feed line)

5 Condensate line

6 Connection reagent bottle, hose nozzle Ø 13.5 mm

7 Condensate elbow

8 Flat gasket

9 Clamp

Before sterile liquid can be added to the vessel via the resterilisable feed line, the various components such as block valves (also known as sterile cross) and the container, e.g. the reagent bottle, must be prepared appropriately:

1) Sterilisation in the autoclave: the block valve (sterile cross) **13.16.02 / 13.16.04** and the container/reagent bottle are sterilised separately in the autoclave.
2) Full sterilisation: the block valve (sterile cross) **13.16.01 / 13.16.03** is mounted and in situ sterilised with the vessel.
3) Sterilisation of the feed line: the block valve (sterile cross) **13.16.02 / 13.16.04** is mounted, feed line is sterilised.

The following sections describe these steps in detail.

4.2.1 Autoclaving the Block Valve 13.16.02 / 13.16.04 and Reagent Bottle

To autoclave the block valve **13.16.02 / 13.16.04**, proceed as follows:

Procedure

1. Prepare/equip the reagent bottle for sterilisation in the autoclave. For details, see the chapter “Preparing Reagent Bottles” in the main chapter “Before Cultivation”.

Choose hose lengths in such a way that the hoses reach from the reagent bottle via the pump to the block valve **13.16.02 / 13.16.04** without tension or kinks when the feed line is connected.

2. Depending on the application: Fill the reagent bottle, close the top plate and label it according to its contents, or fill reagent bottle under sterile conditions after autoclaving, if necessary.

3. Connect the hose line of the reagent bottle to the block valve **13.16.02 / 13.16.04** and secure with cable ties.

4. Close both valves.

5. Autoclave everything together at 121 °C for e.g. 30 to 60 minutes.

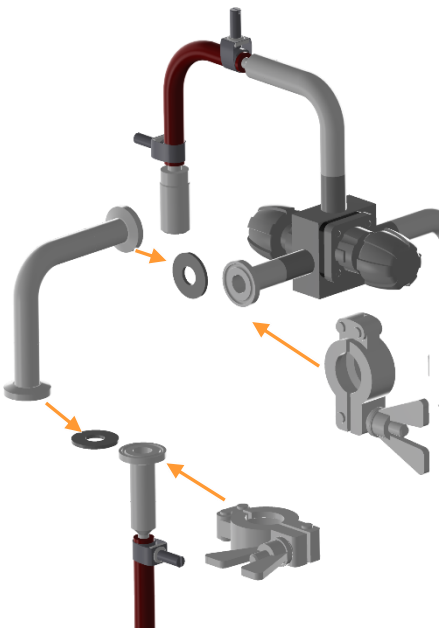
4.2.2 Sterilising Block Valve 13.16.01 / 13.16.03 In Situ

To sterilise block valve **13.16.01 / 13.16.03** with the vessel, proceed as follows:

Procedure

1. Connect the connection nozzle to block valve **13.16.01 / 13.16.03**, insert into a 19 mm port in the vessel top plate and manually screw tight.

Ensure that the connection nozzle has an intact O-ring.



2. Use the clamps to connect the condensate elbow to block valve **13.16.01 / 13.16.03** and connect to the condensate line.

Ensure that the flat gaskets are placed between the connection flanges.

3. Sterilise together with the vessel.

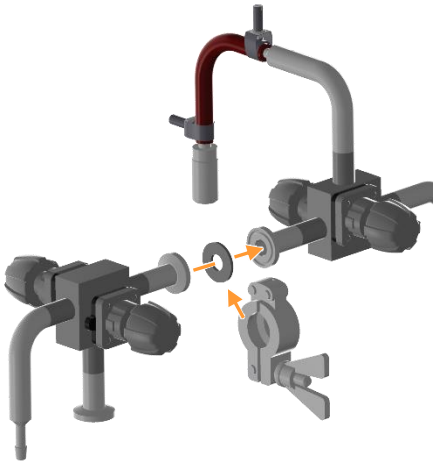
The sterilisation process is described in detail in the chapter “Full Sterilisation” of the main chapter “Operation Touch Screen Software”.

4.2.3 Sterilising the Feed Line

Once the full sterilisation and the sterilisation in the autoclave are completed and the components have cooled down:

Procedure

1. Loosen the clamps and remove them along with the condensate elbow from block valve **13.16.01 / 13.16.03**.

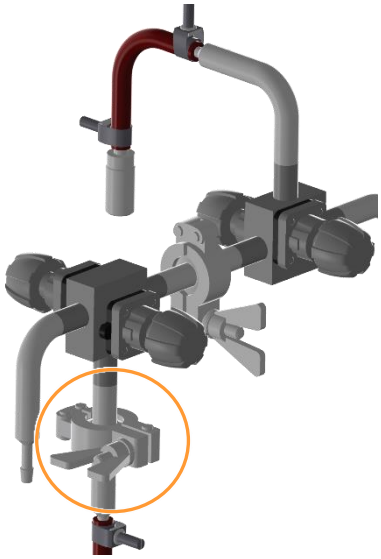


2. Use on clamp to **c**onnect block valve **13.16.02 / 13.16.04** (reagent bottle not pictured) to block valve **13.16.01 / 13.16.03**.

   Ensure that the flat gasket is placed between the connection flanges.

INFORMATION

Both valves remain closed and the hose line on the reagent bottle remains disconnected!



3. Use the second clamp to connect the condensate line to the block valve **13.16.02 / 13.16.04**.

   Ensure that the flat gasket is placed between the connection flanges.

4. Connect the reagent bottle to the pump.

   For details, see the chapter “Preparing the Pumps” in the main chapter “Before Cultivation”.

5. Sterilise the feed line.

   The sterilisation process is described in detail in chapter “SIP Feed Line Sterilisation” of the main chapter “Operation Touch Screen Software”.

After finishing the sterilisation, all components of the resterilisable feed line are sterile and ready for cultivation.

4.3 Steam Generator

A steam generator integrated into the device is available with more or less power, depending on the vessel volume:

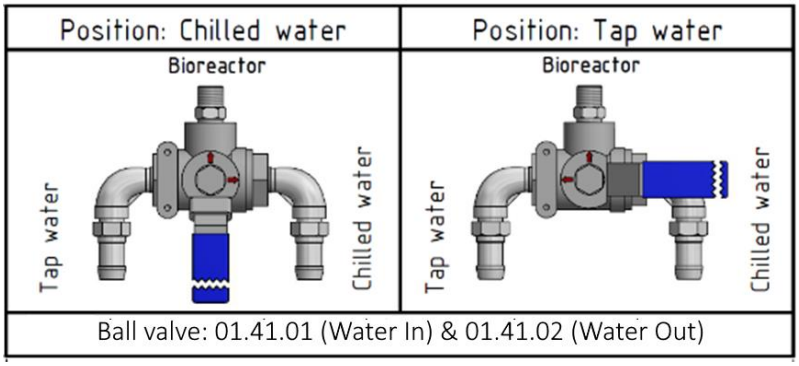
Steam generator power	Total volume of vessel
6 kW / 8 kg/h	15 litres
10 kW / 14 kg/h	30 litres
	42 litres

The steam generator is used for the sterilisation of the vessel and peripheral devices and is also used for heating, depending on the temperature control system chosen.

4.4 Switchover Tap Water / Chilled Water

If a cooling water system provided by the operator is available or a recirculating chiller, which is available separately, is used, 3-way ball valves **01.41.01** (water inlet) and **01.41.02** (water outlet) are used to switch between tap water and chilled water.

A sticker that indicates the different positions of the 3-way ball valves is placed on the rear of the instrumentation cabinet.

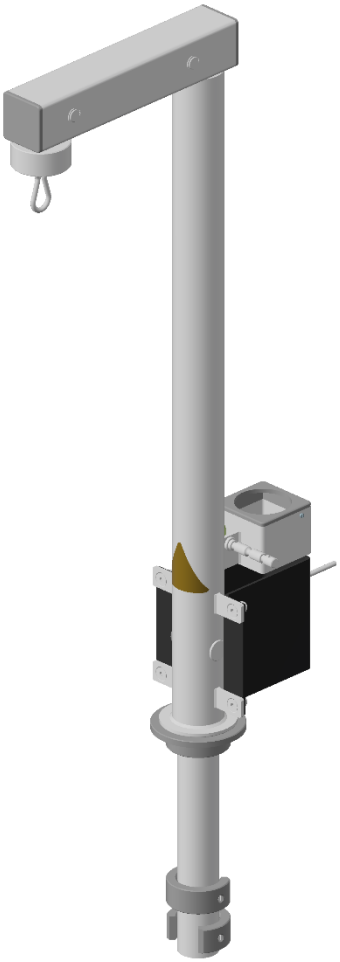


Suitable instructions for the process are also displayed in various dialogue boxes in the touch screen software.

4.5 Recirculating Chiller

Chilled water for the device can also be provided by a separately available recirculating chiller. In this case, the optional 3-way ball valve valves **01.41.01** and **01.41.02** are required for switching between tap water and chilled water, as in the case of an in-house cooling water system and are automatically integrated into the device.

4.6 Lifting Device for Vessel Top Plate



A lifting device is available for lifting and lowering the vessel top plate. This device is installed on the central column of the basic unit and operated using a winch. We recommend using a lifting device in particular for vessels with a total volume of 30 litres and 42 litres.
All information regarding function, operation, technical data and safety is available in the separate operating manual.

4.7 Level Measurement

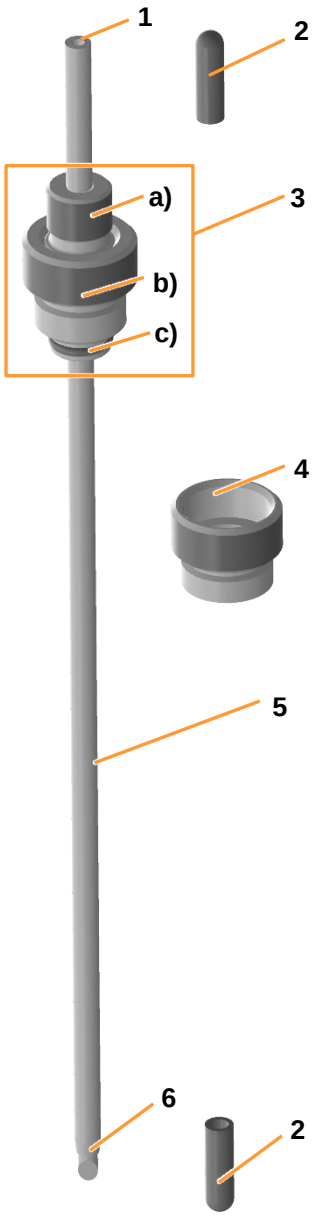
The level sensor detects the level of culture liquid in the vessel. It is mounted in such a way that it touches the liquid down to the lowest possible level of the vessel. As soon as the sensor detects liquid, a signal is generated (*output* of the parameter *Level* = 100 %).

This signal can be used as required for level control in the vessel in order to keep the working volume in the vessel constant. This can be done, for example, by using a simple cascade to control the feed pump or an optional pump that pumps liquid either into or out of the vessel. Special configurations are possible on request.

Options

Technical specifications	
Sensor	Conductive, height can be adjusted
Control	Not pre-configured ex-factory [1)]
Range	0 / 100 % (OFF/ON)

[1)] *A simple cascade can be used, for example, to set a feed pump for open-loop control.*



The level sensor is supplied with a separate septum collar and two protective caps that cannot be sterilised. The mounting depth of the level sensor can be adjusted when the hollow screw is loosened.

1 Sensor head cable connection
2 Protective cap
3 Clamping adapter with hollow screw (a) and threaded housing with thread (b) and fixed O-ring (c)
4 Septum collar
5 Sensor shaft with transparent insulation
6 Sensor tip (sharp!)

In contrast to the antifoam sensor, the level sensor is not hollow and can therefore not be sterilised in situ with the vessel. The level sensor is therefore mounted in the port without a septum collar.

INFORMATION

The septum collar that is included in the delivery offers the option to separately autoclave the level sensor and the antifoam sensor and to equip the port in the vessel top plate with septum and septum collar.

4.7.1 Mounting the Level Sensor and Connecting the Sensor Cable

The mounting depth of the level sensor should be set neither too high nor too low. To keep it sterile, it must not be pushed deeper into the vessel after sterilisation. Pulling out, however, is possible even during cultivation and bears a significantly lower risk of contamination.

Mounting

Please note the following points before mounting:

- The level sensor is equipped with transparent insulation that must be intact, as a continuous signal is generated otherwise.
- The clamping adapter must be equipped with an intact O-ring.

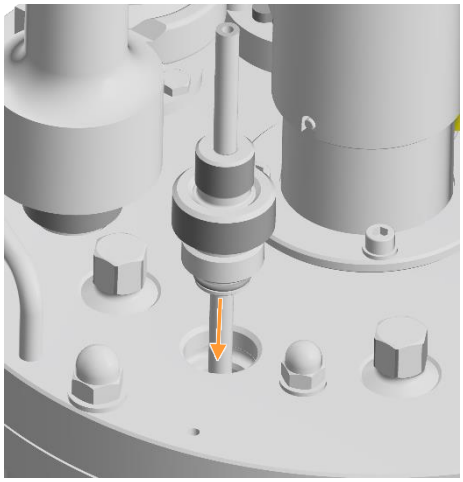
ATTENTION

If the level sensor is fixed too tightly in the clamping adapter, or the mounting depth of the level sensor is changed while the hollow screw on the clamping adapter is tightened, the transparent insulation may be damaged.

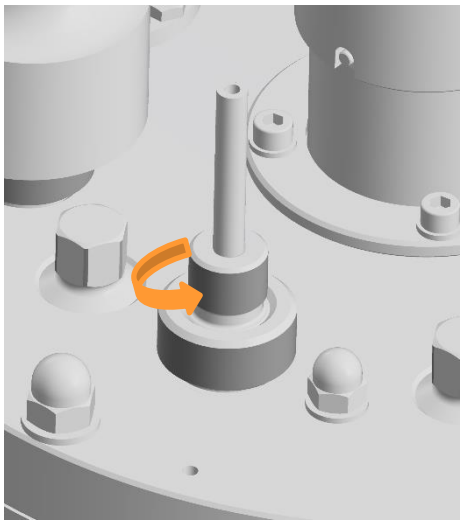
Proceed as follows:

Procedure

1. Remove the protective caps from the level sensor.



2. Manually screw the level sensor into the 19 mm port in the vessel top plate.



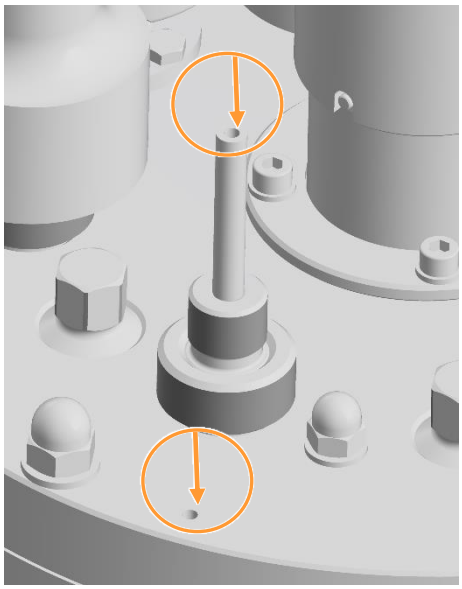
3. Carefully loosen the hollow screw by hand.

4. Adjust the level sensor to the desired mounting depth.
5. Carefully tighten the hollow screw by hand.

Cable connection

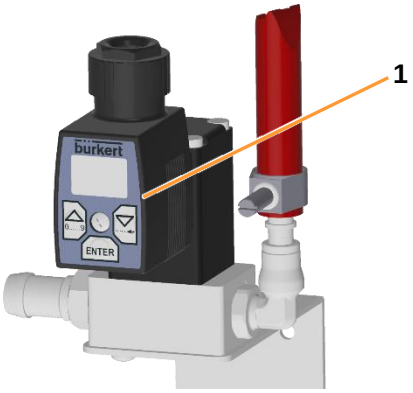
To connect the level sensor, insert the two banana connectors of the sensor cable as follows:

Procedure



1. Insert the red banana plug into the connector on the top of the sensor head.
2. Insert the black banana plug into the drill hole for ground connection in the vessel top plate.

4.8 Pressure Control

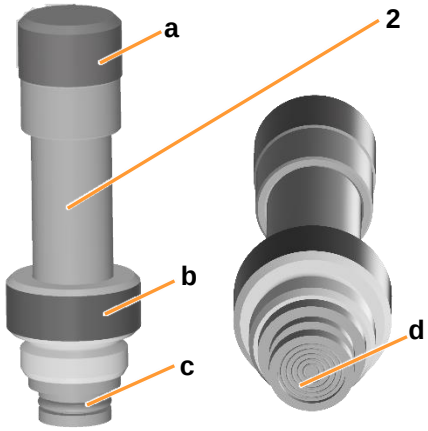


The pressure in the vessel is measured using a piezo-resistive pressure transmitter and controlled with a pressure control valve in the exit gas line.

1 Pressure control valve **03.11.01** (*exit gas*)

2 Pressure sensor **08.31.01**

The measurement values and the setpoint are displayed in the *Pressure* parameter in the touch screen software.



The pressure sensor is equipped with a fixed O-ring (c) and a hollow screw (b) for mounting in a 19 mm port in the vessel top plate. The cable connector is protected with a steel cap (a). A protective cap (not pictured) protects the sensitive steel membrane (d) of the sensor from damage.

Technical specifications	
Sensor	Piezo-resistive pressure transmitter
Control	Proportional valve with electronic open-loop control
Control range	0 to 1.5 bar
Accuracy	Measurement and control: ± 0.1 bar

4.8.1 Mounting and Connecting the Pressure Sensor

The pressure sensor must be mounted and connected prior to sterilisation.

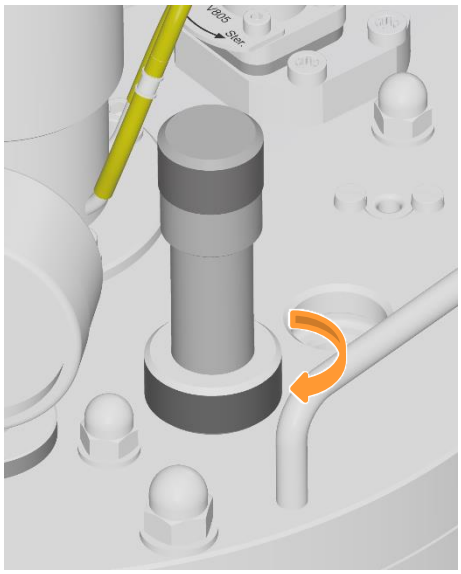
Proceed as follows:

Procedure

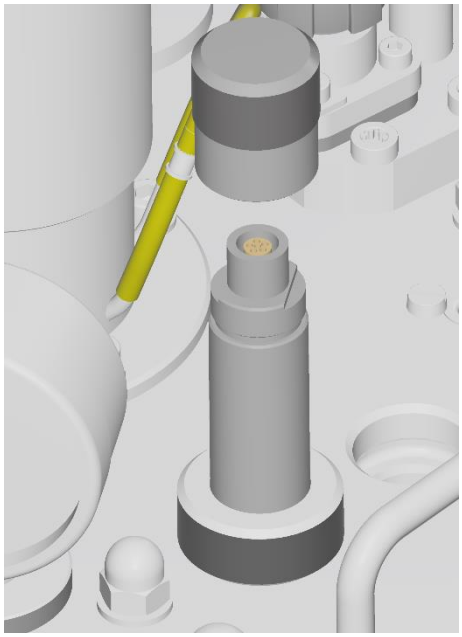
1. Carefully remove the protective cap from the steel membrane of the pressure sensor.

ATTENTION

The steel membrane is very delicate and can be damaged by friction or knocks from hard objects.



2. Carefully insert the pressure sensor with fixed O-Ring into the 19 mm port and tighten it on the hollow screw by hand.



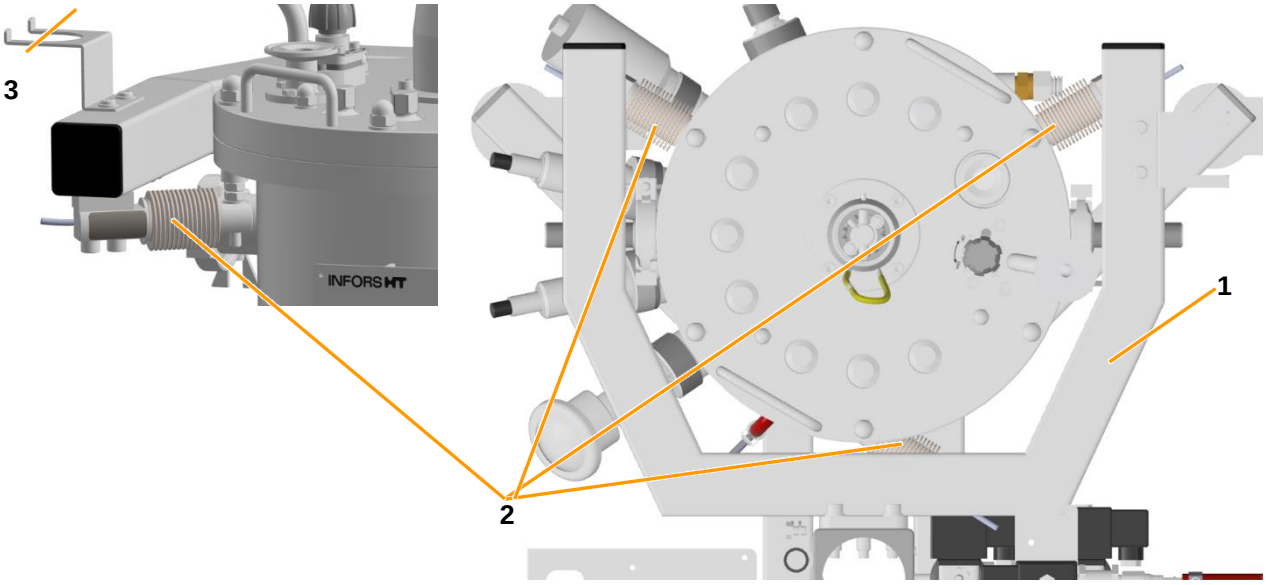
3. Manually remove the steel cap from the cable connector.

4. Connect the sensor cable. In doing so, align the red marking of the cable connected with the red marking on the sensor connector.

4.8.2 Maintenance

The pressure sensor is generally maintenance free. The re-calibration cycle depends on the conditions under which it is used. However, we do recommend annual re-calibration by the sensor's manufacturer.

4.9 Weight Measurement – Weighing System Vessel



1 Weighing system frame
2 Load cell (3 x)
3 Holder for exit gas cooler

The weighing system of the vessel consists of a frame with three load cells. The frame is bolted to the central column of the device. The load cells are evenly distributed on the underside of the frame. Bolts on the underside of the vessel flange serve as load introduction points of the vessel.

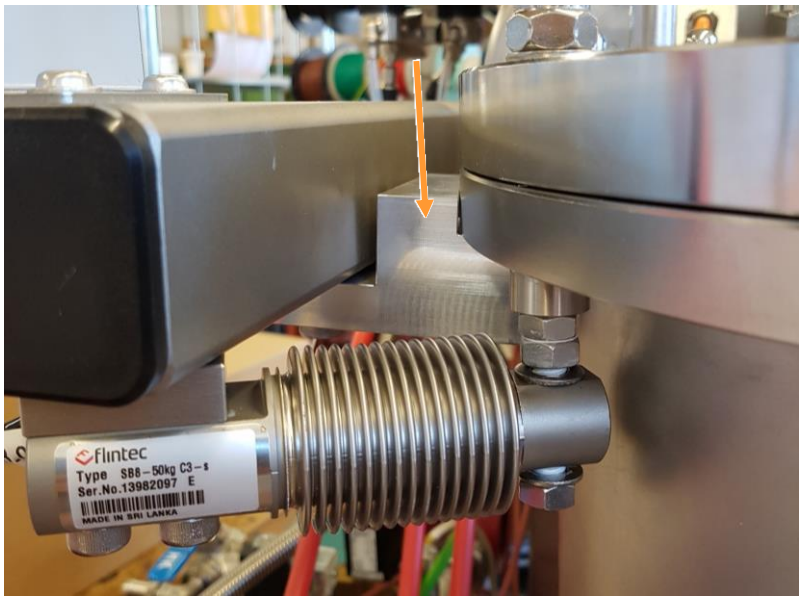
Measured values are displayed in the touch screen software in parameter *Weight*. The weight display can also be tared there.

The holder for hanging the exit gas cooler during e.g. preparatory work on the vessel is located on the frame.

Technical specifications	
Measurement system	Beam load cell (3 x)
Measurement accuracy	± 100 g

4.9.1 Transportation safety device

To protect the load cells from damage during transport, a transportation safety device is attached to the frame of the weight measurement. This means that two plates (see figure below) are screwed to the right and left on the underside of the frame.



The plates prevent the load from being applied to the load cells. The plates are only removed by qualified personnel when the device is installed and they are handed over for safekeeping. The transportation safety device must be fitted before any transport of the device.

4.10 Turbidity Measurement

The Optek ASD25-N measurement sensor is used to determine the turbidity of the culture. The turbidity can be used to draw conclusions regarding the biomass concentration in the culture.

The system consists of a sensor (single channel light absorption) with an integrated transmitter.

Options

Technical specifications		
Sensor type	ASD25-N	
Selection of optical path lengths	OPL01	for very high cell densities
	OPL05	for higher cell densities
	OPL10	for lower cell densities
Absorption measurement range	0 to 4 CU	
Manufacturer	Optek	

The ASD25-N sensors supply a non-linearised turbidity measurement for the culture. This can be linearised manually using the soft sensor in eve®, for example, in order to determine correlation with factors such as the biomass concentration or optical density.

INFORMATION

If the temperature of the sensor increases to above 65 °C during operation in the medium, an automatic switch off takes place. Once the medium has cooled down, the measurement is continued automatically.

For more information, see the separate documentation from the sensor's manufacturer. Read this documentation before using the turbidity sensor and follow the instructions contained therein.

4.10.1 Calibrating the Sensor

Optek sensors are pre-calibrated ex-factory. Inserts are available for reference measurement.

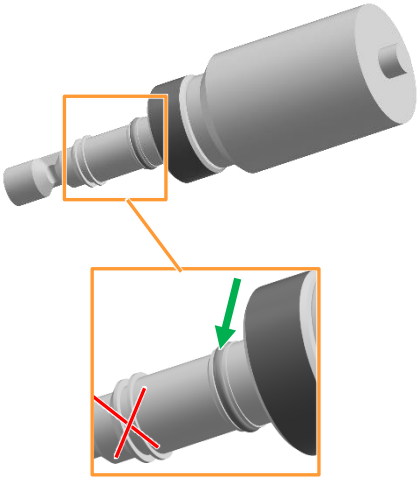
Due to the different light absorption of different media, zero point calibration of the turbidity sensor should be performed before each cultivation process. This can be done either **before or after** in situ sterilisation, depending on the application in question. For more details, see the chapter "Turbidity Sensor Calibration" in the main chapter "Operation Touch Screen Software".

4.10.2 Mounting the Sensor and Connecting the Cable

Due to the position, length and angle of the Ingold nozzle on the vessel, the mounting position of the turbidity sensor is pre-defined. It prevents a gas connection at the port on the top, and medium can drain from sapphire windows. This position also prevents contact with other built-in-parts in the vessel.

Proceed as follows:

Procedure



1. Ensure that there is an intact O-ring in the upper groove of the sensor.

INFORMATION

When the sensor is delivered, the O-ring is placed in the correct groove (the green arrow in the image on the left indicates the position).

2. Insert the turbidity sensor into the Ingold nozzle.
3. Tighten the coupling nut manually.
4. Connect the sensor cable.

4.10.3 Interferences Turbidity Measurement

Interference		
Displayed value is not plausible/unusual		
Possible cause	**Remedy**	**By**
Sensor cable is twisted or kinked or not connected correctly.	Ensure that the cable is not kinked or twisted. Connect properly if necessary.	Operator
Sensor is not calibrated	Calibrate the zero point	Operator
Sapphire windows are dirty	Carefully clean the sensor	Operator
Defective sensor cable	Replace the cable	INFORS HT service technician
Defective sensor	Replace sensor	Operator

4.11 Exit Gas Analysis

To allow the user to draw conclusions regarding the status of the culture while the bioprocess is still underway, the CO_2 and O_2 measurements are often taken and analysed in the exit gas flow of the bioreactor.

4.11.1 Gas Sensor

For exit gas analysis, combined CO_2 and O_2 sensors of the type BlueInOne Ferm or Cell as well as BlueVary by the manufacturer BlueSense are available.

Gas sensor measurement ranges

Gas sensor type	Vol. % O_2	Vol. % CO_2
BlueInOne Ferm Blue Vary	1.0 to 50 [1)]	0 to 10
BlueInOne Cell Blue Vary	0 to 100 [2)]	0 to 10

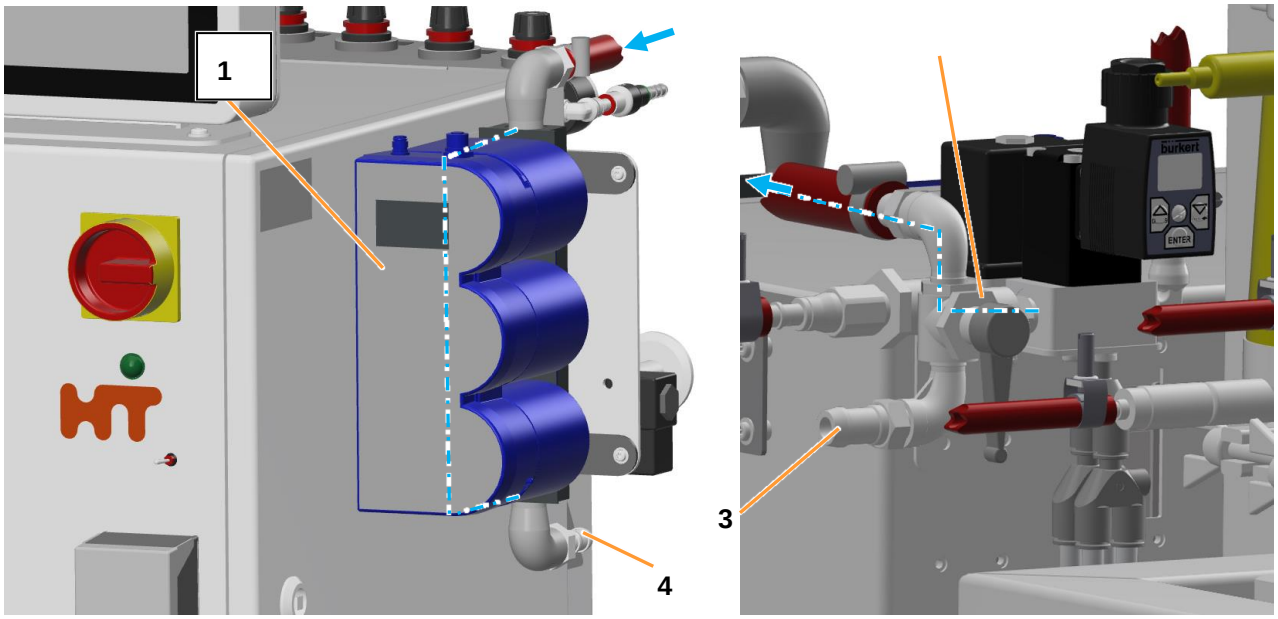
1) *only suitable for aerobic bioprocesses*

2) *only suitable for aerobic and anaerobic bioprocesses*

For more information on safety, use, maintenance and technical data, see the separate documentation from the sensor's manufacturer.

4.11.2 Connection and Exit Gas Routing

The gas sensors are pre-installed ex-factory. The figure shows gas sensors of the type Blue Vary as an example.



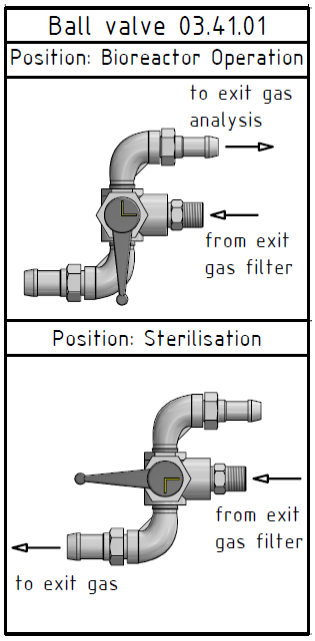
1 Gas sensors BlueVary

2 3-way ball valve **03.41.01** (here: position Bioreactor Operation = exit gas analysis)

3 Direct outlet of exit gas (without exit gas analysis)

4 Outlet of exit gas from exit gas analysis

(both connections for an exit gas system/hose provided by the operator)



During an ongoing bioprocess, exit gas is routed through the gas sensors. During sterilisation, it must be discharged directly into the operator's exit gas line to protect the sensors from moisture. The operator manually makes this switch using the 3-way ball valve **03.41.01**.

The flow direction of exit gas as well as the 3-way ball valve positions are indicated on the sticker placed on the instrumentation cabinet.

- Position **Bioreactor Operation** = exit gas analysis
- Position **Sterilisation** = direct output

Suitable instructions for this process are also displayed in various dialogue boxes in the touch screen software.

4.11.3 Calibration

1-point calibration must be carried out once per month and during initial commissioning in order to guarantee exact measurement results. This is done directly on the gas sensor itself. The procedure is described in the separate documentation provided by the manufacturer BlueSens.

4.11.4 Replacing the BlueVary Gas Sensor Cartridge

The max. operating time of a BlueVary gas sensor cartridge amounts to 9000 operating hours. Once this limit is reached, measurement is no longer possible. I.e. there is no measurement value output anymore and the display turns red. The gas sensor cartridge must be replaced by the sensor manufacturer.

4.12 pCO_2 Measurement

Saturation of dissolved carbon dioxide (CO_2) in the culture is measured by a digital CO_2 sensor with integrated temperature sensor. Measured values in hPa are displayed on the associated transmitter and also in the touch screen software.

Technical Specifications	
Type of sensor	InPro5000i, ISM (digital)
Measurement principle	potentiometric
Type of transmitter	M400
Measurement range	0 to 1000 hPa
Manufacturer sensor & transmitter	METTLER TOLEDO

The displayed value of parameter *pCO_2* in the touch screen software is set to a range of 0 hPA to 1000 hPA analogous to the displayed value of the transmitter.

Mounting and Calibration

The pCO_2 sensor is mounted in an Ingold nozzle in the vessel. For this purpose, the sensor is supplied with the appropriate sensor adapter from the sensor manufacturer. The sensor is calibrated directly at the transmitter and according to the manufacturer's specifications.

For detailed information about technical data, use and maintenance of the pCO_2 sensor and transmitter, refer to the separate documentation from the sensor manufacturer.

4.13 Redox Measurement

The reduction/oxidation potential (redox) in the medium is measured using the redox sensor. Depending on the variant selected, the measurement system is equipped and configured for analogue sensors by the manufacturer METTLER or digital sensors by the manufacturer HAMILTON.

Variant METTLER analogue

- Classic combined sensor (oxidation reduction potential measurement against a reference)
- Type: 405-DPAS-SC-K8S
- Measures the reduced potential in the medium in the range from -2000 mV to +2000 mV.

To use the sensor, the device must feature a corresponding connection.

Variant HAMILTON digital

- Classic combined sensor (oxidation reduction potential measurement against a reference) with integrated electronics
- Type: Easyferm Plus ORP ARC
- Measures the reduced potential in the medium in the range from -1500 mV to +1500 mV.

If the device is configured for HAMILTON sensors, the redox sensor can be connected instead of the pO_2 sensor. If the sensor is configured in addition to the HAMILTON pO_2 sensor or if the device is configured for METTLER sensors, an additional connecting cable is required.

Calibration

The redox sensor is usually not calibrated/adjusted. HAMILTON system: Calibration is possible with a corresponding redox buffer solution using a HAMILTON Arc Handheld or a HAMILTON Arc USB cable. Both of these are available separately from the sensor manufacturer.

Mounting

The redox sensor is mounted into an Ingold nozzle in the vessel. For this, the sensor is supplied with a suitable insertion housing by the sensor's manufacturer.

For details on the technical data, usage and maintenance requirements for the redox sensors, see the separate documentation provided by the sensor manufacturers.

4.14 Permissive Measurement

Sensors of the ABER Futura systems measure the permittivity (also: *capacitance*) and conductivity of the culture. This measured data can be used to determine a correlation with the live biomass concentration, for example, using the soft sensor in eve® or data evaluation.

The sensor with the corresponding transmitters must be purchased directly from the manufacturer ABER. INFORS HT offers a connection to the transmitter on the basic unit.

Measured parameters	Value	Unit
Permittivity	0 to 400	pF cm^{-1} range
Conductivity	0 to 40	mS cm^{-1} range

Calibration is performed according to the manufacturer's guidelines directly on the transmitter.

All information about the ABER Futura system is available in the separate documentation provided by the manufacturer.

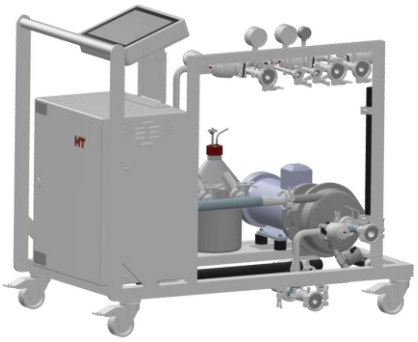
4.15 Pump(s)

In addition to the four pumps available as standard, two additional analogue peristaltic pumps (*Feed 2* and *Feed 3*) can be integrated. As for the standard analogue feed pump, its speed can be variably adjusted in steps of 0.1 % within a range from 0 % to 100 %.

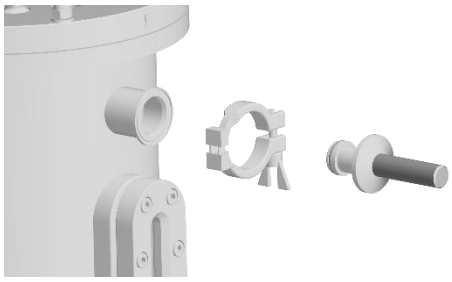
External Pump(s)

One or more Watson Marlow 120U/DV external peristaltic pump(s) are also available. The number of possible external pumps depends on the options already available.
Like the other analogue peristaltic pumps, the pump speed is adjustable and can be set in steps of 0.1 % within a range of 0 % to 100 %.
For further information on safety, use, maintenance and technical data of the pump(s), refer to the separate documentation of the pump manufacturer.

4.16 Mobile CIP Unit TechCIP



For automatic cleaning of the bioreactor, the mobile CIP unit TechCIP is available from the device manufacturer. The cleaning process with the mobile CIP unit and its operation in general are described in detail in the separate operating manual.



To be able to clean the bioreactor with the CIP unit, an adapted vessel design of the Techfors-S is required. In this case, the vessel has two additional Tri-clamp ports with blanking plugs in the upper vessel section.

5 Accessories, Consumables and Hoses

The device is delivered with different accessories and consumables by default. These standard items are listed in the tables below and apply to any of the tree available vessel sizes.

Description	Application
Reagent bottle, 500 mL	Reagents
Hexagon socket spanner WAF 17	Blanking plugs 19 mm ports
Septum (inoculation diaphragm) Ø = 19 mm, MVQ-silicone, transparent	For inoculation 19 mm ports
Cable tie, Polyamid 2.4 x 85 mm, black	Attachment silicone hoses and pump hoses
Hose connector 1/8'' x 1/8'', PVDF	Connection to pump hose with ID = 2.5 mm

5.1 Connection Kit

The connection kit contains the following hose and hose attachment material for all three vessel sizes:

Hose type	Ø mm	Application
Pump hose (Marprene/Bioprene)	3.2 x 6.4	Reagent bottle connection to peristaltic pumps
Pressure hose	8.0 x 14.5	Gas connection
Pressure hose	10.0 x 17.0	Steam connection
Pressure hose	12.5 x 21.0	Condensate

Attachment	Ø mm	Application
Hose clamp	17.0	Hose connection inlet air/gas
Hose clamp	19.0	Hose connection water inlet & outlet and steam inlet
Hose clamp	12 – 22	Hose connection condensate

Standard accessories and additionally available accessories are described in the following chapters.

5.2 Reagent Bottles

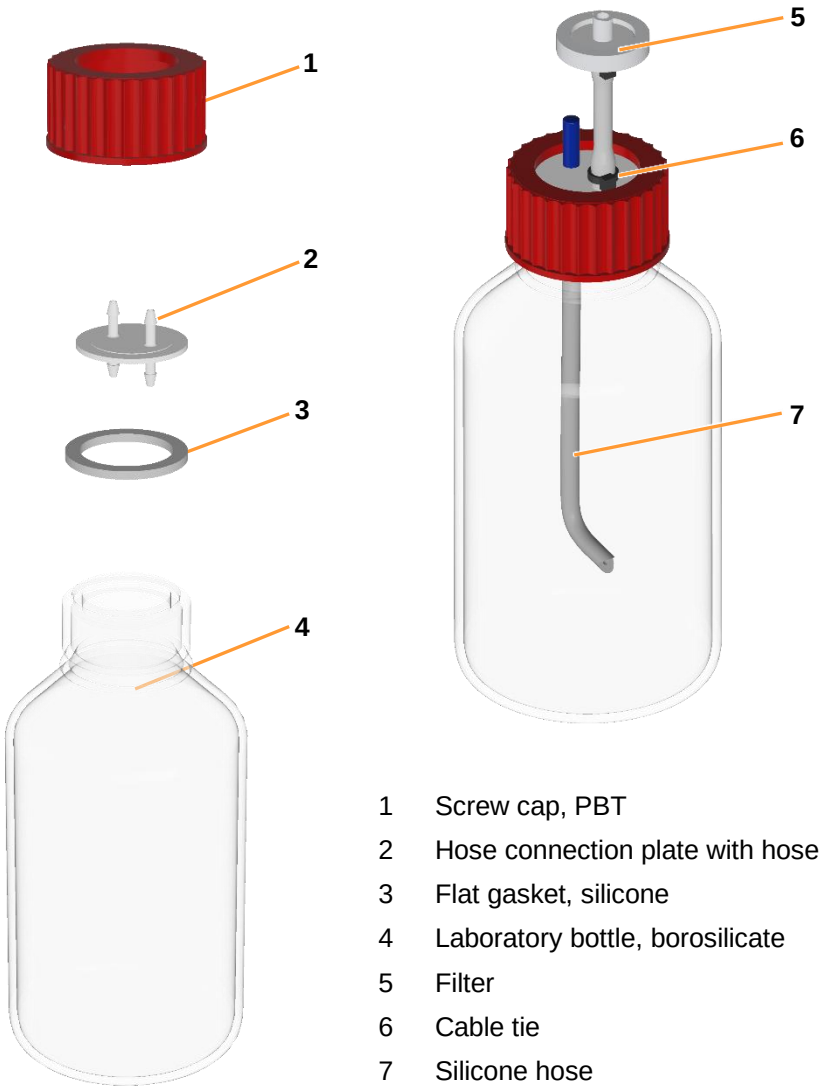
Different sizes of borosilicate reagent bottles are available for adding reagent and nutrient solution:

Size	Hose Ø
500 mL [1)]	2 x 6 mL
1000 mL	3 x 5 mm
2000 mL	3 x 5 mm
5000 mL	3 x 5 mm
10,000 mL	3 x 5 mm

1) 4 units included in the starter set

Accessories, Consumables and Hoses

Reagent bottles are equipped before delivery. There are two hose connections on the top plate. One is equipped with a short piece of silicone hose with a filter for pressure equalisation. The second connection is equipped with a piece of silicone hose at the other end, inside the bottle.



1 Screw cap, PBT
2 Hose connection plate with hose nozzles, PVDF
3 Flat gasket, silicone
4 Laboratory bottle, borosilicate
5 Filter
6 Cable tie
7 Silicone hose

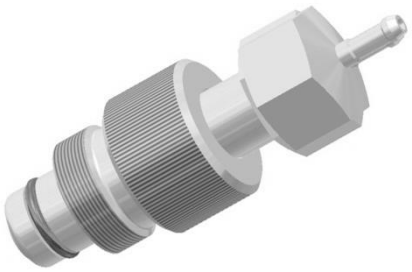
For details on preparation, autoclaving and the connection of a pump, see the chapter “Preparing Reagent Bottles” in the main chapter “Before Cultivation”.

5.3 Push Valves

The push valve enables an aseptic connection between a laboratory bottle and the bioreactor for sterile adding of nutrient solution, reagents etc.

Two push valve designs are available:

- Push valve with hose connection
- 4 inlet push valve with four hose connections for up to four laboratory bottles.

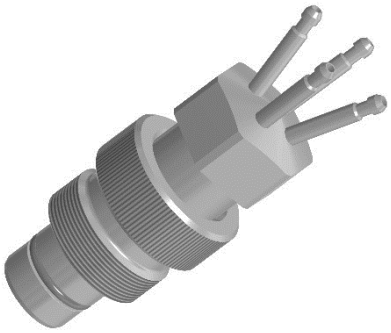


Push valve

Hose connection	Inside Ø	3.0 mm
	Outside Ø	6.0 mm

With fixed O-ring.

A thread is used for mounting in the 19 mm port.



4 inlet push valve

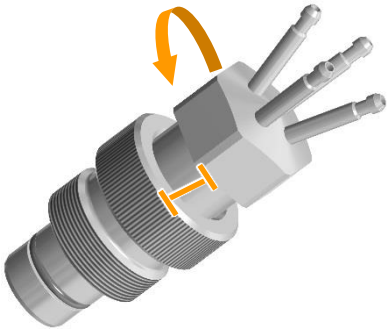
Hose connection	Inside Ø	2.0 mm
	Outside Ø	4.0 mm

With fixed O-ring.

A thread is used for mounting in the 19 mm port.

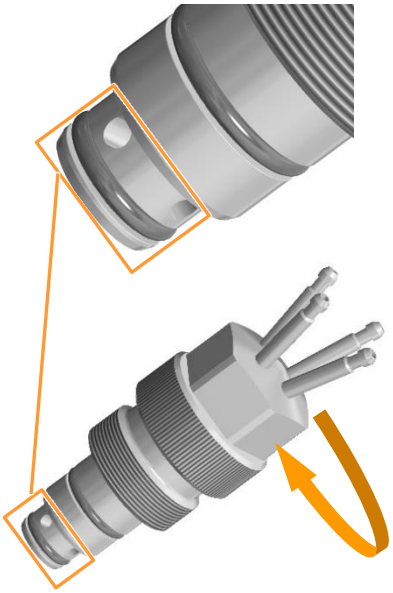
Preparation and use of a push valve mainly comprise the following three steps:

1) Separate sterilisation in the autoclave: The entire push valve (closed!) and laboratory bottle(s) fitted with hose and filter are sterilised separately in the autoclave.
2) In situ sterilisation with the vessel: The exposed part of the (closed!) push valve is sterilised together with the vessel.
3) Cultivation: The push valve is opened.



Closing

Turn the rotary piston counter-clockwise. The lower part of the rotary piston is retracted. The upper part protrudes from the valve body.



Opening

Turn the rotary piston clockwise. The lower part of the rotary piston is pushed out. The distance between the valve body and rotary piston is reduced.

5.4 Inoculation Needles

Inoculation needles are used for feeding liquids into the vessel, which cannot be in situ sterilised. These liquids may be e.g. the inoculum or heat-sensitive reagents.

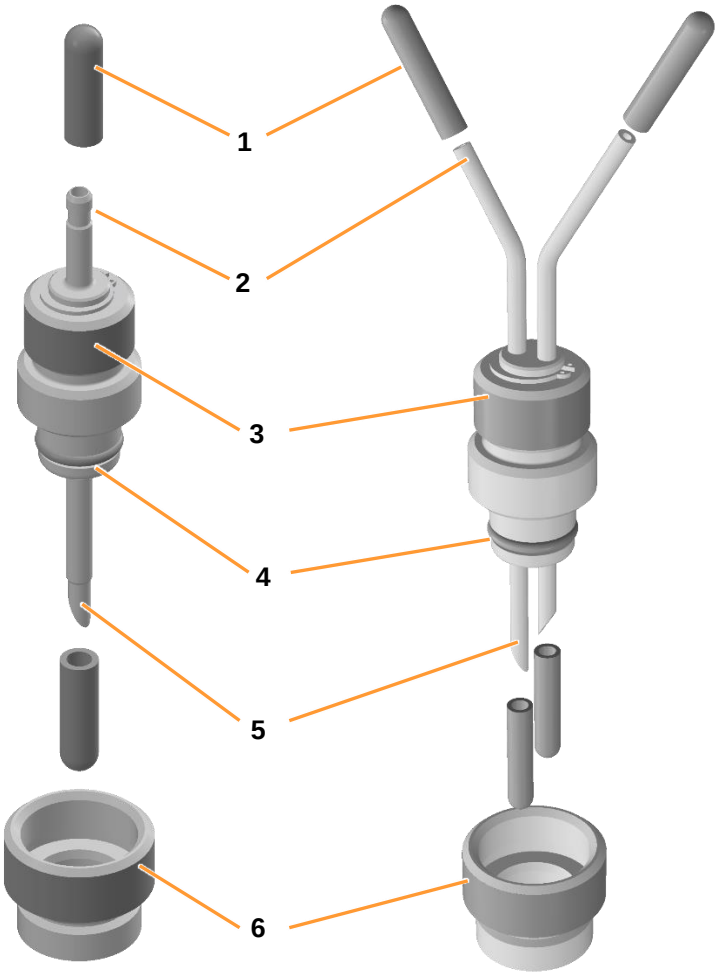
If using an inoculation needle, then a septum (inoculation membrane) must be fitted along with a septum collar in the appropriate port in the vessel top plate. The inoculation needle is connected with the reagent bottle and autoclaved. The liquid, e.g. the inoculum, which shall be added into the vessel, is filled into the reagent bottle under sterile condition, shortly before addition. The septum is then pierced with the inoculation needle, which is screwed into the septum collar.

Inoculation needles are purchased with a septum collar. Inoculation needles have an oblique tip to facilitate the piercing. The hose connection and the very sharp needle tip are covered with non-autoclavable(!) protective caps.

Accessories, Consumables and Hoses

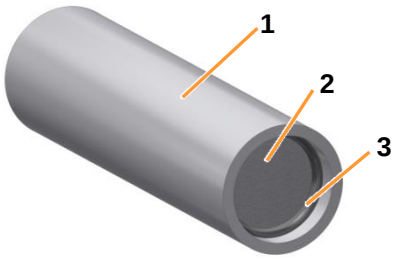
For details about preparation of an inoculation needle refer to the main chapter “Before Cultivation”, chapter “Preparing Inoculation Needles”.

Inoculation needles are available in two versions. The picture below shows a single inoculation needle and a double inoculation needle.



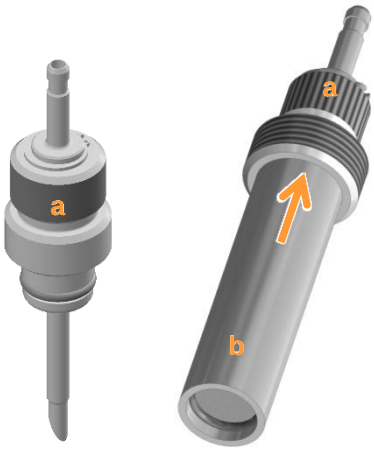
1	Protective cap (non-autoclavable!), 2 or 4 pcs.	4	O-Ring D = 2,5 x 15 mm, EPDM
2	Hose connection (OD = 6.0 mm), 1 or 2 pcs.	5	Needle (ID = 4 mm), 1 or 2 pcs.
3	Hollow screw	6	Septum collar

5.5 Sterile Sheath



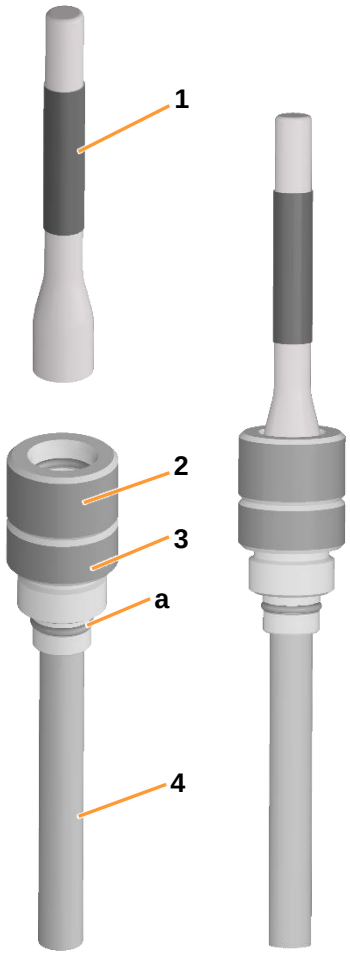
Sterile sheaths are used for inoculation needles for separate sterilisation in the autoclave.

1 Sterile sheath (ID = 19 mm)
2 Filter disc
3 O-ring



Instead of wrapping the inoculation needle (a) in aluminium foil, the sterile sheath (b) is placed on the inoculation needle.

5.6 Vessel Light



The vessel light consists of a torch and clamping screw with thread and O-ring for screwing into a 19 mm port in the vessel top plate. A glass lens is integrated. A is screwed into the retaining collar and serves to fix the torch.

1 Torch
2 Clamping screw
3 Threaded housing with O-ring (a)
4 Glass lens

6 Transport and Storage

The following specifications are based on transport and storage of an unpacked device at the provider's site.

6.1 Transport

WARNING

Improper transport, the use of incorrect auxiliary equipment and careless handling of the device may lead to injuries and severe property damage.

The following points must be observed when transporting the device internally (relocation):

- Transport safety devices supplied with the device must be mounted before relocating the device in order to protect it against damage.
- Work at least in pairs and, where applicable, use suitable auxiliary equipment when transporting the device.
- Especially when using auxiliary tools, it is important to observe that the device's centre of gravity is not in the middle.

6.2 Storage

- Before each time they are put into storage, decontaminate, thoroughly clean and dry the vessel and all accessories [1)].
- Store the device and its components clean, dry and protected against dust, dirt and liquids.
- Store the device and its components in a cool place with low air humidity but protected against frost.
  - Storage temperature: 5 °C to 55 °C
  - Relative air humidity, non-condensing: 10 % to 95 %.
- Protect the device from aggressive media, direct sunlight and mechanical vibrations.

1) *Maintain and store sensors produced by other manufacturers in accordance with the separate documentation.*

7 Installation and Commissioning

Installation and commissioning may only be carried out by the manufacturer's qualified personnel or personnel authorised by the manufacturer.

After installing the device, the first step is to fill the temperature control circuit. This remains filled afterwards and is only emptied in exceptional cases during any repair or service work.

After connecting the motor cable, the basic functions of the bioreactor are briefly tested in a test run.

As this work must not be carried out by the operator, it is not the subject of this operating manual.

In the following, therefore, only the connection conditions to be observed by the operator and the energies to be provided are listed.

⚠ WARNING

Installation and commissioning require qualified and experienced personnel. Faulty installation may lead to perilous situations or severe loss of property.

Installation and commissioning are to be carried out by the manufacturer's associates only. This also applies to installation and recommissioning after relocation of the device.

7.1 General Location Requirements for Installation

The following requirements must be met for the installation of the device:

- The figures and ranges specified in the main chapter "Technical Data", chapters "Connection Values" and "Operating Conditions" must be observed.
- The device must only be installed inside a laboratory or a laboratory-like environment.
- The installation site must be level, sufficiently stable and able to bear loads.
- There must not be any sources of electrical interference near the device.

7.2 Minimum Distances

The device must be installed with a minimum spacing of 150 mm from walls, ceilings or other devices.

Furthermore, it must be considered, that the vessel top plate and its built-in-parts can be easily lifted from the vessel and removed. This must be considered when calculating the distance between the device and the ceiling.

7.3 Power Supply

The in-house power supply to the device must meet the following requirements:

- 1 phase, L1 + N (neutral) + PE (earth)
- Type 230 V (± 5 %) / 50 Hz
- Type 200 to 230 V (± 5 %) / 60 Hz

The power supply must be constant.

The power supply must be secured on-site by means of an FI switch (RCD – Residual Current Device) of RCCB type B.

Steam generator (option)

The (optional) steam generators have separate power connections and are provided with the following connector:

- Type 6 kW: CEE16/5
- Type 10 kW: CEE32/5

The on-site power supply must meet the following requirements:

- 400 V (± 5 %)
- 50 / 60 Hz
- 3 Phases L1 + L2 + L3 + N (neutral) + PE (earth)
- Secured by means of FI switch (RCD – Residual Current Device) of RCCB type B.

For detailed information on the technical data, usage and maintenance requirements for the steam generator, see the separate documentation provided by the manufacturers. Read the manuals BEFORE commissioning and follow the instructions!

7.4 Water and Condensate

On site, the water supply of the device comes from tap water. The additional connection of an internal cooling water system or an optional, separate recirculating chiller is also possible.

If a cooling water system is available, the 3-way ball valves **01.41.01** (inlet) and **01.41.02** (outlet) installed on the device can be used to manually switch between tap water and chilled water.

ATTENTION

An incorrect position of the manual 3-way ball valves for tap water / chilled water can lead to overfilling or overflow of the on-site cooling circuit.

Tap water and chilled water

The on-site supply of tap water and, if applicable, chilled water must meet the following requirements:

- Constant water supply with a pressure of 2.0 ± 0.5 bar
- “Very soft” or “soft” water quality ($CaCO_3$ concentration 0 mmol L^{-1} to 1.5 mmol L^{-1})

ATTENTION

Cooling water additive containing alcohol can damage the components of the temperature control system.

Water outlet and condensate

Tap water / chilled water and condensate must be drained as follows:

- The drain must be heat resistant (max. 100 °C) and free from backpressure.
- The drain must not be in the immediate vicinity of the operator.

CAUTION

Hot water and/or steam can leak from the water and condensate outlet!

- The contaminated condensate must be drained safely and disposed of in an environmentally friendly manner.

WARNING

Health risk and environmental hazard due to contaminated condensate!

Hoses

- Use only pressure-resistant and intact hoses.
- Use only hoses with an appropriate diameter; an adapter may be used, if necessary.
- Secure hoses using hose clamps.

7.5 Process Gas

Depending on the selected gassing strategy, there exist up to three connections on the device for the process gasses air (compressed air), O_2 and N_2.

Irrespective of the number and type of gasses used, the on-site supply for each individual process gas must meet the following requirements:

- Constant gas supply at a pressure of 3.0 to 6.0 bar
- Gas(es) is/are dry, clean and free of oil and dust; (recommended) pre-filter: 10 µm
- Recommended compressed air quality as per DIN ISO 8573-1: Class 1,2,3,4

WARNING

Using contaminated gases carries a risk of explosion which may cause serious injuries and loss of property!

Depending on the configuration of the device, up to three mass flow controllers are installed.

ATTENTION

Use of oily or wet compressed air may lead to damage to the mass flow controller!

Hoses

- Use only pressure-resistant and intact hoses.
- Use only hoses with an appropriate diameter; an adapter may be used, if necessary.
- Secure hoses using hose clamps.

7.6 Exit Gas

Ensure the following on the house side:

- The exit gas is safely discharged by means of a suitable, gas-tight hose.
- The exit gas line is higher than the exit gas filter.
- The working environment is equipped with an adequate ventilation system, depending on the application.

7.7 Steam

The steam supply to the device is on the house side or via an optional integrated steam generator and must meet the following connection requirements:

- Constant steam supply at a pressure of 2.0 ± 0.2 bar
- Quality: steam must be of clean steam quality and can be guided through a filter with a filtration size of 5 micron.

Required amount of steam for each vessel size

Vessel size	vessel & filters for inlet air and exit gas	Periphery
15 L TV	≈ 8 kg/h	1 kg/h
30 L + 42 L TV	≈ 14 kg/h	1 kg/h

Water requirements for integrated steam generator (if available)

- Constant water supply at a pressure of at least 3 bar
- Water quality $CaCO_3$ concentration 0 mmol L^{-1} to max. 0.53497 mmol L^{-1}

For detailed information on the connection requirements as well as technical data, usage and maintenance of the steam generator, see the separate documentation provided by the manufacturer.

Read the manual before initial commissioning and follow the instructions given therein.

Hoses

- Use only pressure-resistant and intact hoses.
- Use only hoses with an appropriate diameter; an adapter may be used, if necessary.
- Secure hoses using hose clamps.

⚠ CAUTION

Escaping steam can lead to scalding and burns!

7.8 Safety Valves

⚠ CAUTION

If the safety valve of the vessel is triggered, steam, hot and/or contaminated liquid or dangerous gases can escape from the overpressure-venting pipe, depending on the process phase and vessel content of the bioreactor.

If the safety valve of the temperature control system is triggered, steam or hot water can escape depending on the process phase of the bioreactor.

In order to ensure that medium escaping from the vessel or the temperature control system is safely discharged when the safety valve is triggered, the following must be ensured on site:

- The outlets of the overpressure-venting pipes of the safety valves are equipped with suitable gas-tight, heat- and pressure-resistant hose or pipe lines. Their inner diameters must not be smaller than the inner diameters of the overpressure-venting pipes.
- The hose / pipelines are designed in such a way that the contents are safely discharged and disposed of in an environmentally friendly manner.
- The hose / pipe lines must not have any backpressure or may not exceed the following values:
  - Safety valve vessel: max. 15 % of the set pressure
  - Safety valve temperature control system: max. 10 % of the set pressure.

8 Before Cultivation

The following chapters describe the preparatory work before starting the cultivation process. This essentially comprises:

- Preparing the vessel and accessories:
  - Checking seals (O-rings) on built-in-parts and vessel
  - Mounting built-in-parts

ATTENTION

Using tools when mounting/removing built-in-parts including blanking plugs on the vessel and on the top plate can damage these and result in inseparable screw connections!

– Mount/remove built-in-parts by hand.

– Screw in (hand-tight) and loosen 19 mm blanking plugs with the hexagon socket spanner provided.

  - Filling the vessel
  - Preparing sensors and other accessories
- In situ sterilisation – general information

INFORMATION

The actual sterilisation processes are described in detail in the main chapter “Operation Touch Screen Software”.

WARNING

Any manipulation on a vessel with residual energy can lead to dangerous situations.

Before any manipulation, check the vessel pressure on the manometer and, if required, put the vessel into non-pressurised condition.

8.1 Securing the Position of the Device

Ensure that the device stands safely on its working site and cannot roll away before beginning any work.

⚠ CAUTION

Uncontrolled rolling of the device contains a risk of injury and loss of property.

Always lock the brakes of the swivel castors on the base frame!

8.2 Preparing the Vessel and Accessories

The vessel top plate must be lifted in order to be able to check and, if necessary, correct the fitting of the seal (O-ring) on the vessel top plate, the baffles and the position of the impellers. Depending on the application, this is also required for filling the vessel. To do this, the inlet air filter as well as the exit gas cooler with exit gas filter and inlet air filter must be removed.

The safety valve on the vessel top plate does not necessarily have to be removed. Depending on the type and length of the hose/pipe-line on the overpressure venting pipe of the safety valve installed by the operator, however, this might have to be removed.

Prior to in situ sterilisation, all required built-in-parts and accesso-ries such as inoculation needles, reagent bottles etc. have to be prepared accordingly. This also applies to all sensors used.

8.2.1 Uncoupling the Motor

The two cables for power supply and control of the motor are plugged into the motor when the device is installed and then re-main connected permanently. In routine operation, the motor merely needs to be coupled and uncoupled.

Prior to uncoupling the motor from the drive hub, ensure the follow-ing:

⚠ CAUTION

The motor is heavy! Work in pairs when coupling and uncou-pling the motor.

- The bioreactor is stopped, the system has been shut down and the device is switched off on the main switch.
- The vessel is de-pressurised

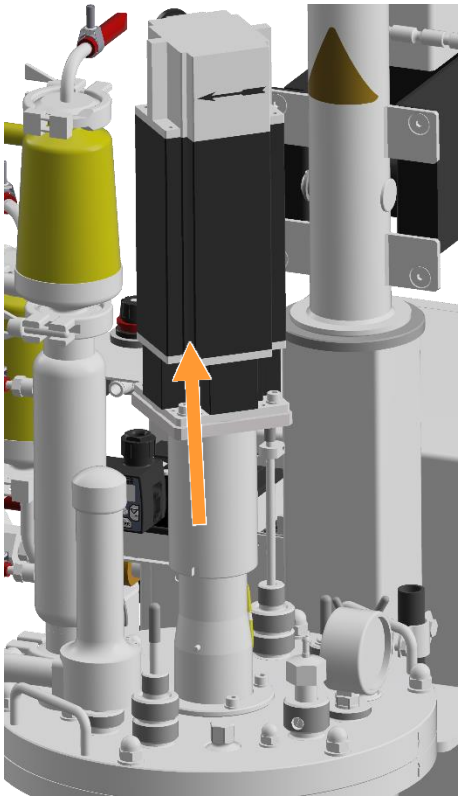
- The motor has cooled down

⚠ CAUTION

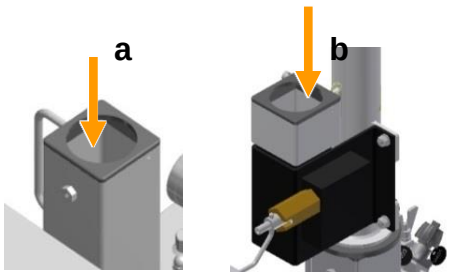
Touching the motor during operation or during the cool-down phase can cause slight burns.

Proceed as follows:

Procedure



1. Get a second person to help lift the motor. If necessary, lightly shake the motor to loosen it from the drive hub.



2. Do one of the following with the motor:

a) Place it in the holder on the central column.

Or, if necessary:

b) Place it in the holder of the lifting device for the vessel top plate.

8.2.2 Removing the Exit Gas Cooler with Filter and the Inlet Air Filter

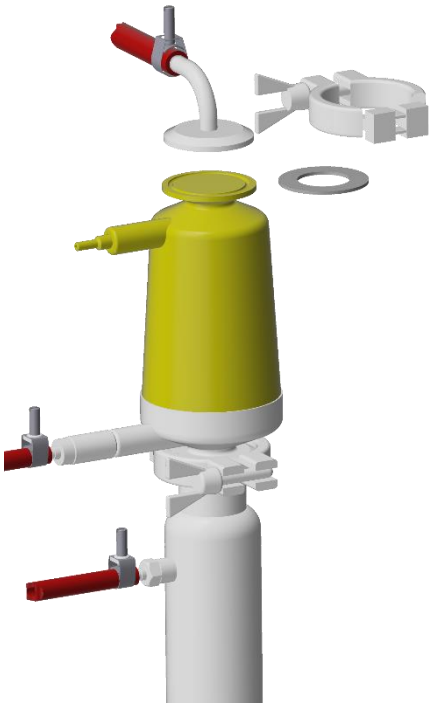
Before removing the vessel top plate, the inlet air filter as well as the exit gas cooler with exit gas filter must be removed from the vessel top plate.

Exit gas cooler and filter

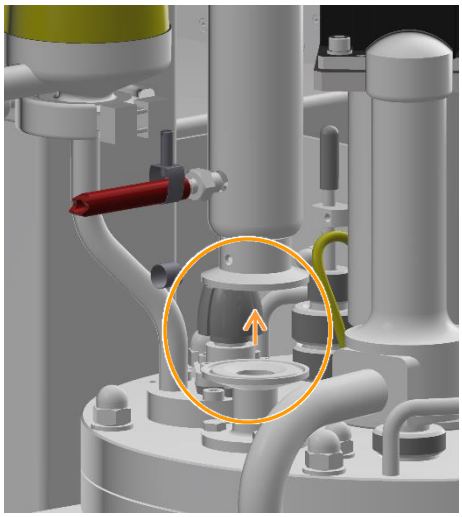
The exit gas cooler and exit gas filter can be removed as a unit. However, to do so, the exit gas hose line must be removed.

Proceed as follows:

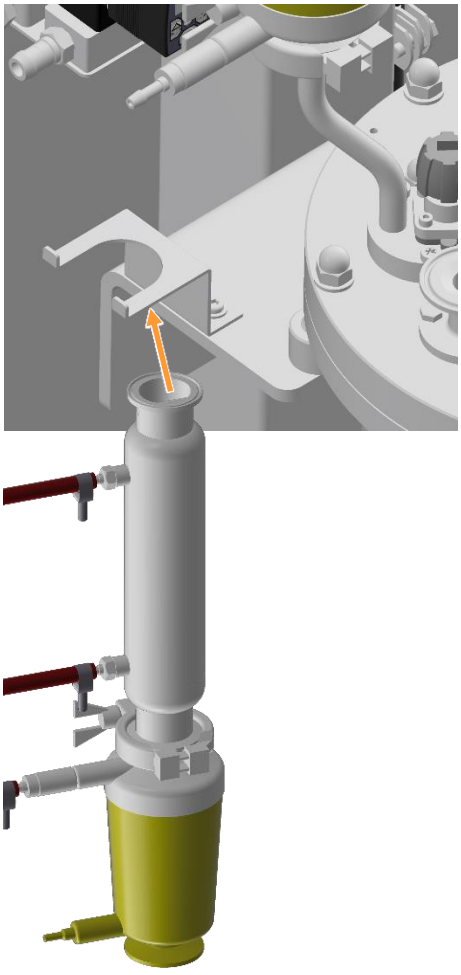
Procedure



1. Open the clamp between the exit gas filter and the exit gas hose.
2. Remove the clamp and flat gasket. Ensure that the two parts are not lost.
3. Remove the exit gas hose.
4. Remove the clamp and flat gasket between the exit gas cooler and connection flange on the vessel top plate in the same way and put them aside.



5. Remove the exit gas cooler.



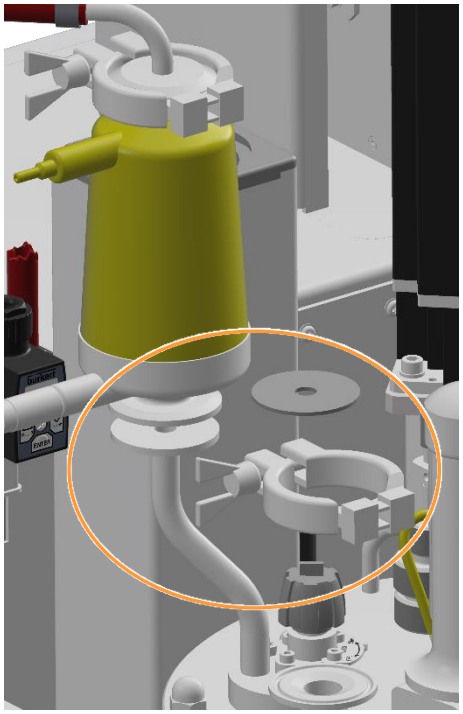
6. Turn over the exit gas cooler and place it in the holder on the vessel mounting.

Inlet air filter

The inlet air/gas hose line does not necessarily have to be removed here.

Proceed as follows:

Procedure



1. Open the clamp between the inlet air filter and connection flange on the vessel top plate.
2. Remove the clamp and flat gasket. Ensure that the two parts are not lost.
3. Remove the inlet air filter.

INFORMATION

Due to its light weight, the inlet air filter does not require a special holder. It can hang loosely on the hoses.

8.2.3 Removing the Vessel Top Plate

In order to check O-rings on certain built-in-parts and on the vessel top plate itself, it is necessary to remove it.

Before you begin, ensure the following:

- The bioreactor is stopped, the system is shut down and the device is switched off at the main switch
- The vessel is non-pressurised.
- Any cable or hose connections between vessel top plate and basic unit or instrumentation cabinet are disconnected

ATTENTION

Cables or hoses connecting the vessel or its built-in-parts with the instrumentation cabinet or frame can break, if they are not disconnected before removing the vessel top plate.

The heavy vessel top plate can either be lifted manually or with an appropriate lifting device. In both cases two people are needed.

CAUTION

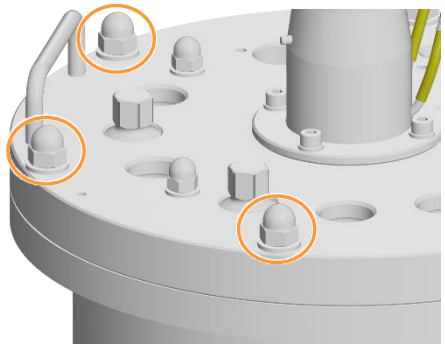
The vessel top plate is heavy. Risk of injuries due to inappropriate handling of the vessel top plate!

INFORMATION

The use of the optional lifting device of the manufacturer of the device is recommended due to the heavy weight of the vessel top plate. Assembly, Operation and Maintenance of the lifting device are described in detail in the separate user manual.

Proceed as follows:

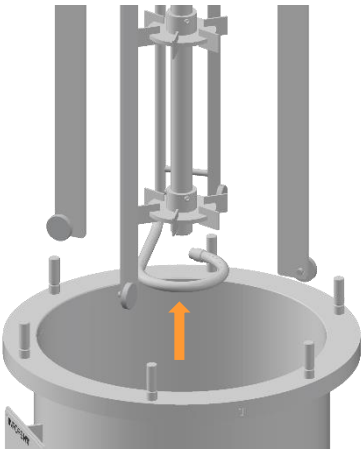
Procedure



1. Loosen the capped nuts (M10) of the vessel fixing using a wrench (17 mm).
2. Remove the capped nuts and the metal washers.
3. Disconnect any cable or hose connections between vessel top plate and basic unit or instrumentation cabinet.

Manual procedure (2 people)

4. Carefully lift the vessel top plate horizontally out of the vessel holding it on both handles.



Ensure that the baffles, the sparger or the stirrer do not come in contact with the inside of the vessel.

ATTENTION

Knocking built-in components against the inside of the vessel can cause micro scratching. In these circumstances, the certified vessel finish (inside) can no longer be guaranteed.

5. Carefully place the vessel top plate on its lid-side on an appropriate surface and ensure it cannot tilt over or fall down.

ATTENTION

The stirrer shaft is delicate! A distorted stirrer shaft leads to unbalanced mass during operation which can damage the mechanical seal and the bearings in the hub of the drive shaft.

8.2.4 Checking Impellers, Baffles and Top Plate Seal

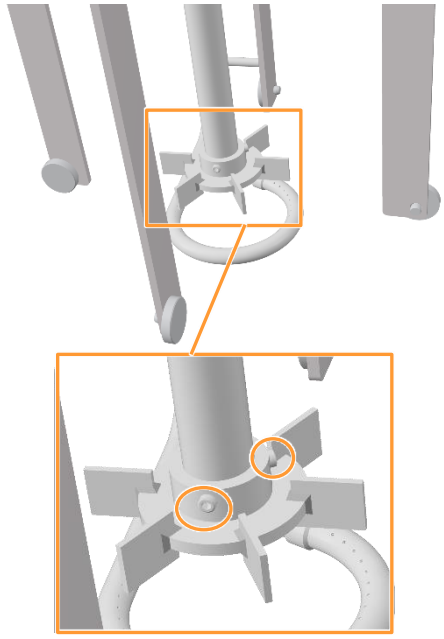
Before fitting the vessel top plate, the correct seat of the impellers, baffles and the top plate seal must be checked.

Stirrer shaft and impellers

ATTENTION

Manipulations on the mechanical seal can damage it!

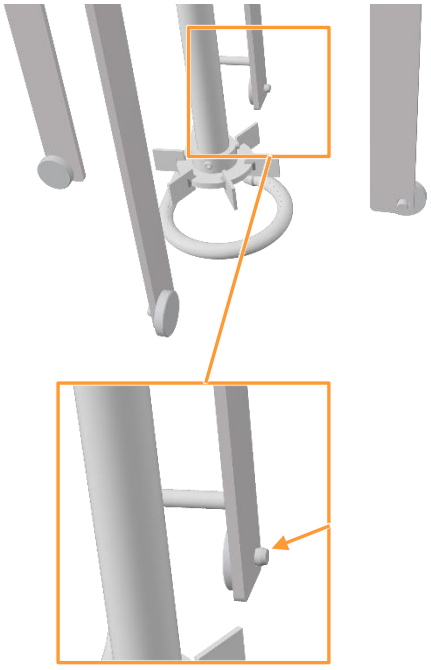
Procedure



1. Ensure that the impellers on the stirrer shaft are set to the desired height and sit tightly.

   If necessary, loosen the grub screws (M5x6, 2 pc. per impeller) on the impellers, correctly position the impellers and retighten the grub screws.

Baffles



2. Ensure that all four spacers are placed on the baffles and fit tightly.

3. Ensure that the four baffles are correctly affixed to the vessel top plate: Washers are fitted and cap nuts (M8) are tightened.

Top plate seal (O-ring)

4. Ensure the O-ring (top plate seal) is intact and firmly seated in the groove.

8.2.5 Filling the Vessel and Mounting the Top Plate

It's easiest to fill the vessel without the vessel top plate. In this case, all vessel built-in-parts such as sensors, which are to be mounted in the Ingold nozzles, must be prepared and mounted first.

Depending on the medium used and user requirements, the vessel is either filled with a heat-resistant medium or with water. For details, see the chapter "In Situ Sterilisation - General Information".

If the vessel top plate is mounted, the vessel can also be filled via port in the top plate.

The vessel top plate can be lifted and lowered either manually or by using a suitable lifting device. This is a two person job in either case.

INFORMATION

We recommend using the device manufacturer's optional lifting device due to the weight of the vessel top plate. Assembly, operation and maintenance of the lifting device are described in detail in the separate operating manual.

CAUTION

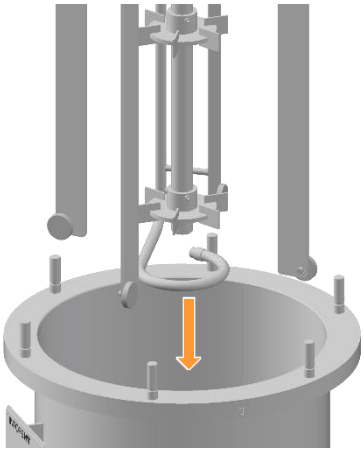
The vessel top plate is heavy. There is a risk of injury in case of incorrect handling!

Manual procedure (2 people!)

To mount the vessel top plate, proceed as follows:

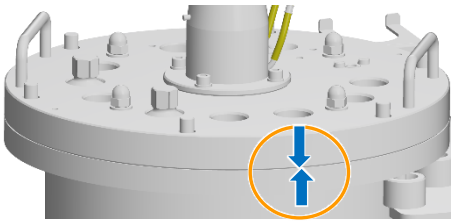
Procedure

1. Lift the vessel top plate on the two handles.



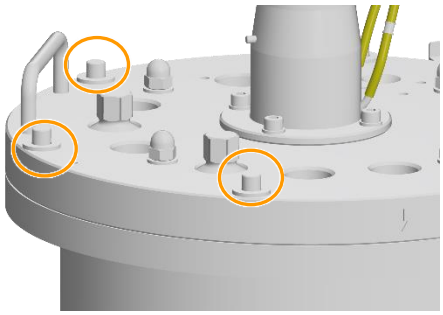
2. Align the vessel top plate with the centre above the vessel and lower it slowly.

Ensure that baffles, sparger and stirrer shaft do not hit the inside of the vessel.



3. Fit the studs on the vessel flange into the threaded holes in the vessel top plate.

Two engraved arrows on the vessel top plate and on the flange of the vessel indicate the correct position of the vessel top plate.

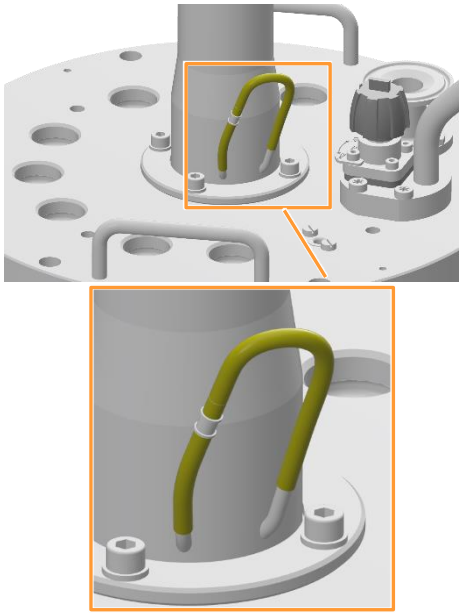


4. Fit the washers.

5. Fit the cap nuts (M10) and tighten them crossways with a wrench (17 mm).

8.2.6 Checking Lubrication of the Mechanical Seal

The mechanical seal must always be lubricated. This can easily be checked.



The silicone hose on the flange of the drive hub must be completely filled with glycerine, top it up as necessary. For details see the main chapter “Cleaning and Maintenance”, chapter “Lubricating the Mechanical Seal”.

ATTENTION

A mechanical seal, which has not been adequately lubricated is destroyed when running dry!

8.2.7 Mounting the Manometer

The manometer **08.30.01** for displaying the vessel pressure must be mounted in a 19 mm port in the vessel top plate prior to sterilisation.

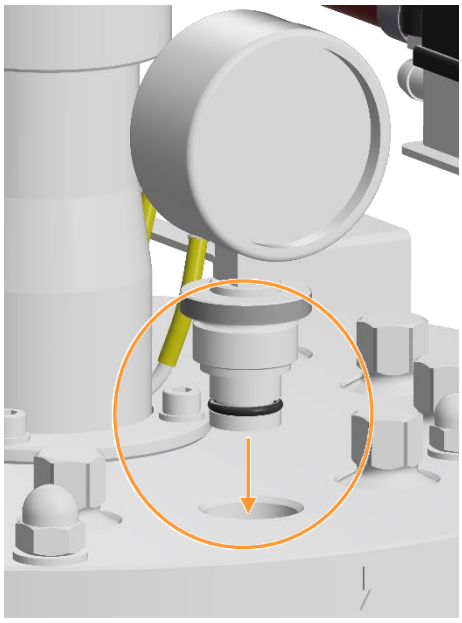
ATTENTION

The steel membrane of the manometer is very delicate and can be damaged by friction or knocks from hard objects.

Carefully mount the manometer by hand!

Proceed as follows:

Procedure



1. Carefully insert the manometer with fixed O-ring into the port.
2. Manually screw down the manometer.
   Ensure that the manometer is screwed in straight.

8.2.8 Mounting the Safety Valve

The safety valve, which secures the vessel against excessive overpressure, must always be mounted.

WARNING

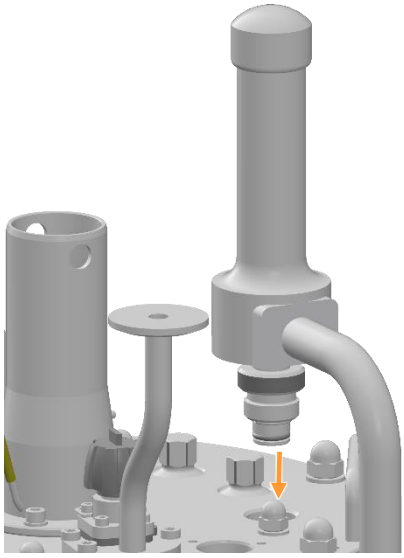
If the safety valve is not mounted, possible overshoot of permitted pressure in the vessel cannot be relieved in a safe manner.

This may lead to bursting or slew round of pressurised components!

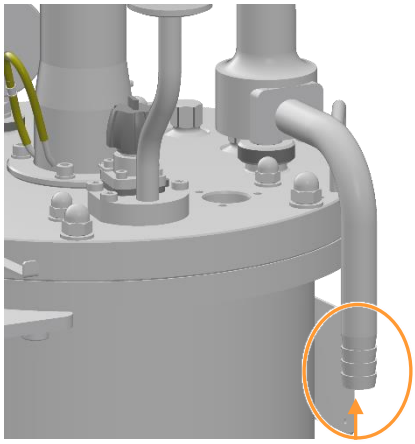
Detailed information about the safety valve can be found in the separate documentation of the safety valve.

Proceed as follows:

Procedure



1. Insert the safety valve with fixed O-ring into the 19 mm port and screw tight by hand.



2. Ensure that the operator-side hose or pipe line is connected to the overpressure-venting pipe, connect it, if necessary.

   For details refer to chapter “Safety Valves” in the main chapters “Setup and Function” and “Installation and Initial Operation”.

3. Ensure that the safety valve is closed. If necessary, turn the lifting device clockwise (CLOSED engraving is visible).

   Refer to main chapter “Setup and Function” chapter “Safety Valve Vessel” for details about the lifting device.

8.2.9 Preparing the Reagent Bottles

Reagent bottles are autoclaved separately together with inoculation needles, the antifoam sensor as well as any push valves and/or the block valve **13.16.02 / 13.16.04** of the resterilisable feed line. The bottle that is filled aseptically with the stock culture (inoculum) shortly before inoculation is also autoclaved separately and prepared in the same way as the reagent bottles.

Reagent bottles are fitted with a filter for pressure equalisation. Pump hoses are delivered separately. Silicon hoses or, depending on on-site specifications, weldable hoses for sterile hose connections are not included in the scope of delivery.

ATTENTION

Damaged hoses and/or clogged filters can lead to undesirable pressure ratios in the reagent bottles.

– Each reagent bottle is fitted with an open pressure equalisation line and a clean and dry filter.
– Use only clean and intact hoses and affix these properly.

The following section describes in detail how a reagent bottle with silicone hose and pump hoses is prepared for separate autoclaving and subsequent connection to the pumps.

Proceed as follows:

Procedure

1. Unscrew the bottle lid.
2. Fit a piece of silicone hose onto one of the two hose connections inside the bottle lid.

   Choose the length so that the hose end does not touch the bottom of the bottle. Otherwise, the hose may get sucked against the bottom and no longer be able to pump liquid.

INFORMATION

Alternatively, the hose end can be cut at an angle. In this case, the hose end can touch the bottom of the bottle.

3. Secure the hose with a cable tie.

Before Cultivation

4. Screw on the bottle lid.

   Ensure the rubber seal between bottle neck and lid sits and seals correctly.

5. Fit a long piece of silicone hose onto the upper end of the hose connection on the outside of the bottle lid.

   Choose the length of the hose so that it reaches from the reagent bottle to the pump without tension or sharp kinks.

6. Fit a short piece of silicone hose onto the second hose connection on the outside of the bottle lid.
7. Fit the filter on a short piece of hose.

8. Secure the hoses with cable ties.
9. Before autoclaving, thoroughly rinse the hose of the reagent bottle with distilled water.
10. Label the reagent bottle in accordance with its content.
11. Depending on the application: Fill the reagent bottle and close with the lid, or fill reagent bottle under sterile conditions after autoclaving, if necessary.

ATTENTION

Use of highly corrosive hydrochloric acid HCl as reagent causes damage to components made of stainless steel such as the ports in the vessel top plate and the actual vessel top plate.

Use only non-corrosive acids such as phosphoric acid.

INFORMATION

Fill reagent bottles with heat-resistant reagents only. Sterilise non-heat-resistant feed solution separately and only transfer it to the reagent bottle after autoclaving.

12. Use a hose connector to connect the silicone hose with a piece of pump hose and another piece of silicone hose.

    The length of the entire hose must be chosen so that it reaches from the reagent bottle via the pump to the inoculation needle etc. in the vessel top plate without tension or sharp kinks.
13. Connect the hose to the inoculation needle etc.
14. Secure all hose connections with cable ties.
15. Loosely cover the filter and inoculation needle etc. with aluminium foil.
16. Clamp off the hose with the clamp.
17. Autoclave everything together at 121 °C for e.g. 30 to 60 minutes.

8.2.10 Preparing the Inoculation Needles

Inoculation needles are separately autoclaved along with the reagent bottles and where appropriate, with the seed bottle for later inoculation.

Before Cultivation

Proceed as follows:

Procedure

1. Carefully remove the protective caps from the inoculation needle.

   The figure to the left serves as an example for any inoculation needle.
2. Keep the septum collar ready for equipping the port in the vessel top plate.

3. Connect the hose line of the prepared reagent bottle to the inoculation needle.

   For details refer to chapter “Preparing the Reagent Bottles”.
4. Secure all hose connections with cable ties.
5. Lightly cap the filter on the reagent bottle with a little aluminium foil and wrap the inoculation needle in aluminium foil or fit the needle into a sterile housing.
6. Clamp off the reagent hose line with a hose clamp.
7. Autoclave the whole assembly together for e.g. 30 to 60 minutes at 121 °C.

After autoclaving and enough time to cool down, the hoses on the reagent bottles must be connected to the pumps, refer to chapter “Preparing the Pumps” for details.

The inoculation needles are screwed into the ports in the vessel top plate AFTER in situ sterilisation, which were equipped with septum collars and septa BEFORE the in situ vessel sterilisation.

Proceed as follows:

Procedure

1. Loosen the blanking plug and unscrew it from the septum collar in the port.

> **INFORMATION**
>
> A few drops of 70% ethanol can be placed on the septum surface as an additional protection against contamination.

2. Remove the aluminium foil or sterile housing from the inoculation needle.
3. Instantly pierce the needle through the septum.
4. Screw the inoculation needle into the septum collar.

The reagent and pump hoses can be filled now, refer to chapter “Preparing the Pumps” for details.

Adding of the inoculum using an inoculation needle is described in main chapter “Cultivation”, chapter “Inoculation with Inoculation Needle”, too.

8.2.11 Preparing the Push Valves

Prior to in situ sterilisation, single or 4 inlet push valves must be autoclaved together with the reagent bottles. After autoclaving and sufficient cool-down time, the reagent bottles are connected to the pumps and the closed (!) push valve is screwed into the port in the vessel top plate.

The subsequent in situ sterilisation has the effect that the part of the push valve that was exposed after autoclaving is now sterilised.

8.2.11.1 Autoclaving

To prepare a push valve for use, proceed as follows:

Procedure

1. Prepare the reagent bottle as described in chapter “Preparing Reagent Bottles”.
2. Connect the reagent bottle to the push valve.

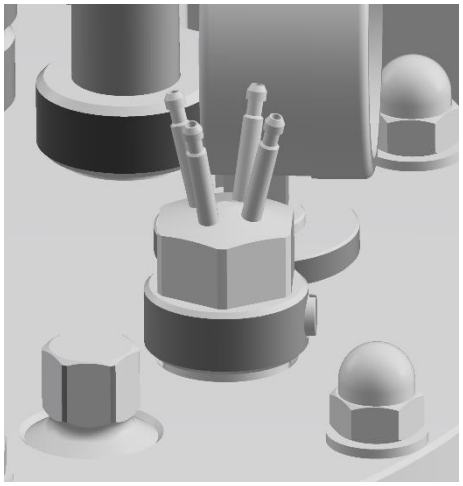
   When using a 4 inlet push valve, up to four reagent bottles can be connected.
3. Close any unused connection on the 4 inlet push valve.
4. Ensure that the push valve is closed, close it if necessary.

5. Secure the hoses with cable ties.
6. Lightly cover the filter of the reagent bottle(s) and the push valve with aluminium foil.
7. Pinch off the hoses with clamps.
8. Autoclave everything together at 121 °C for e.g. 30 to 60 minutes.

8.2.11.2 In situ Sterilisation

After autoclaving and sufficient cool-down time, the following work has to be carried out:

Procedure



1. Manually screw the (closed!) push valve into the 19 mm port in the vessel top plate.

   The figure on the left is an example showing a mounted 4 inlet push valve without hoses.

2. Connect the reagent bottle(s) to the pump(s).

   For details, see the chapter “Pumps”.

8.2.11.3 Cultivation

After in situ sterilisation, the push valve has to be opened. Following this, the hose of the corresponding pump is filled. For details, see the chapter “Pumps”.

8.2.12 Preparing the Resterilisable Feed Line

If a resterilisable feed line is present, its components must be prepared accordingly.

For details on the individual steps see the chapter “Resterilisable Feed Line” of the main chapter “Options”.

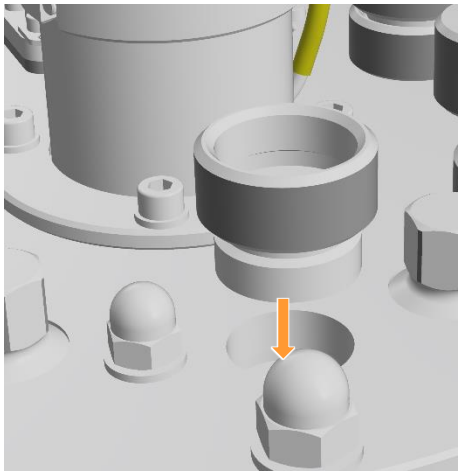
8.2.13 Equipping the Ports with Septa (Piercing Membranes) and Collars

If working with the piercing method for later inoculation, addition of corrective reagent, antifoam reagent and nutrient solution, then the ports in the vessel top plate must be equipped with septa and septum collars. This also applies to the port, where the antifoam sensor is to be mounted.

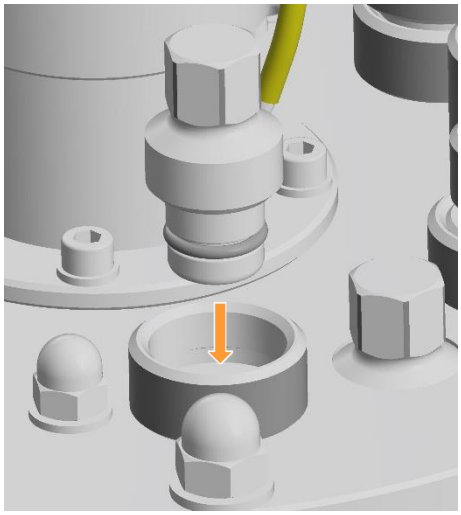
Proceed as follows:

Procedure

1. Loosen and remove the blanking plug using the hexagon socket spanner provided with the device.
2. Insert the septum into the port.



3. Screw the septum collar into the port by hand.



4. Screw the blanking plug with fixed O-ring into the septum collar by hand.

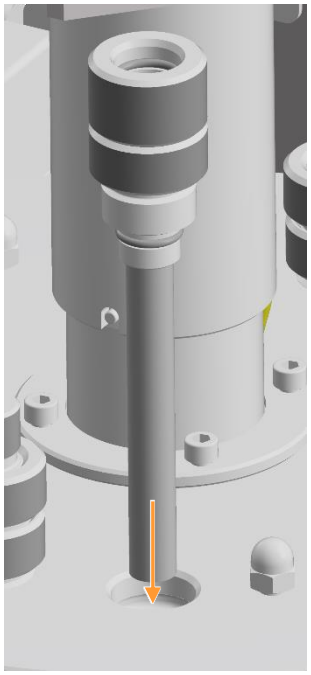
   Tighten it with the hexagon socket spanner hand-tight.

8.2.14 Mounting the Vessel Light

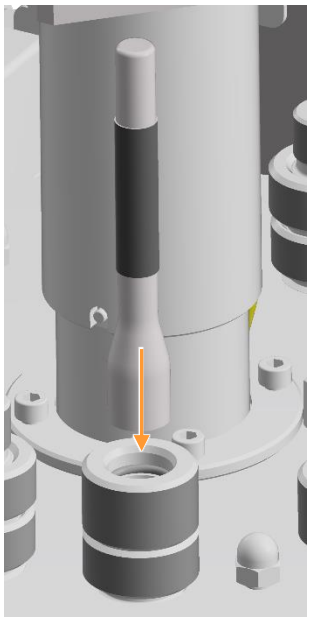
If present, the vessel light is mounted in a 19 mm port in the vessel top plate.

Proceed as follows:

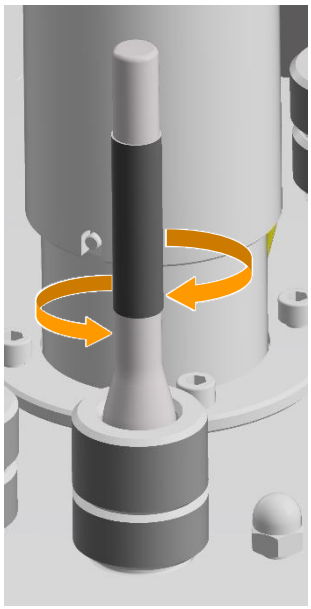
Procedure



1. Insert the glass lens in the threaded housing with a fixed O-ring into the 19 mm port and screw it in by hand.



2. Place the torch in the clamping screw.



The torch can be switched on or off by turning it clockwise/counter-clockwise.

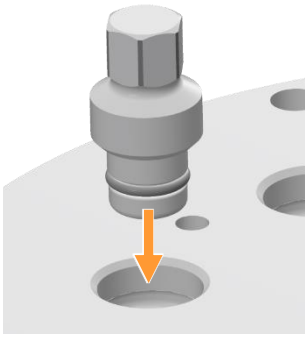
8.2.15 Closing the Unused Ports and Nozzles

All unused ports and nozzles in the vessel top plate and on the vessel be closed with blanking plugs before sterilisation.

Proceed as follows:

Procedure

Blanking plug vessel top plate

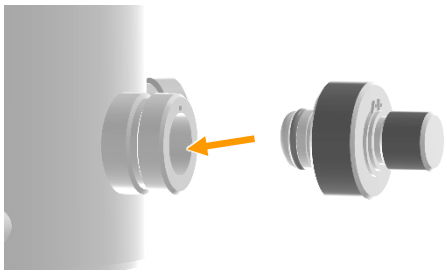


1. Screw the blanking plug with fixed O-ring into the 19 mm port by hand.

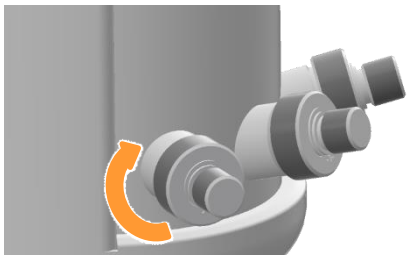
2. Tighten the blanking plug hand tight using the hexagon socket spanner provided with the device.

Blanking plugs Ingold nozzles

Procedure



1. Insert the blanking plug with fixed O-ring into the Ingold nozzle.



2. Screw the blanking plug hand tight.

8.2.16 Preparing the Pumps

8.2.16.1 Calibrating the Pumps

If need be, pumps should be calibrated before beginning a cultivation process. This provides an accurate value for the actual pumped volume of liquid delivered in mL, respectively in g.

The pumps must be calibrated before autoclaving the reagent bottles and before in situ sterilisation. For details of the procedure refer to the main chapter “Operation Touch Screen Software”, chapter “Calibrating the Pumps”.

8.2.16.2 Connecting the Pumps to the Reagent Bottles

The reagent bottles must be connected to the pumps after autoclaving and enough time to cool down.

Proceed as follows:

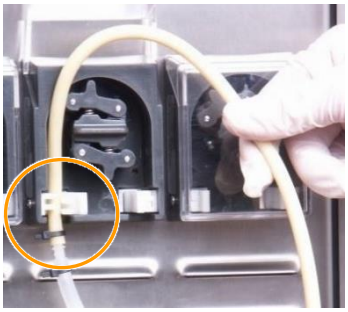
Procedure

1. Place the reagent bottle onto the tray below the instrumentation cabinet.
2. Fold up the pump cover.

Observe the direction of rotation (clockwise) of the pumps:

3. Thread the pump hose from left to right into the clamps and around the pump head.

4. Press the left clamp inwards and insert the pump hose at the same time.
5. Release the clamp.



The pump hose is fixated by the left clamp now.

6. Lay the pump hose around the pump head and lightly push it in.

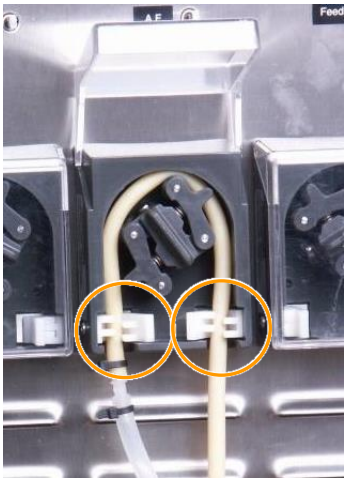
7. Slowly turn the pump head clockwise with one hand and guide the hose with the other hand at the same time.

⚠ CAUTION

Operating the pump electrically and inserting the pump hose at the same time can lead to bruising the fingers and damage to the pump hose!

Always turn the pump head with the hand when inserting the pump hose.

8. Press the right clamp inwards and insert the pump hose at the same time.
9. Release the clamp.

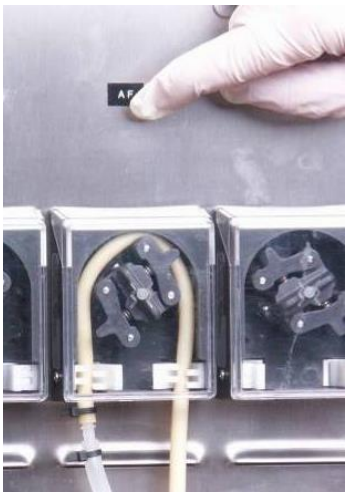


The pump hose is threaded in and fixated by both clamps now.

10. Fold down the pump cover.

8.2.16.3 Filling the Pump and Reagent Hoses

The pump and reagent hoses can either be filled using the rocker switches on the instrumentation cabinet or by pressing the corresponding buttons in the touch screen software for manual or time-controlled filling.



Filling via rocker switches

Proceed as follows:

- Tip the rocker switch to the right side: the pump runs forwards (clockwise), liquid is pumped into the vessel.
- Tip the rocker switch to the left side: the pump runs backwards (counter-clockwise), liquid is pumped back into the reagent bottle.

Filling via touch screen software

For details about filling via touch screen software refer to the main chapter „Operation Touch Screen Software", chapter "Filling and Emptying the Pump Hoses".

8.2.17 Preparing the Sensors

The sensors available as standard include the temperature, pH, pO_2 and antifoam sensors. These sensors must be prepared appropriately before they are used. This might include calibration and autoclaving, mounting and connection. This work is described in the following sections.

The sensors for measuring level, pressure, turbidity, redox, pCO_2, permittivity and O_2 / CO_2 in the exit gas are described in the corresponding chapters of the main chapter "Options".

Commissioning, maintenance and use of the sensors from third-party manufacturers are described in detail in the sensor manufacturers' separate documentation. Strictly follow the instructions therein!

8.2.17.1 Preparing the Antifoam Sensor

The antifoam sensor must be equipped with a silicone hose and a reagent bottle and wrapped up in aluminium foil and autoclaved like inoculation needles.

The antifoam sensor should be adjusted in its mounting depth before separate sterilisation in the autoclave. It should be mounted

too low rather than too high. Pulling it up during cultivation carries a much lower risk of contamination than pushing it down.

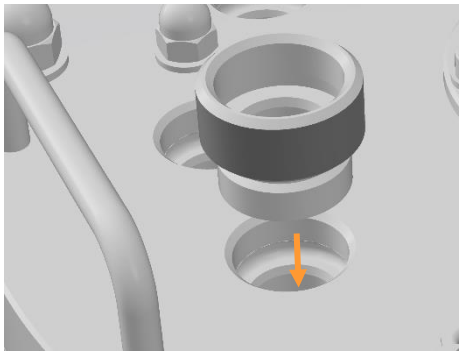
ATTENTION

If the antifoam sensor is fixed too tightly in the clamping adapter, or the mounting depth of the sensor is adjusted with a tight hollow screw, the insulation of the sensor may be damaged!

Preparation for autoclaving

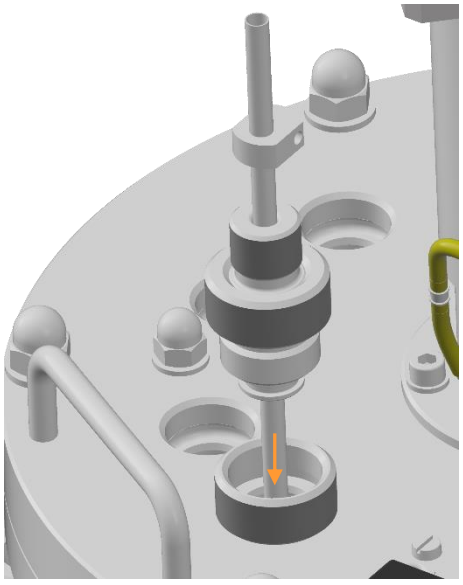
To prepare the antifoam sensor before autoclaving, proceed as follows:

Procedure

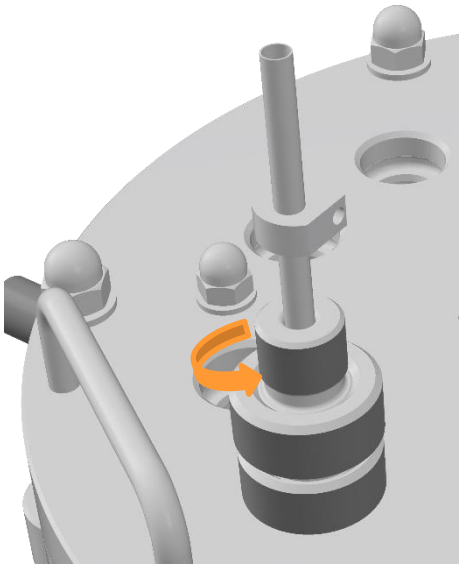


1. Screw the septum collar by hand into the 19 mm port in the vessel top plate.

2. Remove the protective caps from the antifoam sensor.

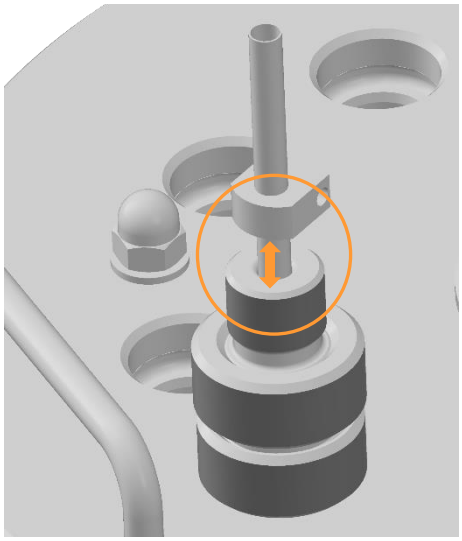


3. Screw the antifoam sensor by hand into the septum collar.



4. Carefully loosen the clamping screw by hand.

5. Adjust the antifoam sensor to the desired mounting depth.



Ensure that the antifoam sensor head does not touch the hollow screw, otherwise a constant signal will be generated when the sensor is connected.

6. Carefully tighten the hollow screw by hand.
7. Loosen and remove the antifoam sensor from the septum collar.
8. Loosen and remove the septum collar and put aside for later use.
9. Connect the antifoam sensor with a reagent bottle filled with antifoam agent and sterilise in the autoclave.

   For details refer to chapter “Preparing the Reagent Bottles”.

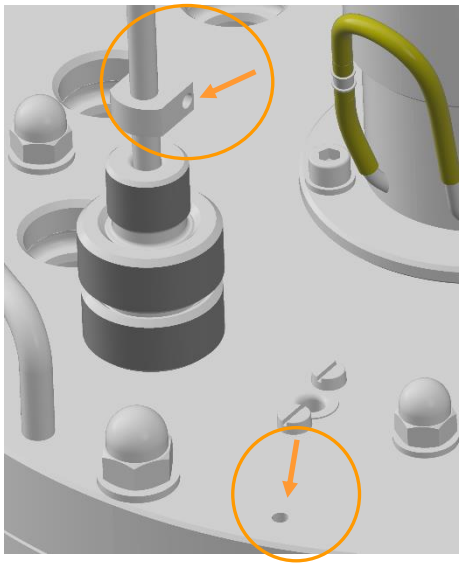
8.2.17.2 Mounting the Antifoam Sensor and Connecting the Sensor Cable

Proceed for the mounting (piercing through the septum) with the antifoam sensor the same way as with an inoculation needle after separate autoclaving and after in situ vessel sterilisation.

Refer to chapter “Preparing the Inoculation Needles” for details.

To connect the antifoam sensor cable, plug in the banana connectors as follows:

Procedure



1. Insert the red banana connector into the lateral hole of the antifoam sensor.
2. Insert the black banana connector into the ground connection in the vessel top plate.

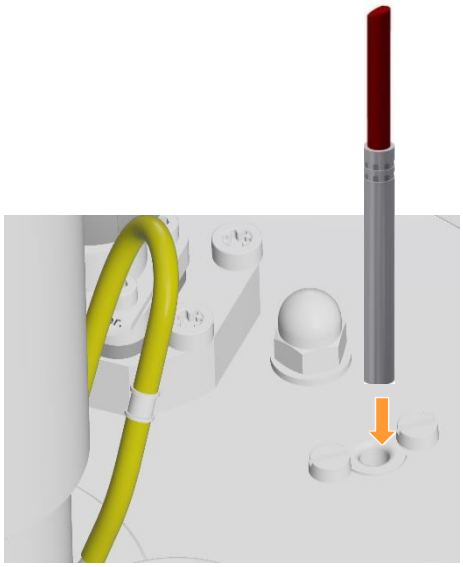
8.2.17.3 Mounting the Temperature Sensor

The mounting of the temperature sensor varies depending on the size of the vessel. For vessels with 15 L and 30 L TV, the temperature sensor does not have a plug connection. For vessels with 42 L TV, the temperature sensor is mounted in an Ingold nozzle.

Proceed as follows:

15 L and 30 L TV

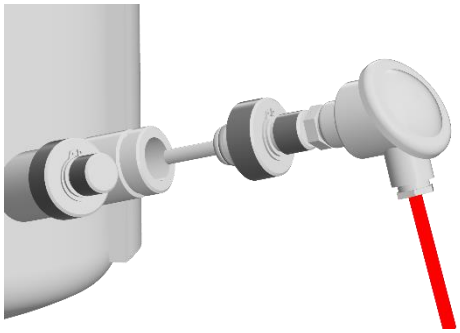
Procedure



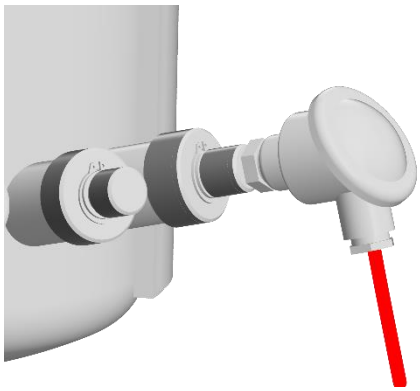
1. Insert the temperature sensor up to the stop (which can be felt) in the immersion pocket in the 10 mm port in the vessel top plate.

42 L TV

Procedure



1. Insert the temperature sensor (with fixed O-ring on the screw-in socket) in the Ingold nozzle.



2. Manually tighten the coupling nut clockwise and straighten the sensor at the same time.

   Ensure that the temperature sensor is straight and sits neatly.

8.2.17.4 Calibrating the pH Sensor

The calibration of a pH sensor must always be performed before the sterilisation. The calibration is described in detail in the chapter “pH Sensor Calibration” of the main chapter “Operation Touch Screen Software”.

INFORMATION

If the pH sensor has already been calibrated externally, the bioreactor will use this data and there is no need for calibration on the operating panel. This only applies to digital pH sensors.

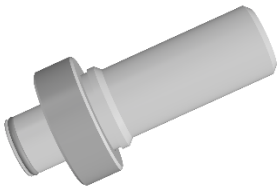
8.2.17.5 Mounting and Connecting the pH Sensor

The pH sensors, which vary depending on the pH measurement system used, are supplied with a suitable insertion housing for mounting in the Ingold nozzle. The insertion housings serve as sensor adapters and also protect the sensors from physical damage.

Insertion housings

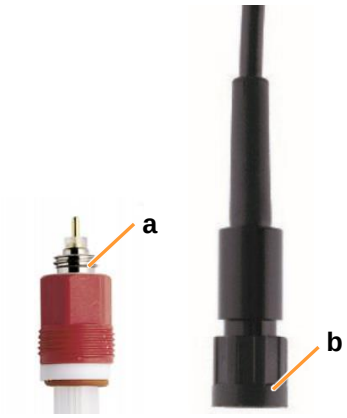
The pH sensors manufactured by METTLER are supplied with the suitable insertion housing of the type InFit 761 with cable kink protection.

The pH sensors manufactured by HAMILTON are supplied with the insertion housing of the type Flexifit U Bio.



The sensor and cable connections of the pH sensors differ depending on the pH measurement system used.

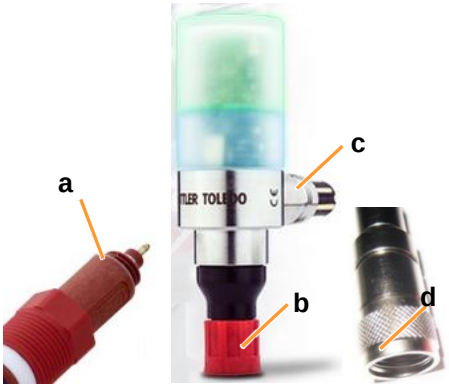
Sensor and cable connections



METTLER analogue Type 405-DPAS-SC-K8S/120	Sensor head connection (a)	K8S
	Cable bushing (b)	AK9

ATTENTION

The sensor cable shield can be damaged by buckling or twisting. This may lead to faulty measurements.

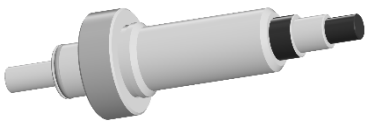


METTLER digital Type InPro 3253i	Sensor head connection (a)	ISM
	Cable bushing (d)	VP8
Head transmitter M100	Plug connection for sensor (b)	
	Plug connection for cable (c)	

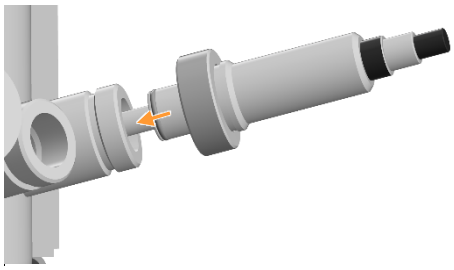
HAMILTON digital Type Easyferm Plus ARC	Sensor head connection (a)	VP8
	Cable bushing (b)	VP8

Proceed as follows:

Procedure



1. Insert the sensor into the insertion housing according to the sensor manufacturer's guidelines.



2. Insert the sensor into the Ingold nozzle and tighten it manually using the coupling nut.

3. If applicable, fit the cable kink protection according to the manufacturer's specifications prior to connecting the cable.

4. Connect the sensor cable.

All information on safety, use, maintenance and technical data of the sensors and insertion housing is available in the separate documentation from the sensor manufacturers.

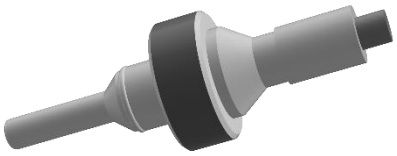
8.2.17.6 Calibrating the pO_2 Sensor

A 1-point calibration to 100 % is usually sufficient for exact measurement and should be carried out before each cultivation. If required, a 2-point calibration to 100 % and 0 is also possible.

The calibration is described in main chapter "Operation Touch Screen Software", chapter "pO_2 Sensor Calibration".

8.2.17.7 Mounting and Connecting the pO_2 sensor

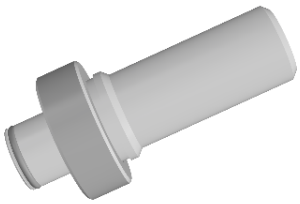
The pO_2 sensors, which vary depending on the pO_2 measurement system used, are supplied with a suitable insertion housing for mounting in the Ingold nozzle. The insertion housings serve as sensor adapters and also protect the sensors from physical damage.



Insertion housings

Analogue pO_2 sensors manufactured by METTLER are designed in such a way that they can be directly mounted in the Ingold nozzles.

Digital pO_2 sensors manufactured by METTLER are supplied with the suitable insertion housing of the type InFit 761 with cable kink protection.

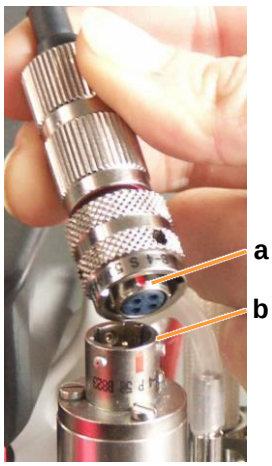


The pO_2 sensors manufactured by HAMILTON are supplied with the insertion housing of the type Flexifit U Bio.

The sensor and cable connections of the pO_2 sensors differ depending on the pO_2 measurement system used.

Sensor and cable connections

METTLER analogue Type InPro 6820/25/080 (amperometric, polarographic)	Sensor head connection (a)	T-82
	Cable bushing (b)	T-82



ATTENTION

The sensor cable shield can be damaged by buckling or twisting. This may lead to faulty measurements.

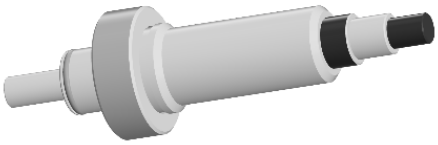
Before Cultivation

METTLER digital Type InPro6860i	Sensor head connection (a)	VP8
	Cable bushing (b)	VP8

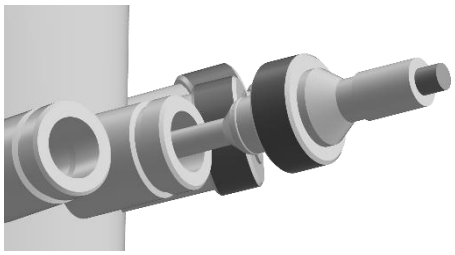
HAMILTON digital Type Visiferm DO ARC	Sensor head connection (a)	VP8
	Cable bushing (b)	VP8

Proceed as follows:

Procedure



1. Insert the sensor into the insertion housing according to the sensor manufacturer's guidelines.



2. Insert the sensor into the Ingold nozzle and tighten it manually using the coupling nut.

3. If applicable, fit the cable kink protection according to the manufacturer's specifications prior to connecting the cable.

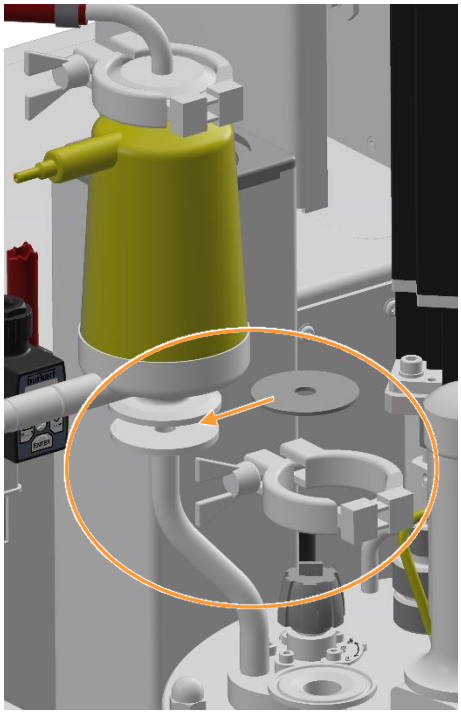
4. Connect the sensor cable.

All information on safety, use, maintenance and technical data of the sensors and insertion housing is available in the separate documentation from the sensor manufacturers.

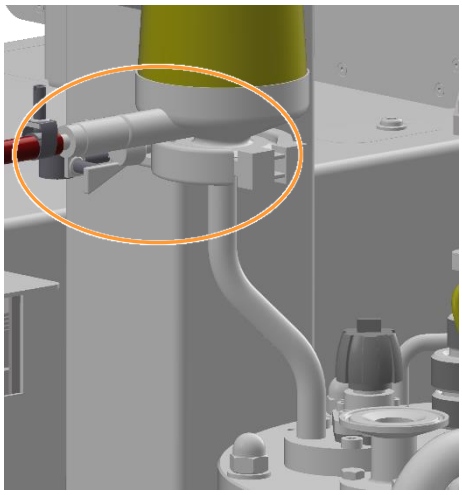
8.2.18 Mounting the Exit Gas Cooler and Filter and the Inlet Air Filter

To remount the inlet air filter and the exit gas cooler with exit gas filter, proceed as follows:

Procedure



1. Place the flat gasket and flange of the inlet air filter flush on the flange of the vessel top plate.



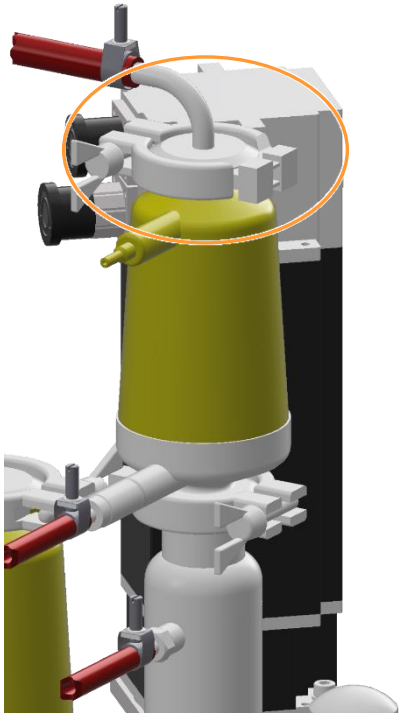
2. Place the clamp around both flanges, close and screw tight.

3. Remove the exit gas cooler from the holder and turn it around.

Before Cultivation

4. Place the flat gasket and exit gas cooler onto the flange on the vessel top plate in the same way as the inlet air filter and secure them with a clamp.

5. Place the flat gasket and flange of the exit gas hose flush on the flange of the exit gas filter.



6. Secure the exit gas hose with a clamp.

8.2.19 Checking the Inlet Air/Gas and Exit Gas Lines and Filters

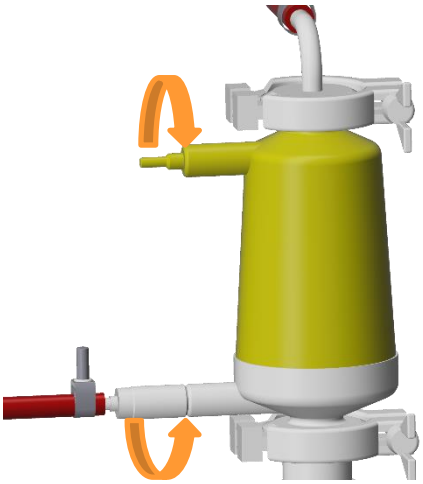
A blocked inlet air or exit gas line or clogged filters may result in poor venting/gassing of the culture or even completely interrupting it. This leads to overpressure in the vessel, which may be released in a non-sterile manner via leaky vessel connections and gaskets.

A humid/wet exit gas filter may get colonised by microorganisms which are growing through the exit gas line. This may contaminate the culture.

Therefore, check and ensure the following points:

- The air supply is correctly installed and turned on.

  The air supply must be turned on throughout the vessel sterilisation process so that no vacuum occurs during the cooling phase in the vessel sterilisation process.
- The filters for inlet air and exit gas are clean and dry. They are fitted correctly.



- Unused twist valves on both filters are closed.

  Close them by turning them clockwise as necessary.
- Twist valves with hose connections to inlet air filter and exit gas filter are open.

  Open them by turning counter clockwise as necessary.
- All hoses sit neatly and are secured with hose clamps.
- All hoses are intact; they are neither kinked nor damaged.

8.2.20 Coupling the Motor

⚠ CAUTION

Touching the motor during operation or during the cool-down phase can cause slight burns.

Before Cultivation

> **CAUTION**
>
> The motor is heavy! Work in pairs when coupling and uncoupling the motor.

Proceed as follows:

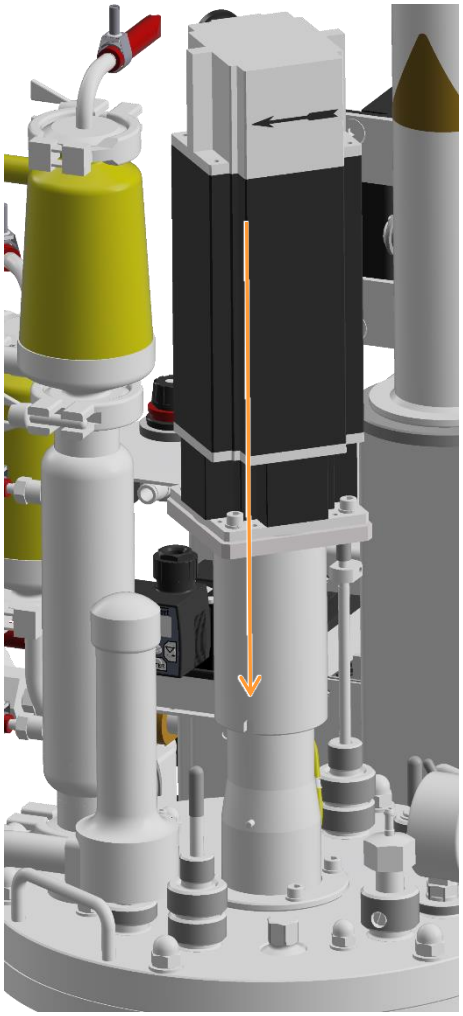
Procedure

1. Lift the motor from:

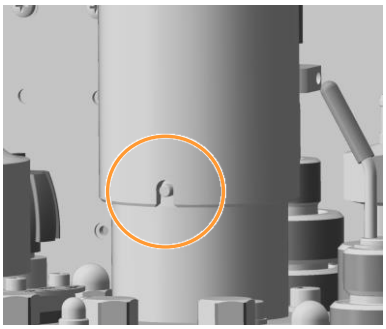
a) the opening in the central column.

OR, if applicable:

b) the holder on the lifting device for the vessel top plate.



2. Plug the motor onto the drive hub of the vessel top plate.



In doing so, align the groove on the motor with the pin on the drive hub. A different position is not possible. The motor is thus held in its position.

8.2.21 Checklist before in situ Sterilisation

Check and ensure the following items before in situ sterilisation:

Vessel
The baffles are fitted with spacers and mounted.
The impellers are fitted at the desired position on the stirrer shaft.
The vessel top plate seal (O-ring) sits tightly in the groove, the vessel top plate is mounted.
The safety valve is mounted, its lifting device is closed. The outlet of the overpressure venting pipe is equipped with a suitable hose/pipeline.
The manometer is mounted.
Unused ports in the vessel top plate and Ingold nozzles on the vessel are closed with blanking plugs
Port(s) is/are equipped with septum, septum collar and blanking plug, if applicable.
The vessel is filled with sufficient liquid for sterilisation.
The mechanical seal is lubricated.
The motor is coupled.

Reagent bottles and pumps
Reagent bottles are prepared for separate sterilisation in the autoclave (adding method via inoculation needle) OR Reagent bottles are sterile and connected to the vessel via pumps (adding method: push valve / resterilisable feed line)
Pumps are calibrated

Inoculation needles, (optional) push valves, (optional) resterilisable feed line
The inoculation needles are connected to reagent bottles and/or a suitable vessel for inoculum and wrapped in aluminium foil.
Closed push valve(s) is/are installed in port(s) after separate sterilisation in the autoclave. 4 inlet push valve: unused hose connections are closed with a pinched off piece of hose.
Block valve **13.16.01** / **13.16.03** of the resterilisable feed line is mounted. Block valve **13.16.02** / **13.16.04** with reagent bottle is ready for separate sterilisation in the autoclave.

Filters
All filters are clean and dry.
Unused twist valves on filters for inlet air and exit gas are closed.
Reagent bottles are equipped with filters for pressure equalisation, filters are lightly covered with aluminium foil.

Sensors
The temperature sensor is connected/mounted.
All other available sensors are mounted and, if necessary, calibrated.
The antifoam sensor is adjusted to its correct mounting depth and, with the correct reagent bottle, ready for separate sterilisation in the autoclave.

Harvest/sample valve 05.12.01 and (optional) sample valve 17.13.01
The steam trap(s) is/are mounted
42 L TV vessel: The valve insert with needle is mounted for sampling

8.3 In situ Sterilisation – General Information

There must be enough liquid in the vessel for in situ vessel sterilisation in order to generate a sufficient amount of steam.

The exact evaporation loss during vessel sterilisation cannot be determined. Some liquid evaporates via the inlet air and exit gas lines. This will partly be compensated by adding the inoculum. Furthermore, compensation is possible by adding water before the sterilisation (see *sterilisation method without culture medium*) or by adding separately sterilised medium.

Basically, there are different possible sterilisation methods, but sterilisation is always carried out according to the application and user specifications.

Two commonly used practices are briefly described below.

Sterilising the vessel with culture medium

- Fill the vessel with culture medium
- Sterilise the vessel
- Add sterile water to compensate loss of liquid due to evaporation and if applicable, any heat-labile components under sterile conditions

Sterilising the vessel without culture medium

Also when using heat-labile medium components, or components that, if combined with the medium, are not sterilisable, then the vessel must not be sterilised empty. Proceed as follows:

- Fill the vessel approx. half full with water, to generate sufficient steam in the vessel during sterilisation. Add nutrient salts, if needed.
- Sterilise the vessel.

  Either drain off the residual water after sterilisation or take this into account when adding the culture medium.
- Add the culture medium and inoculum under sterile conditions

  All heat-labile components are usually sterile filtrated and added by injection or with the inoculum afterwards.

INFORMATION

The programmed sterilisation processes are described in detail in the appropriate chapters of the main chapter “Operation Touch Screen Software”.

9 Cultivation

This chapter describes the work necessary for the performance of and after the completion of a cultivation, before the vessel is in situ sterilised again, if applicable, followed by being cleaned and then prepared for another cultivation.

WARNING

The vessel may be under pressure during operation!

Removing mounting parts or the vessel top plate lead to spurting out of liquids and/or rapid exhausting of gasses. This may cause severe chemical burns, burns or intoxication.

Always ensure the vessel is unpressurised before manipulating on mounting parts or on the vessel top plate.

CAUTION

Danger of scalding and burns due to contact with hot surfaces!

The vessel, the pipework and their components can get hot during cultivation and lead to burns!

9.1 Preparing the Medium

Before the first sampling, which usually takes place as a ‘zero sample’ before inoculation, and before the inoculation itself, the medium must be warmed to the desired temperature. If necessary, the pO_2 concentration and the pH are set. The time required for this depends on the working volume.

For details about operation, see the main chapter “Operation Touch Screen Software”.

INFORMATION

Depending on the specifications defined by the user, the pO_2 sensor is calibrated either before the vessel is filled with medium or afterwards, in the prepared medium. Calibration is described in the main chapter “Touch Screen Operation”.

9.2 Sampling

Samples are taken from the vessel to gain material for off-line analysis. The number of samples and method of sampling can vary due to the different analyses carried out by the operator.

A sample can be taken after sufficient cool-down time after sterilisation of the sample valve.

⚠ CAUTION

Risk of burns due to contact with the hot sample valve!

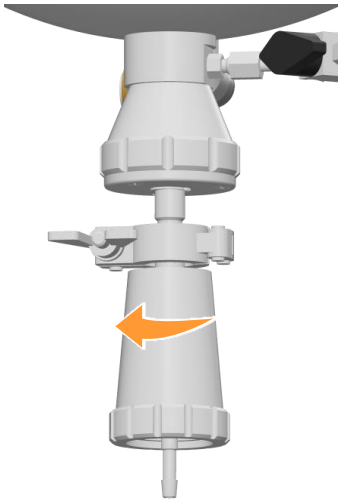
If the optional sample valve **17.13.01** installed in one of the Ingold nozzles is not present, sampling takes place via the combined harvest/sample valve **05.12.01** on the vessel bottom.

The type of harvest/sample valve (bottom valve) varies depending on the vessel size. For details, see the chapter “Harvest/Sample Valve (Bottom Valve) ” of the main chapter “Setup and Function”.

To take a sample, proceed as follows:

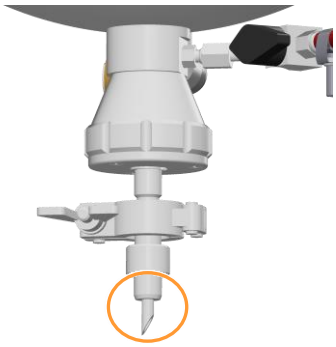
Procedure

1. Have the sample bottle/container ready.



2. Turn the steam trap counter-clockwise to remove it from the needle in the harvest/sample valve.

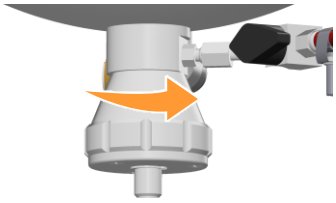
The figure on left shows, as an example, the valve type for the 15 L and 30 L TV vessel.
The steam trap is disconnected from the valve of the 42 L TV vessel and the optional sample valve in the same way.



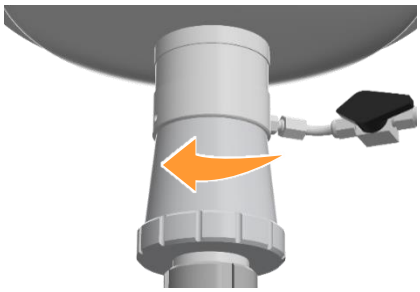
The needle is now visible.

3. Hold the sample bottle under the needle. Or, if necessary, use the needle to pierce the septum on the sample bottle.

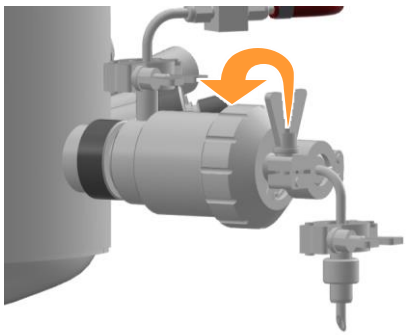
4. Open the valve:



- Valve type 15 L and 30 L TV: Turn the valve clockwise.



- Valve type for 42 L TV: Turn the valve counter-clockwise.



- Valve type optional sample valve **17.13.01:** Turn the valve counter-clockwise.

5. Fill the sample bottle with the required amount of liquid.
6. Close the valve:

- Valve type 15 L and 30 L TV: Turn the valve counter-clockwise
- Valve type for 42 L TV: Turn the valve clockwise.
- Valve type optional sample valve: Turn the valve clock-wise.

7. If applicable, pull the needle out from the septum in the sample bottle.
8. Screw the steam trap to the needle clockwise.

The harvest/sample valve should now be sterilised again to ensure it has cooled down sufficiently for the next round of sampling.

9.3 Inoculation

Check and ensure the following items before inoculation:

- Medium is filled in the vessel.
- Heat labile supplements are separately sterilised and added.
- Reagent bottles are connected to the vessel via the pumps and are filled with reagents and nutrient solution enough for the duration of the entire cultivation.
- The hoses of the reagent bottles are filled.
- The correct operating temperature has been reached.
- The required stirring speed is set.
- The sensors are calibrated, and the control is set correctly (maybe not active yet).
- Utensils for inoculation and the container with the inoculum are ready to use.

There exist different possibilities to add the inoculum. The precise method of inoculation depends on the internal regulations and the kind of used system. Two commonly known methods are described in the following.

- Via inoculation needle and septum: the inoculum drips into the culture. This method contains a high risk of contamination.
- Via push valve: the inoculum drips into the culture. This method requires a sterile hose connection.

9.3.1 Inoculation with Inoculation Needle

Proceed as follows:

Procedure

1. Fill the inoculum under sterile conditions into the prepared container.
2. Unscrew the blanking plug from the septum collar.
3. If wished, place a few drops of Ethanol (70 %) on the septum before piercing.

   If wished: briefly flame the septum collar.
4. Remove the aluminium foil from the inoculation needle.
5. Depending on the application: briefly flame the inoculation needle.
6. Immediately pierce the inoculation needle through the septum.
7. Screw the inoculation needle into the septum collar.
8. Transfer the desired volume of inoculum into the vessel.
9. Clamp off the silicone hose.

   Or: pull the inoculation needle off and close the septum collar with the blanking plug. However, this method does not completely rule out contamination.

9.3.2 Inoculation with Push Valve

For this, the following work must be carried out first:

- The (closed!) push valve with fitted closed piece of suitable [1)] hose is separately sterilised in the autoclave.
- The empty container for the inoculum fitted with a closed piece of suitable hose [1)] is separately sterilised in the autoclave.
- The (closed!) push valve with the closed piece of hose is mounted into the vessel top plate port and in situ sterilised with the vessel.

[1)] suitable for establishing a sterile hose connection

To add the inoculum, proceed as follows:

Procedure

1. Fill the inoculum under sterile conditions into the prepared container.
2. Establish a sterile hose connection with the push valve.
3. Open the push valve and transfer the desired volume of inoculum into the vessel, use the peristaltic pump as necessary.

4. Clamp off the silicone hose, weld it as necessary or close the push valve.

9.4 Harvest

The culture can be harvested at the end of the cultivation process. The easiest and safest way to do so is to prepare for the harvest before the cultivation process ends. For example, get a suitable vessel ready or connect a hose to the harvest valve.

⚠ CAUTION

Risk of burns due to contact with the harvest valve!

There are generally two methods for doing this:

- using gravity (0 bar)

  or
- excess pressure (1.0 bar) – if optional pressure control is available.

Procedure

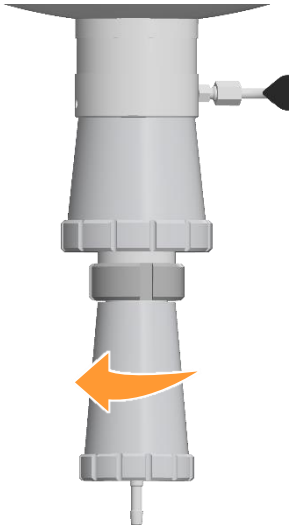
Valve type for 15 L and 30 L TV vessel

1. Open the clamp and remove the steam trap with the flat gasket from the connection flange of the harvest/sample valve..

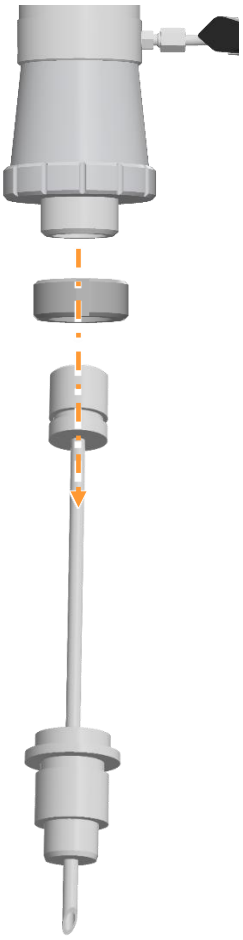
2. Attach the harvest hose with flat gasket and clamp to the harvest/sample valve or place the container underneath the harvest/sample valve.
3. Open the harvest/sample valve clockwise.

Procedure

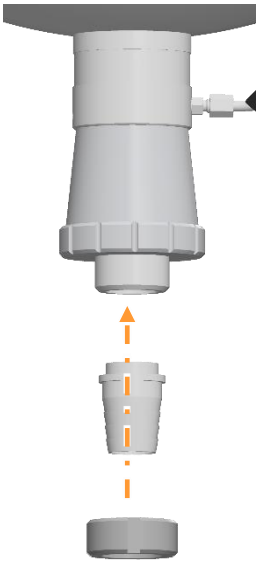
Valve type for 42 L TV vessel



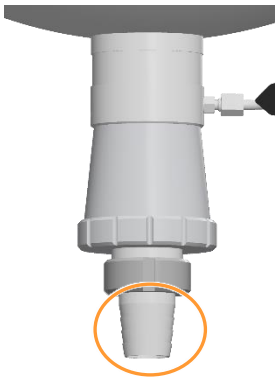
1. Turn the steam trap counter-clockwise to remove it from the needle in the harvest/sample valve.



2. Loosen the groove nut and remove the valve insert with needle.



3. Affix the valve insert with nozzle by using the groove nut.



4. Fit the harvest hose to the nozzle of the harvest/sample valve or place the container underneath the harvest/sample valve.

INFORMATION

If no hose is connected, a valve insert with nozzle does not necessarily have to be connected.

5. Open the harvest/sample valve counter-clockwise.

9.5 Emptying the Vessel

Depending on the user specifications, the vessel can be emptied either before or after sterilisation.

A previously emptied culture vessel filled only with water for sterilisation is easier to clean afterwards.

For emptying the vessel, the same options as for harvesting are available. For more information, see the chapter “Harvest”.

If the culture will not be used further, it must be inactivated according to the current in-house instructions (e.g. by sterilisation or by lowering the pH value), and subsequently disposed of in an environmentally sound manner according to the local regulations.

9.6 Sterilisation after Cultivation

Depending on internal guidelines, some accessories like reagent bottles, hoses, inoculation needles etc. are again separately autoclaved followed by cleaning after completion of the cultivation process. The vessel is in situ sterilised again, too. In particular, this is mandatory because safety related, if carrying out cultivation processes with potentially dangerous, pathogenic or genetically modified microorganisms.

Proceed as follows:

Procedure

1. Empty all hoses of the reagent bottles completely by means of the pumps.
2. Clamp off the hoses and remove them from the pumps.

3. Remove inoculation needles under sterile conditions from the vessel top plate and replace the blanking plugs before in situ sterilisation.

   If in use: close the push valves, sterilise them with the vessel in situ followed by autoclaving them separately.

INFORMATION

After emptying and before autoclaving, it is recommendable to thoroughly rinse the reagent bottle hoses with water. Depending on internal guidelines, the hoses are disposed of in an environmental acceptable manner and new hoses are used for the next cultivation.

4. If applicable, dispose of residual liquid in the reagent bottles in an environmental acceptable manner.
5. Autoclave the whole assembly (reagent bottles, hoses and inoculation needles).

   The components will be sterile and no longer carry a risk of microbial contamination after this process is completed successfully.
6. Carry out in situ sterilisation again.

INFORMATION

In any case, the exact procedure must comply with the internal guidelines and may therefore differ from the procedure described here.

9.7 Emergency Shut-Off

To shut-off the device in dangerous situations, proceed as follows:

Procedure

1. Immediately switch off the device at the main switch.

   The device is de-energised.

   A running cultivation process continues after restarting the device.

   If the mobile CIP unit *TechCIP* from the device manufacturer is in use:

   The software connection to the mobile CIP unit is interrupted and the system alarm *TechCIP communication error* appears on the *TechCIP* touch screen.

2. Resolve emergency shut-off situation.

9.8 Restart after Emergency Shut-Off

CAUTION

Premature restarting in an emergency shut-off situation that has not yet been rectified can be dangerous and result in damage to property.

ATTENTION

A cultivation process that is running when the emergency shut-off is executed, will continue after the device is switched on again. It must be stopped separately via **Stop** if necessary. All other processes remain stopped in any case and must be re-started.

After the fault and the emergency shut-off situation have been resolved, proceed as follows:

Procedure

1. Switch the device on at the main switch.

INFORMATION

If additional switches for the power supply/interruption have been installed on site, the internal safety regulations must be observed.

System alarm *System restarted after a power failure* appears.

2. Restart the desired process(es), abort and restart if necessary.

10 Operation Touch Screen Software

This chapter contains detailed descriptions of all functions of the touch screen software that are accessible to the operator.

Most of the figures in this manual showing the various menus, dialogue boxes and tab pages of the touchscreen software reflect the view of a user with the user authorisation level of *Technician*.

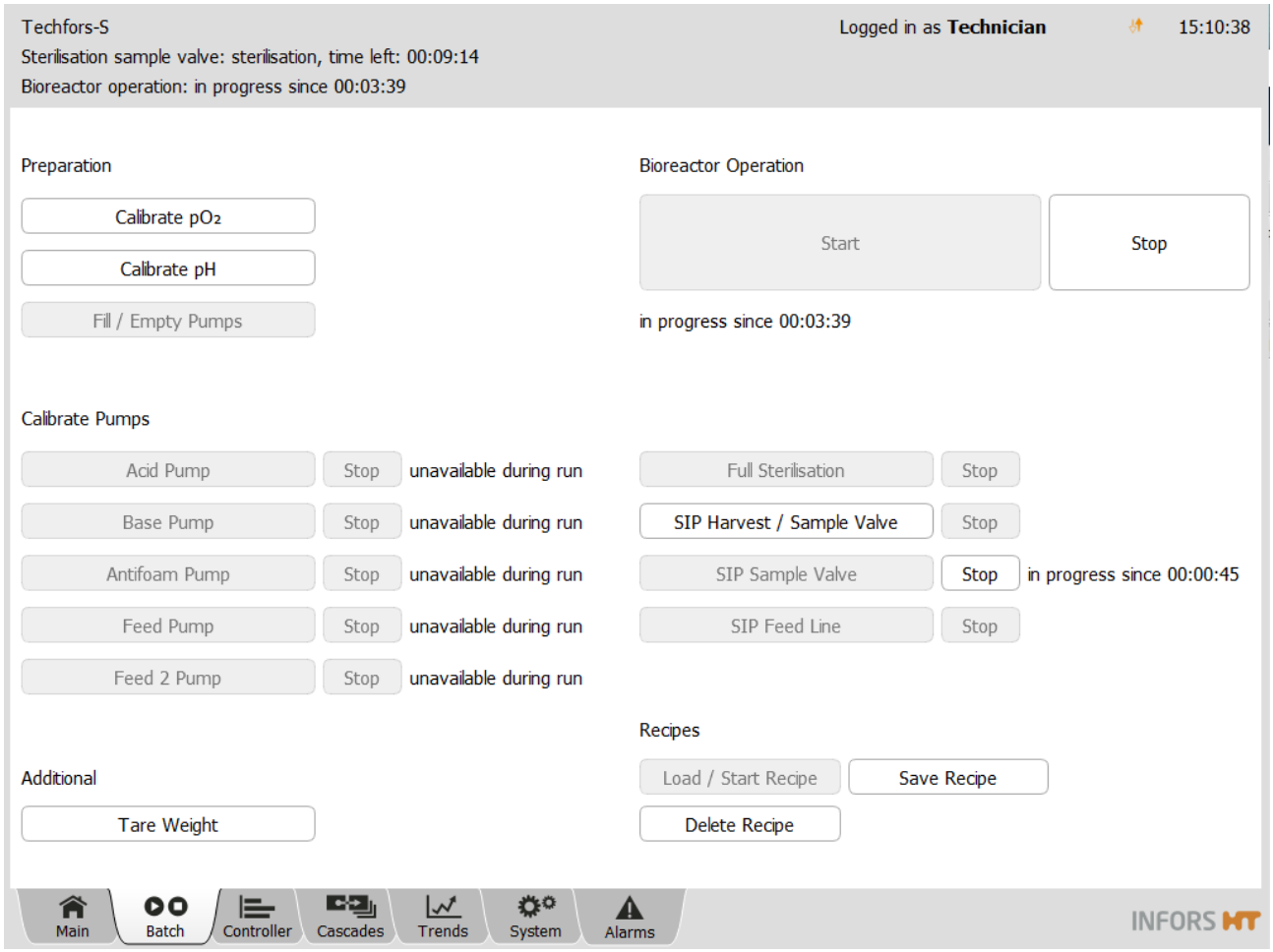
Refer to chapter “Security – User Management”, “User Levels for further information about user levels and access authorisation.

The figures are used as examples and may therefore differ from the actual device configuration.

ATTENTION

Changing settings in the touch screen software by unqualified personnel or personnel with insufficient training may lead to loss of property.

10.1 Screen, Menu Navigation and Control Elements



The screen is divided into the three sections:

Header

shows the name of the device, operating states, login-status and the time.

Two opposing vertical arrows in the header signalise that an external software like e.g. eve® has access to the OPC XML DA server of the touchscreen software. They are flashing while data is transmitted

Main area

shows main menus and submenus, e.g. main menu *Batch*, see figure above. Inputs are made exclusively in the main area.

Footer

comprises 7 tabs which provide access to the 7 main menus.

The tabs are displayed with a grey background. A selected tab is shown light grey.

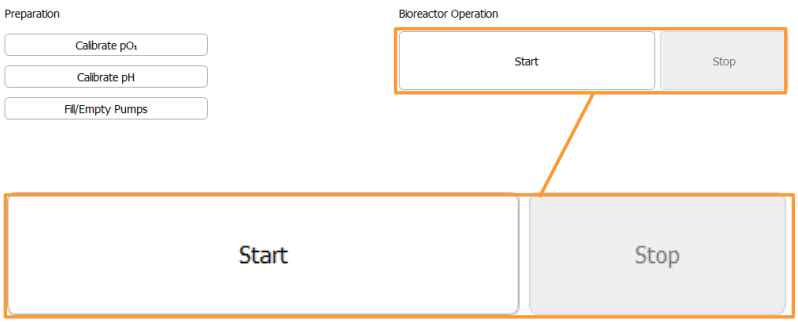
The following main menus are available (from left to right):

- *Main*: shows process parameters and their values, pumps and a few valves of the bioreactor.
- *Batch*: this is where the bioreactor (cultivation process) and all sterilisation processes are started and stopped and sensors and pumps are calibrated.
- *Controller*: shows the parameters of the bioreactor and offers the option of changing values.
- *Cascade*: allows to set up a serial, parallel or parallel serial (mixed) cascade control of one or several parameters.
- *Trends*: shows trends in the parameters, time span between 15 min. and 2 days.
- *System*: provides access to the submenus *Valves*, *Security, Settings, Wipe Screen* and *Shutdown.*
- *Alarms*: shows parameter alarms, user alarms and system alarms.

Buttons

Depending on the selected main menu or submenu and access authorisations, various buttons may be visible and available. Pressing a button either opens a sub menu, or a dialogue box or a tab page.

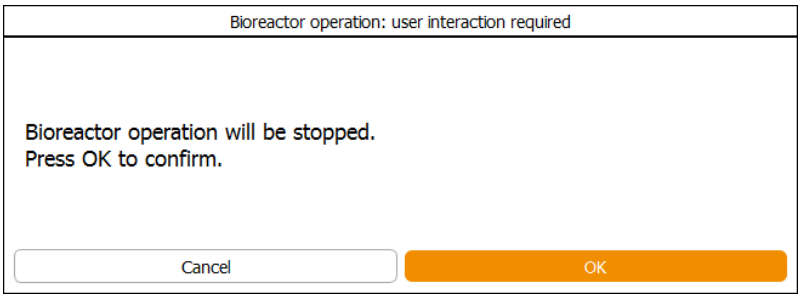
Enabled buttons are white in colour, disabled buttons are grey in colour.



Buttons, which are intended as the next logical step in the procedure, are shown in orange colour, see example in next section.

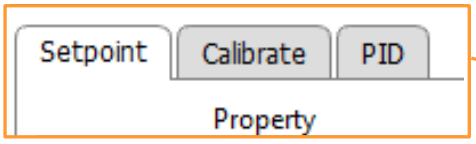
Dialogue boxes and tab pages

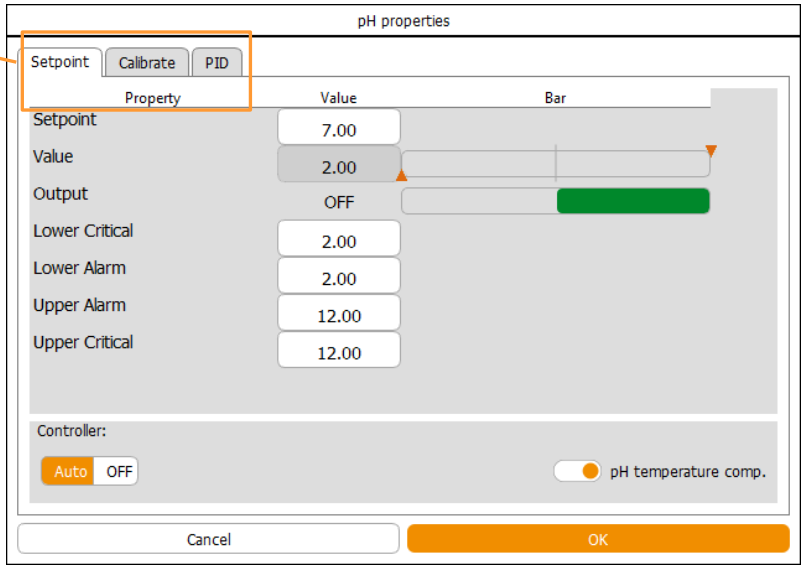
A dialogue box may contain instructions, notes, warnings or general information.



A dialogue box may also contain further buttons, input fields or view boxes and tabs.

Example: *pH properties* dialogue box with tabs which lead to the different parameter options.





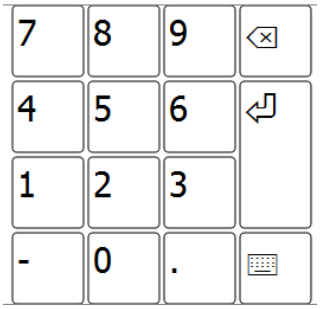
Depending on the parameter and the access authorisations there may be more or less available options for a parameter.

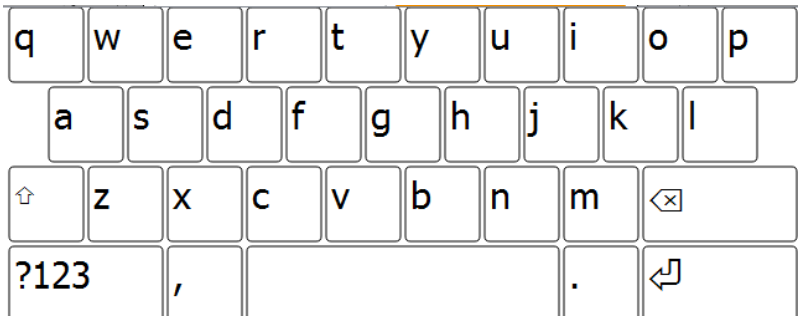
Input fields and view boxes

They are included in various menus, dialogue boxes and tab pages. They either require the inputting of a numerical or an alpha-numerical value or show these values.

Numeric keypad and alphanumeric keyboard

Numerical values are entered using a numeric keypad. Alphanumerical values are entered using an alphanumeric keyboard. After pressing an input field, the appropriate pad/board appears.





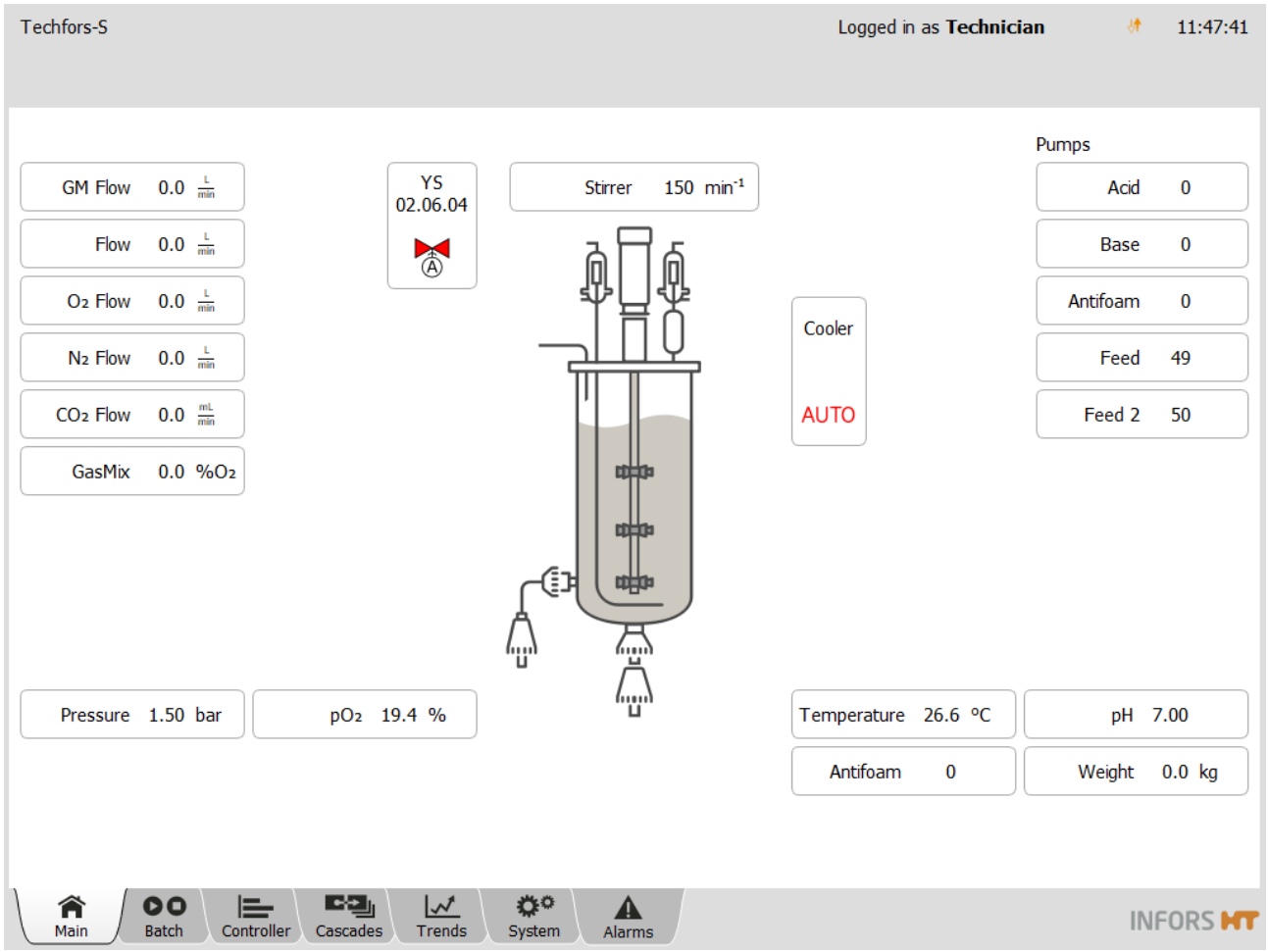
ON / OFF switch

The ON / OFF switch is used in order to switch a function on or off.

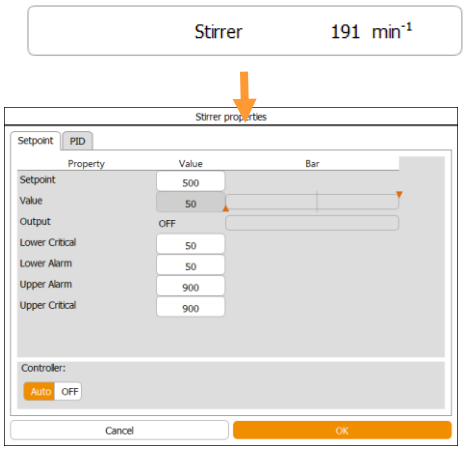
- **ON**: the switch is in orange colour
- **OFF**: the switch is in white colour

10.2 Main Menus

10.2.1 Main – Overview

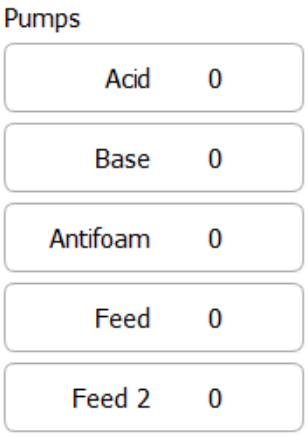


The main menu *Main* charts the bioreactor and some of its valves and offers an overview of its process parameters and pumps according to its configuration.



Parameters

Process parameters and their current measured values are displayed as buttons.
Pressing one of the parameter buttons leads to its options.



Pumps

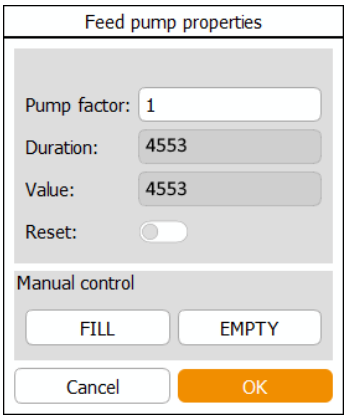
All integrated peristaltic pumps of the bioreactor are displayed as buttons at the right of the screen.
The following four pumps are present by default:

- *Acid*
- *Base*
- *Antifoam*
- *Feed*

The *Feed 2* pump is optional.

The delivered volume (in mL) of a calibrated pump is continuously shown while the bioreactor is running. This numerical value is displayed on the appropriate pump button, as the example for the Feed pump shows on the left. For pumps which are not calibrated, the number of rotations is displayed instead.

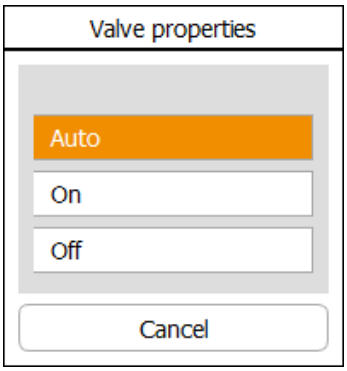
Operation Touch Screen Software



When pressing one of the pump buttons, a dialogue box appears where the number of rotations of the selected pump can be reset to zero. The pump factor calculated during pump calibration is also visible and can be changed manually here.
In addition, the two buttons **FILL** / **EMPTY** are available for the standard pumps. These allow manual filling or emptying of the hoses of the reagent bottles.

Valves

- The **red** colour signifies a closed valve.
- The **green** colour signifies an open valve.
- The letter **A** signifies, that the valve is switched to automatic mode.
- The letter **M** signifies that the valve is switched to manual mode i.e. it is “forced”.

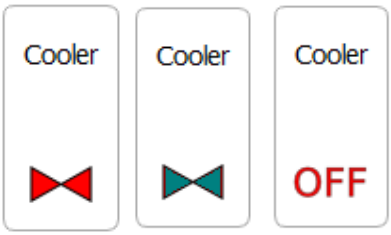


Pressing a valve button opens a dialogue box where the state of the valve can be changed by switching **On**, **Off**, or **Auto** for diagnosis purposes.

ATTENTION

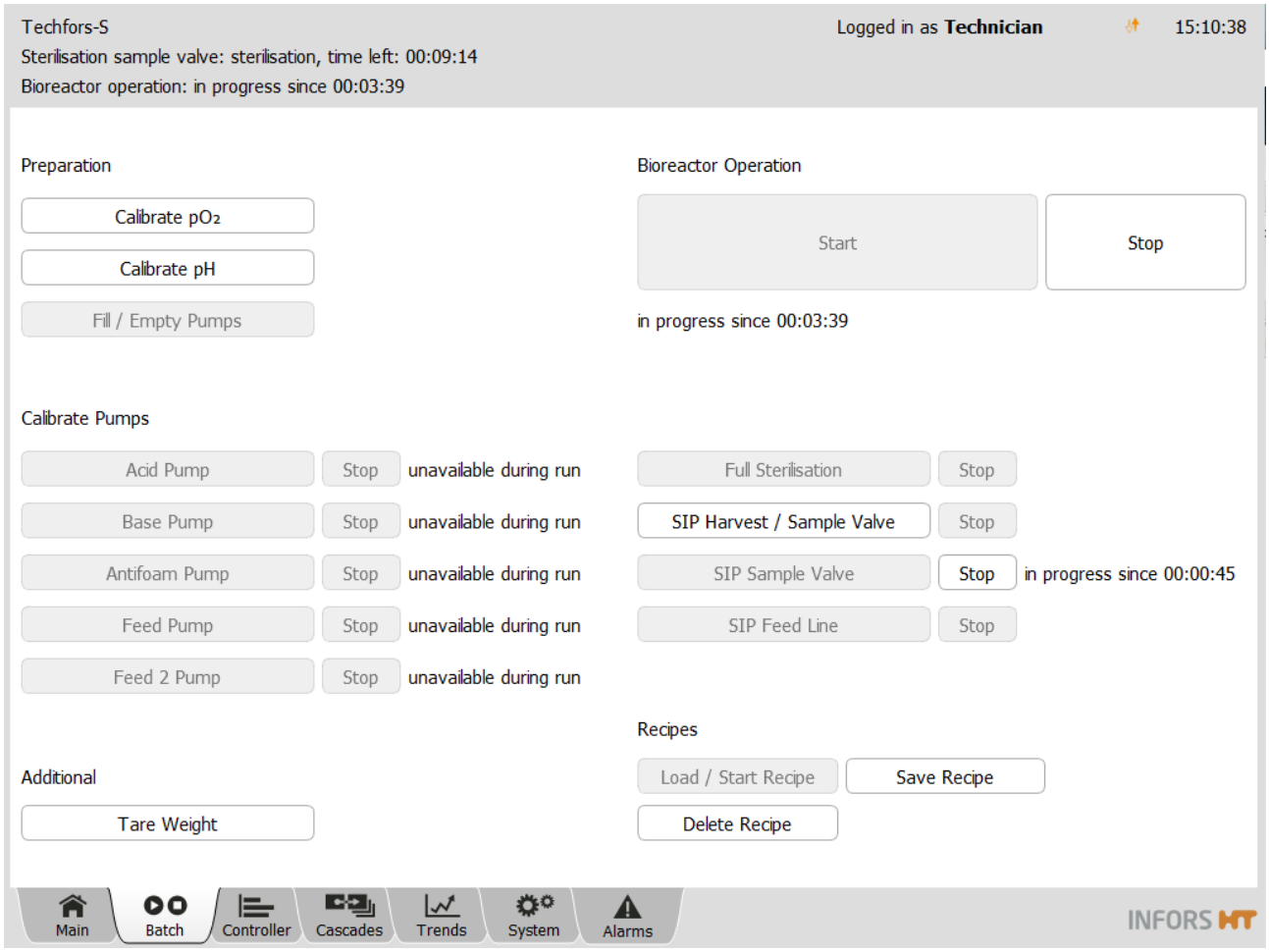
All valves are set to automatic mode (*Auto*) ex-factory. These settings may not be changed!

Exit gas cooler



The **Cooler** button (exit gas cooler) with the valve symbol signifies the valve (**01.06.06**) for the water supply of the exit gas cooler.
The valve automatically opens during the cultivation process (bioreactor is running) and in the cooling phase during full sterilisation when switched to automatic mode.
If this valve is manually switched off, water supply is not possible anymore, the valve remains closed! This is indicated with the word *OFF* in red letters instead of the valve symbol on the **Cooler** button.

10.2.2 Batch – Start Menu



The bioreactor (cultivation process) and all sterilisation processes are started and stopped in main menu *Batch*. If present, this applies to the sterilisation process of the optional sample valve and the optional resterilisable feed line, too.

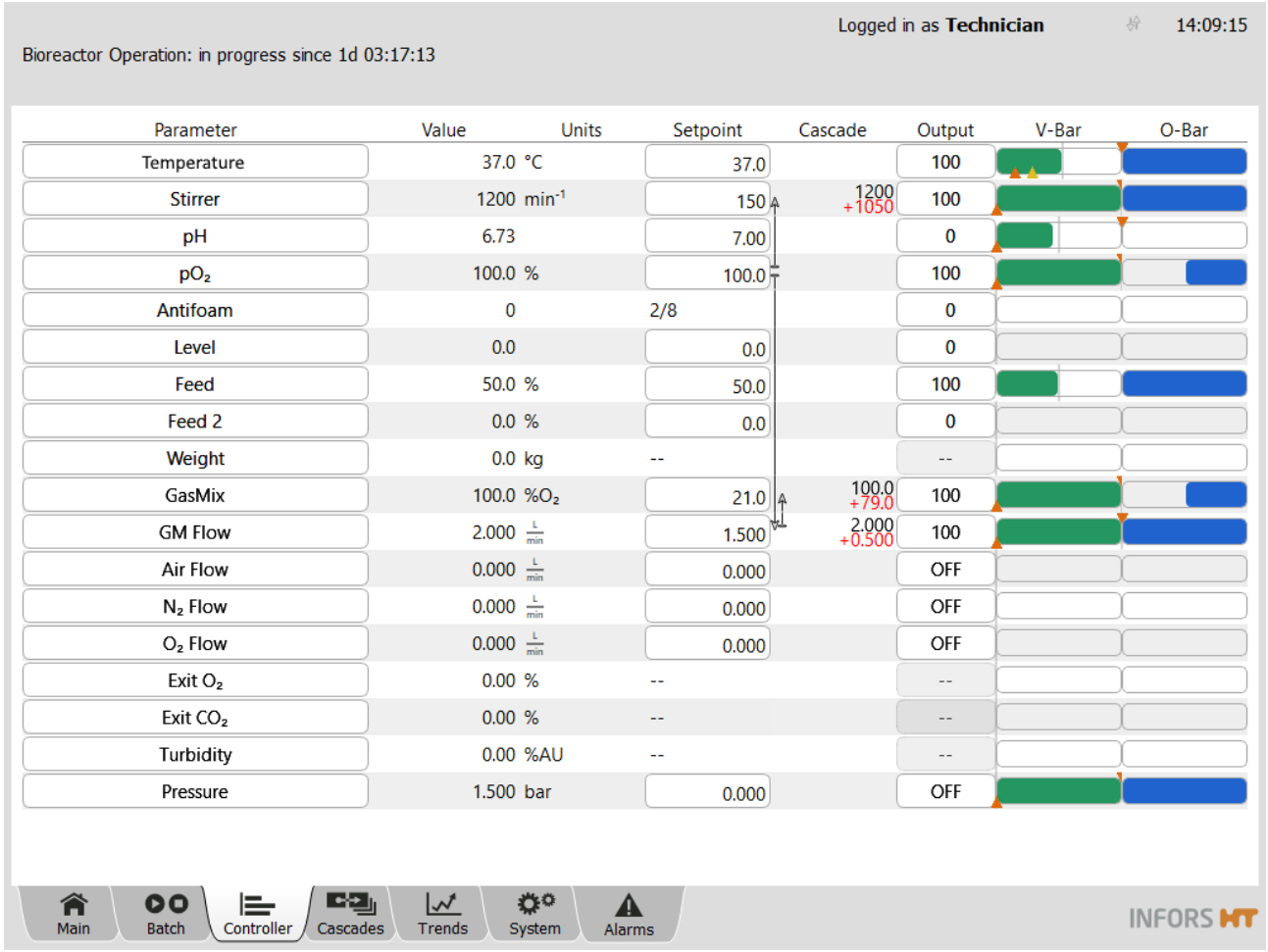
pH and pO_2 sensors and pumps are calibrated in this menu, too. If required, pump hoses can automatically be filled and emptied.

Recipes can be stored, loaded or deleted here. If the optional vessel weighing system is installed, the weight display is tared here.

Depending on the device's configuration, access rights of the operator and operating state of the bioreactor more or less functions are present and enabled.

Detailed descriptions of each function and process can be found in the corresponding chapters in this manual.

10.2.3 Controller – Value Display



The main menu *Controller* shows current values, setpoint values and controller outputs for the parameters of the bioreactor. Settings for parameters can be changed here.

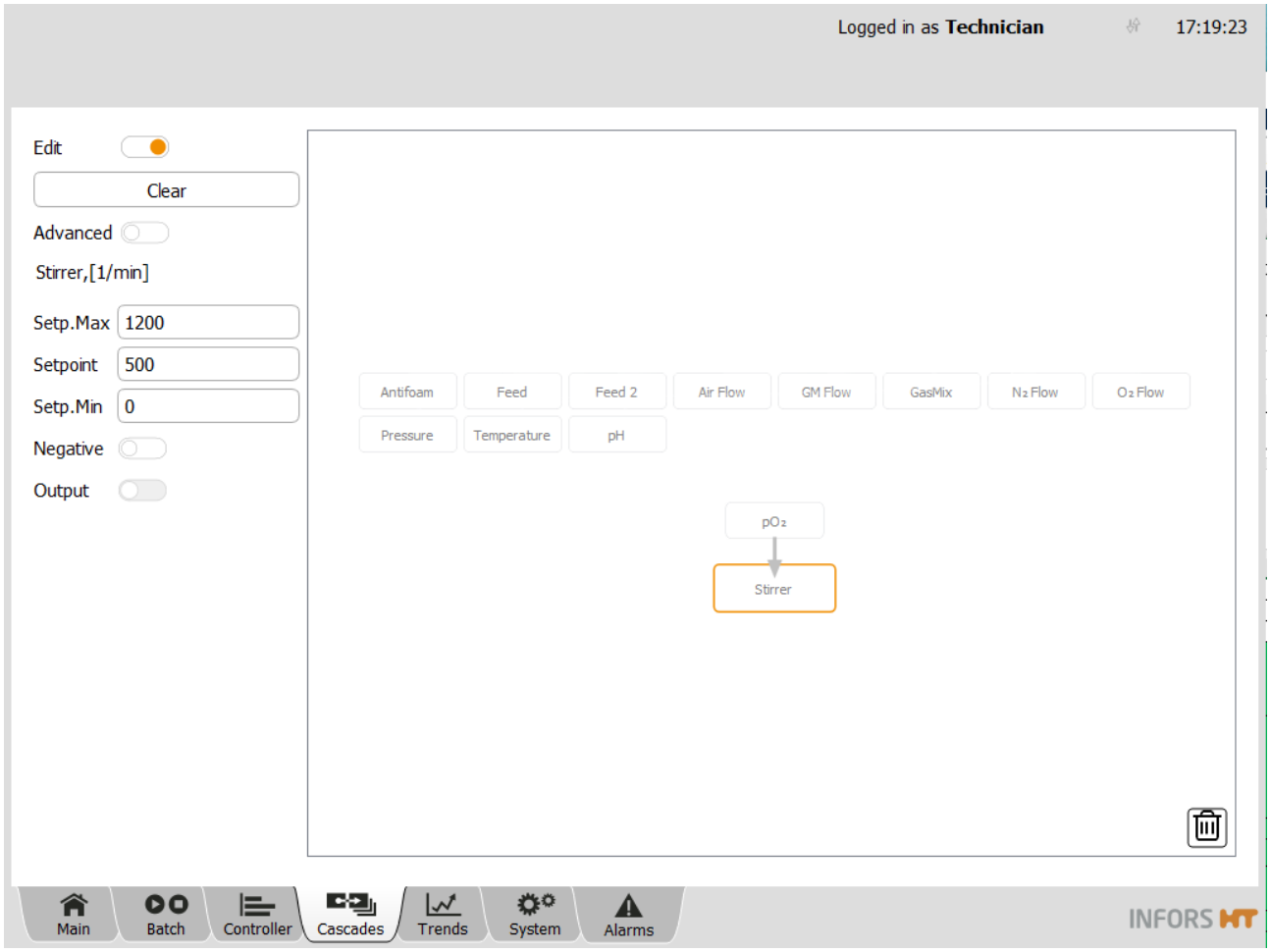
- *Parameter*: lists the available parameters. Pressing the desired parameter button leads to the parameter options, see chapter “Parameter Options”.
- *Value*: displays the actual parameter values
- *Units*: displays the units of the parameters
- *Setpoint*: to enter/change setpoint values of parameters

INFORMATION

When the bioreactor has been stopped, setpoint values in the Controller menu are overwritten with the setpoint values set in the configuration dialogue. See the chapters “Setpoint” and “Setting Setpoint Values, Switching Parameters ON / OFF” for details.

- *Cascade*: indicates, whether and how cascade control is active and which process parameters are used. Settings for a cascade are made in the main menu *Cascade*. A detailed description about cascade control can be found in the chapter “Cascade Control”.
- *Output*: displays the controller output for a parameter in % when the bioreactor is running. A switched off parameter is displayed as *OFF*. When the bioreactor has been stopped, all its parameters are automatically switched off. Parameters can be switched on or off here whilst the bioreactor is running by pressing the controller output (button with displayed value *OFF* or %). This is only possible, if the automatic mode is set in the *Setpoint* option of the parameter concerned.
- *V-Bar* (vertical bar): shows a graph comparing the current value, set value and alarm limits:
  - Grey continuous marking: set setpoint value
  - Yellow marking: set alarm value (lower alarm / upper alarm).
  - Red marking: set critical values (lower critical / upper critical)
  - Green bar: current value is within the alarm limits
  - Yellow bar: current value has exceeded the upper alarm value or dropped below the lower alarm value
  - Red bar: current value has exceeded the upper critical value or dropped below the lower critical value
- *O-Bar* (controller output bar): shows a graph of the current controller output (%). Parameters which are controlled on two sides (e.g. pH and temperature) are shown as a two-part bar.

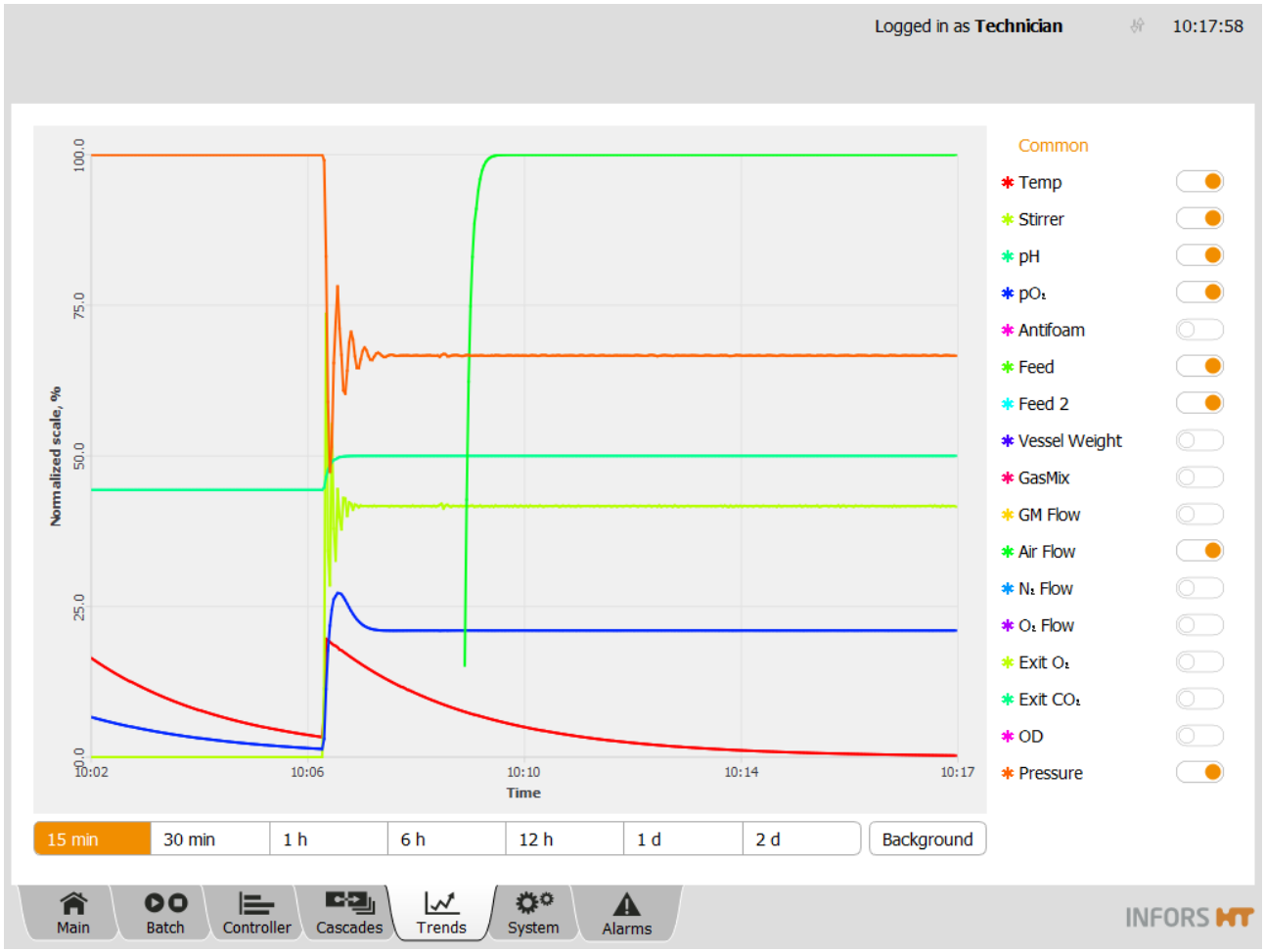
10.2.4 Cascade



The main menu *Cascade* provides the option of setting up a serial, parallel or mixed cascade control of a parameter. This function is mainly used for pO_2 regulation.

The cascade settings are made in the left-hand section of the screen and the main section presents these schematically. The individual process parameters can be added to a cascade by dragging & dropping them. For details about cascade control refer to chapter “Cascade Control”.

10.2.5 Trends – Trend Lines



The touch screen operating unit keeps the current parameter values in a buffer and continuously charts them in the main menu *Trends*. This data can neither be archived nor edited or exported. The main menu *Trends* serves to provide quick information on the progress of the cultivation only.

However, the data can be archived on computer connected via network using e.g. eve®.

The parameters of the bioreactor are listed on the right-hand side of the screen. The **ON/OFF** switch next to each parameter allows to activate/deactivate the display of its trend line in the main area of the screen.

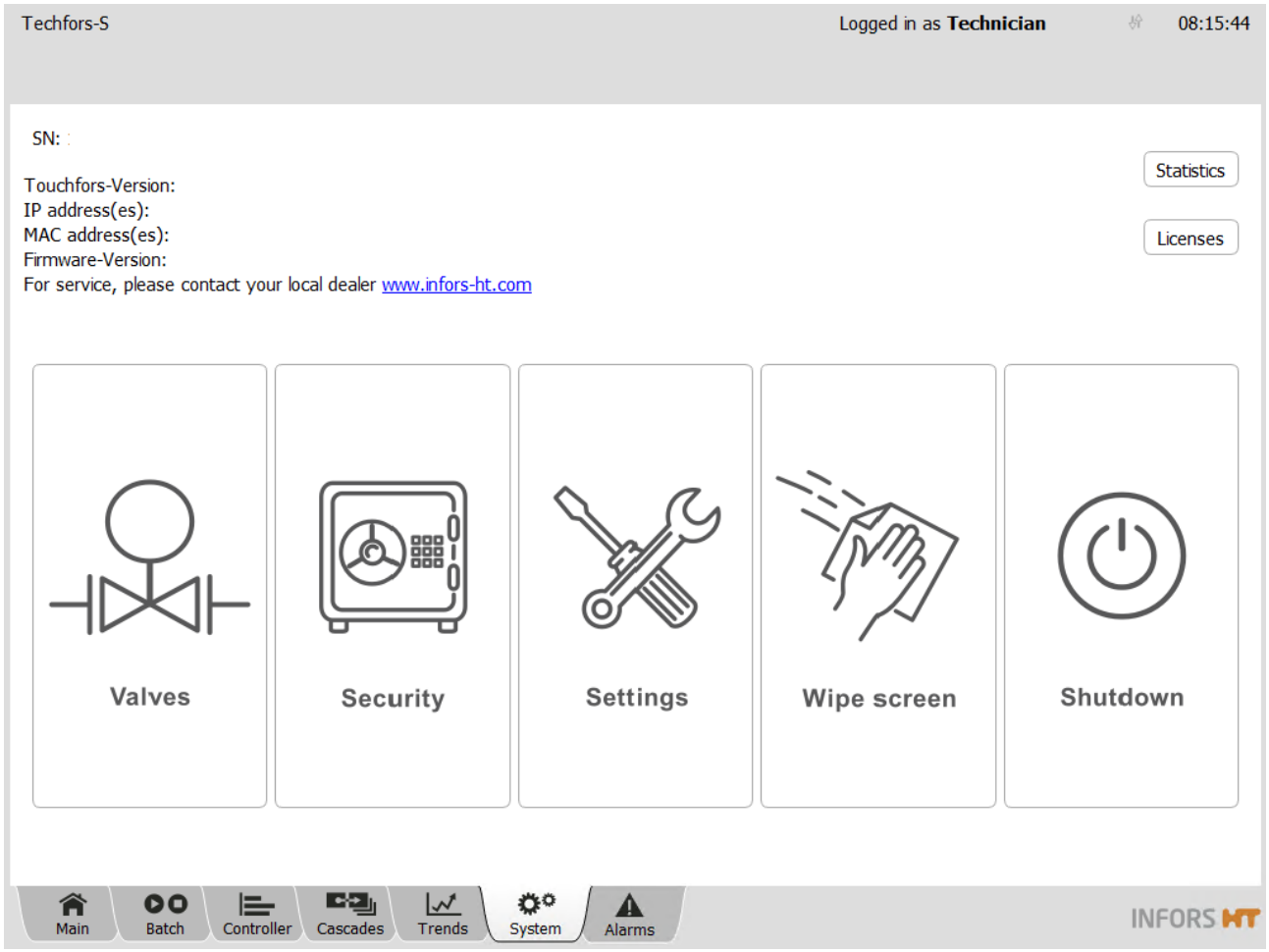
All trend lines are normalised to the value range of the respective parameter. The maximum value (= 100 % of the normalised scale) is located on the top of the diagram, the minimum value (= 0 % of the normalised scale) on the bottom. When a parameter is selected from the list, the labels on the Y axis will switch to the value range of the selected parameter. When *Common* is selected, the labels on the Y axis are reverted to the normalised scale.

The sideways spread of the diagram can be selected via the buttons below the diagram:

- **15 min** and **30 min**: 15 and 30 minutes
- **1 h**, **6 h** and **12 h**: 1, 6 and 12 hour(s)
- **1 d** and **2 d**: 1 and 2 day(s)

The **Background** button allows to change the background colour of the diagram display (white, grey and black).

10.2.6 System – System Settings



The main menu *System* shows the following:

- Serial number
- Software version
- IP address of the system(s)
- MAC (hardware) address
- Firmware version
- Manufacturer's internet address (Domain)

Two buttons are situated in the upper right side of the screen:

- **Statistics**: enables viewing some statistics of the software communication with the control board, i.e. the hardware of the bioreactor. The function is only used for fault diagnosis for the technical support from the manufacturer.

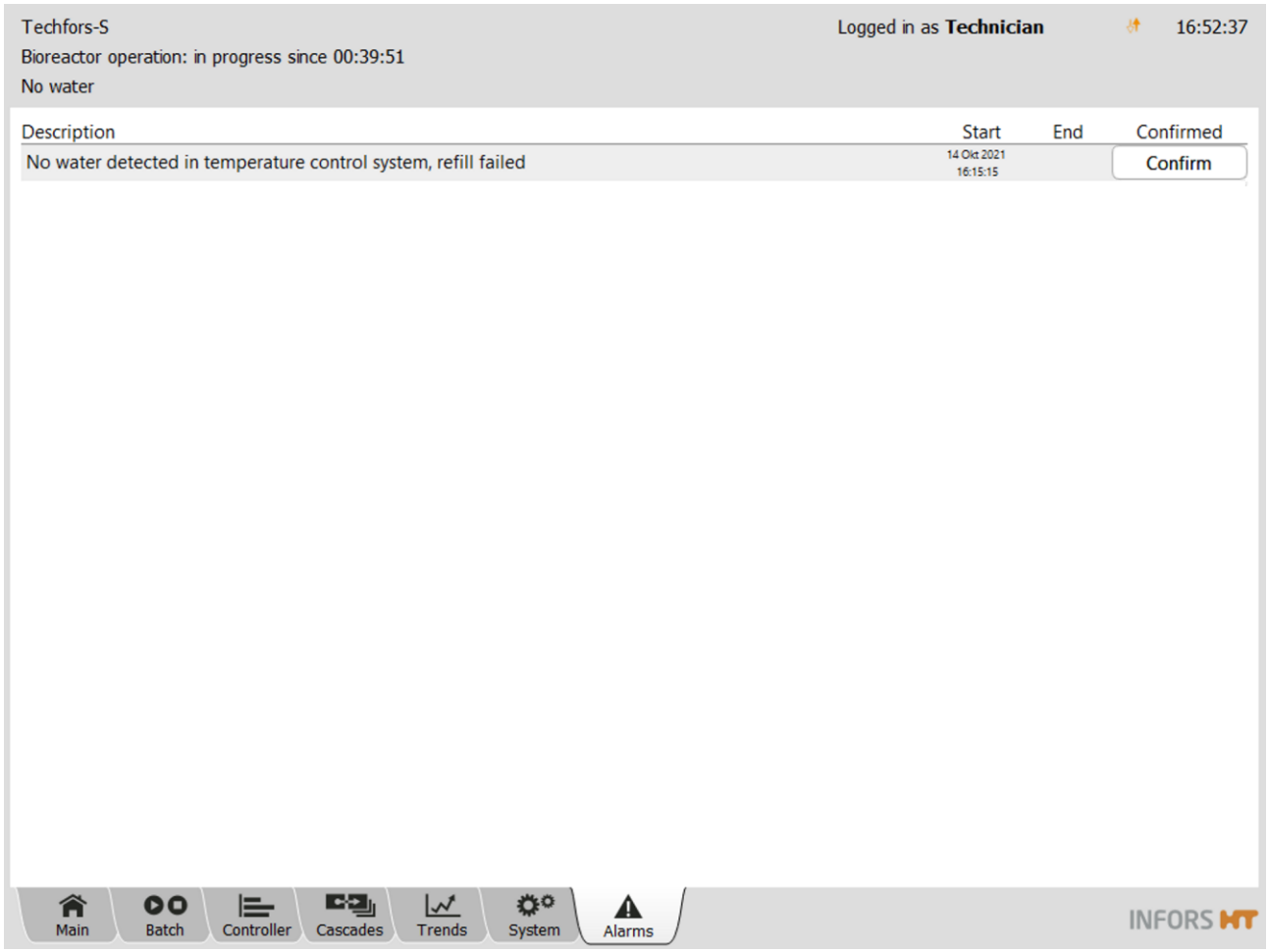
- **Licences**: Opens a menu with the licenses of all software libraries used.

The menu has 5 buttons which access the submenus with various functions:

- **Valves**: displays the status of the digital outputs.
- **Security**: for system log-in and log-off, passwords and user management
- **Settings**: for the system and basic settings of the bioreactor
- **Wipe Screen**: to lock the screen for 20 seconds, e.g. for screen cleaning
- **Shutdown**: to shut down the system

A detailed description of the submenus can be found in the appropriately titled chapters.

10.2.7 Alarms – Parameter Alarms, User Alarms, System Alarms



The main menu *Alarms* lists all parameter alarms of the running cultivation process by time of occurrence. User and system alarms are shown here, too.

Alarms are signalled by the *Alarm* tab flashing light red and dark alternately.

The screen contains the following columns:

- *Description*: describes the alarm
- *Start* and *End*: shows the date and time when the alarm started/ended.
- *Confirmed*: indicates via **Confirm** confirmed alarms with date, time and user.

The following user and system alarms are shown:

User alarm

- *Password Expiry:* the alarm for password expiry will be indicated during 10 days before expiry. Validity duration of the password is set when creating a new user login.

System alarms

- *Difference in board configuration*
- *Invalid modbus map for Parameter xy*

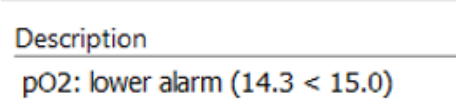
> **INFORMATION**
>
> This alarm can only occur if modbus settings were modified. Modbus settings can only be modified on user level Service.

- *No water detected in temperature control system, refill failed:* no water in the temperature control system or insufficient water supply. For details refer to main chapter “Interferences”, chapter “Interferences Temperature Control System”.
- *No communication*: no communication between control board and operating panel. For details refer to main chapter “Interferences”, chapter “Interferences Basic Operation and Operating Panel”.
- *Requested specialized configuration not installed*: error occured while restoring saved data or during installation of a software update. For details refer to chapter “System Alarm – Difference in board configuration”.
- *System restarted after power failure*: for details refer to main chapter “Interferences”, chapter “Behaviour in Case of Power Interruption”.

10.2.7.1 Parameter Alarms

A parameter alarm occurs as soon as the current value of a parameter is outside the set alarm tolerances.

A parameter alarm is triggered as soon as a value drops below the lower alarm value or exceeds the upper alarm value.

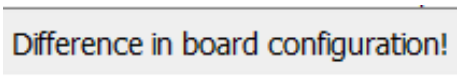


The example in the figure on the left shows: *pO2: lower alarm (14.3 < 15)*. I.e. the current value of parameter pO_2 (= 14.3 %) is below the lower alarm value (= 15 %).

INFORMATION

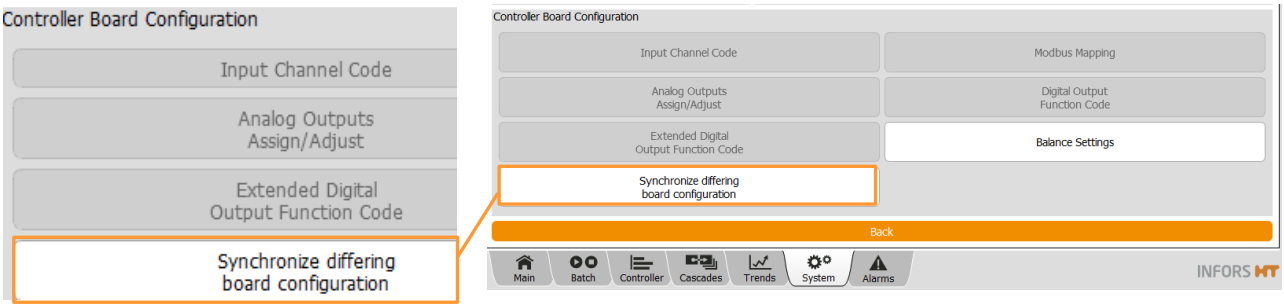
The values in brackets always refer to the current value compared with the setting of the alarm value or the critical value.

10.2.7.2 System Alarm “Difference in board configuration”



A backup of each control board configuration of the device is stored in the touch screen. If there are differences between the backup and the current configuration after a firmware update / exchange of the control board respectively the touch screen, the alarm *Difference in board configuration* will occur. This signifies that the configurations do not correspond with each other.

To enable to select the appropriate configuration, the **Synchronize differing board configuration** appears and is enabled in the *Controller Board Configuration* section of the main menu Settings.



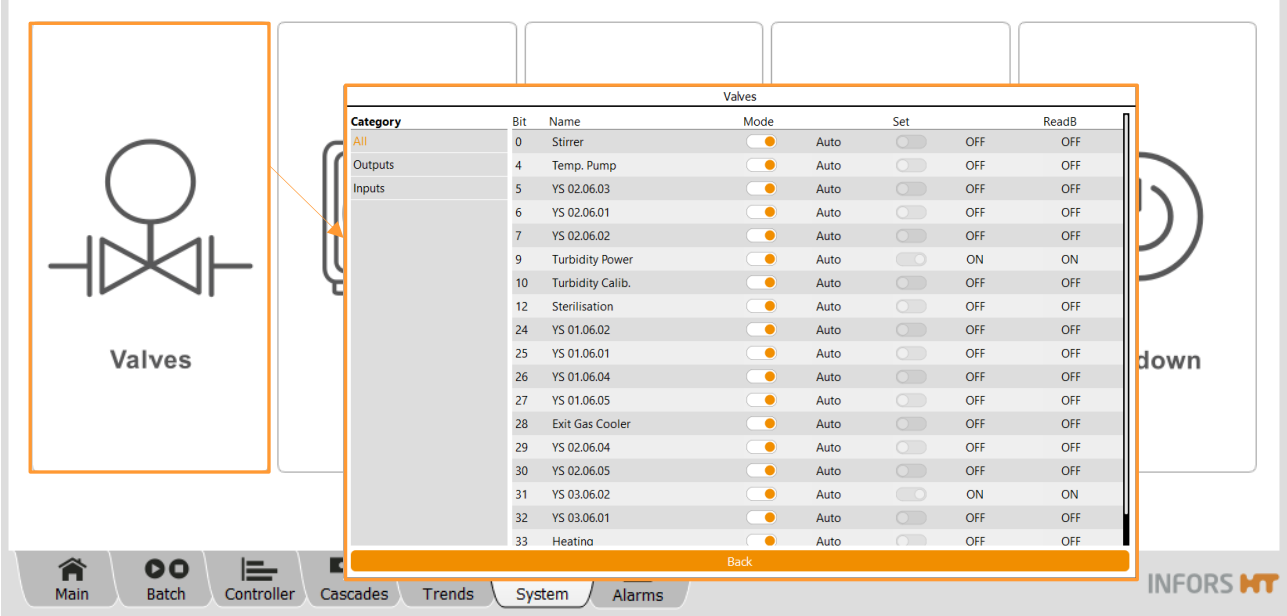
After selection of this function (pressing the button), the menu appears with the two following options:

- **Use current board configuration**: to replace the backup in the touch screen with the current configuration of the control board.
  This is appropriate after exchange of a touch screen.
- **Use stored board configuration**: to overwrite the configuration of the control board with the configuration from the backup.
  This is appropriate after a firmware update, respectively replacement of a control board.

The alarm disappears as soon as the function is executed.

10.3 Submenus

10.3.1 Valves – Digital Controller Outputs



The submenu *Valves* displays the digital outputs and inputs of the control board. The overview is predominantly used for fault diagnosis.

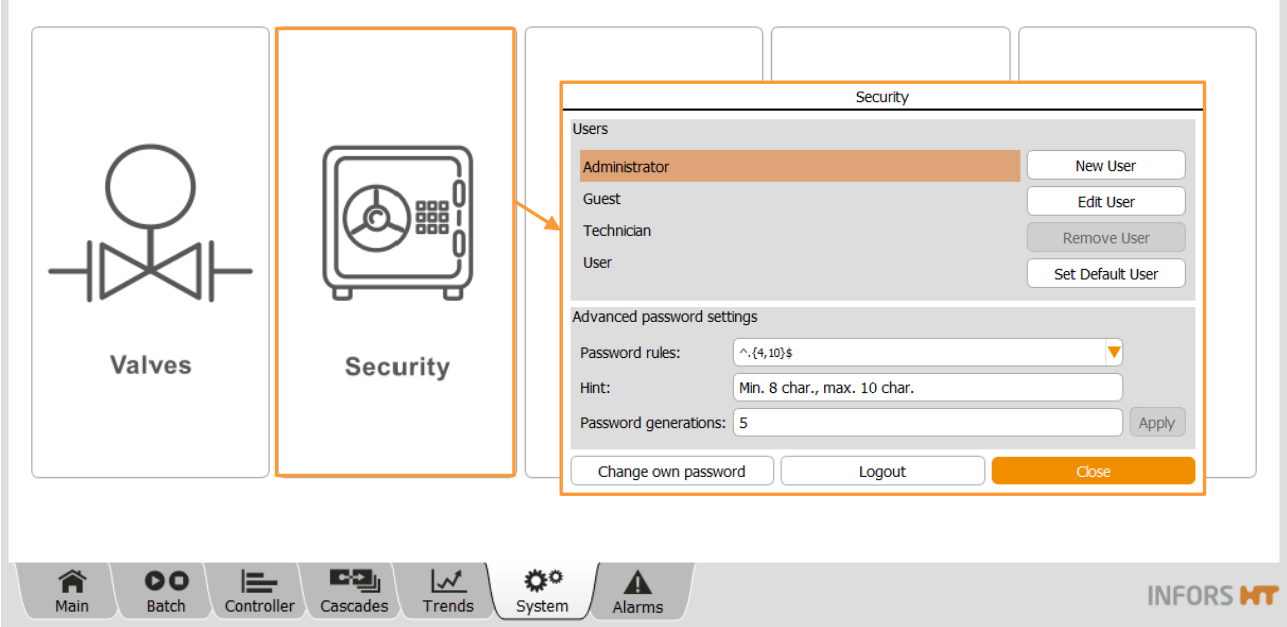
All valves and digital outputs are set to automatic mode (*Auto*) ex-factory. These settings must not be changed!

In column *Category* the view of all (*All*) digital inputs and outputs or only the display of the inputs or outputs can be selected.

The main column shows:

Main column		
Bit / Name		Channel number and designation
Mode	*Auto*	Automatic switching
	Manual	Manual switching, outputs are forced, i.e. the automatic switching is thus disabled.
Set (Switching status of the digital output)	*OFF / ON*	Output is switched off / on
ReadB (electronic feedback channel, which confirms the change in status.	*OFF / ON*	Readback is switched off / on
If the electrical connection is faulty, it is displayed as FALSE		

10.3.2 Security – User Management



The submenu *Security* is used for logging on and off the system. This is where users can also be added or deleted, passwords can be issued, and access authorisations can be assigned.

More or less buttons may be enabled in this menu depending on the access authorisation of the registered user:

- **Login/Logout**: to log on/off to/from the system
- **Change own password**: to change the own password.
- **New User**: to add a new user.
- **Edit User**: to edit user settings.
- **Remove User**: to delete a user.
- **Set Default User/Clear Default User**: to define/delete automatic user login.
- *Advanced password settings*: to define password rules for password security.

The different user levels, access authorisations and functions are described in the following chapters.

10.3.2.1 User Administration

There are five user groups with different access rights. A user is created ex-factory for each user group - except for Service.

User group	User	Password
Guest [1)]	Guest	No password
Users	User	qwertyuiop
Technicians	Technician	qwertyuiop
Administrators	Administrator	qwertyuiop
Service [2)]	---	---

1) *Without access rights, is automatically logged in, if no other user is logged in.*

2) *Is only accessible to qualified INFORS HT service technicians and is blocked for all other users.*

INFORMATION

The factory-defined passwords should be changed and managed accordingly by the authorised person (administrator!) after initial commissioning.

10.3.2.2 Access Authorisations of User Groups

The following tables group the various functions of the touch screen software with an indication of the access authorisations of the user groups. Optional functions are listed, too. These functions are only present with the correspondingly ordered device configuration.

Key:

- V (view) = visible, function cannot be executed
  Visible means that, depending on the function, the button or the menu/dialogue can only be viewed.
- E (execute) = Visible and function can be accessed for execution
  I.e. functions are executable
- Empty field = cannot be viewed and function cannot be executed

BIOREACTOR	User Groups				
	Guests	User	Technician	Admin.	Service
Start / Stop (cultivation)	V	E	E	E	E

STERILISATION Standard	User Groups				
	Guests	User	Technician	Admin.	Service
Full Sterilisation	V	E	E	E	E
SIP Harvest/Sample Valve (Sterilisation harvest/sample valve **05.12.01**)	V	E	E	E	E
STERILISATION Option	Guests	User	Technician	Admin.	Service
SIP Sample Valve (Sterilisation sample valve **17.13.01**)	V	E	E	E	E
SIP Feed Line (Sterilisation feed line)	V	E	E	E	E

RECIPES	User Groups				
	Guests	User	Technician	Admin.	Service
Load/Start	V	E	E	E	E
Save	V	V	E	E	E
Delete	V	V	E	E	E

PUMPS	User Groups				
	Guests	User	Technician	Admin.	Service
Calibrate (Pump calibration)	V	E	E	E	E
Reset (Resetting counter)	V	E	E	E	E
Pump factor (Setting pump factor manually)	V	E	E	E	E
Fill/Empty Pumps (Filling/emptying hoses manually and time-controlled)	V	E	E	E	E

PARAMETER options	User Groups				
	Guests	User	Technician	Admin.	Service
Standard					
Setpoint (changing setpoints)	V	E	E	E	E
Upper/Lower Alarm, Upper/Lower Critical (Setting alarm and critical values)	V	E	E	E	E
Output active ON/OFF (Switching parameters on and off)	V	E	E	E	E
Calibrate pH (Calibrating pH sensor, all variants)	V	E	E	E	E

pH analogue: changing *Slope* and/or *Offset* (*Manual* calibration mode)		E	E	E	E
Calibrating pO_2 sensor, all variants (*Calibrate pO2*)	V	E	E	E	E
pO_2 analogue: Function *USE AS SET-POINT* in calibration menu		E	E	E	E
Function *USE AS SETPOINT* (if present) in calibration menus except for pO_2 analogue				E	E
Calibrate, all except for above mentioned			V	E	E
Calibrate, manually (*Manual* calibration mode), all except for above mentioned				E	E
PID			E	E	E
Options					E
Optional					
Turbidity, *Calibrate* (Calibrating the zero point of turbidity sensor Optek)	V	E	E	E	E
Tare Weight (Taring the vessel weight measurement display)	V	E	E	E	E

CASCADES	**User Groups**				
	Guests	User	Technician	Admin.	Service
Setting a cascade	V	E	E	E	E
Advanced option (Setting an advanced cascade)			E	E	E

TREND LINES (Trends)	**User Groups**				
	Guests	User	Technician	Admin.	Service
Change display settings	E	E	E	E	E

ALARMS	**User Groups**				
	Guests	User	Technician	Admin.	Service
Confirming alarms	V	E	E	E	E

SYSTEM	User Groups				
	Guests	User	Technician	Admin.	Service
Statistics (Viewing statistics of communication between software and bioreactor hardware)	E	E	E	E	E
Licenses (viewing software library licenses)	E	E	E	E	E

DIGITAL INPUTS/OUTPUTS (System / Valves)	User Groups				
	Guests	User	Technician	Admin.	Service
Manually switching digital inputs and outputs	V	V	E	E	E

USER MANAGEMENT (System / Security)	User Groups				
	Guests	User	Technician	Admin.	Service
Login (Logging on to the system)	E	E	E	E	E
Logout (Logging out from the system)		E	E	E	E
Change Password (Changing password)		E	E	E	E
Advanced password settings (configuring password rules)				E	E
New User (Adding a new user)		V	V	E	E
Remove User (Deleting a user)		V	V	E	E
Edit User (Changing user settings)		V	V	E	E
Set Default User (Setting automatic user login)		V	V	E	E
List of all users				V	V

SYSTEM SETTINGS (System / Settings)	User Groups				
	Guests	User	Technician	Admin.	Service
Settings					
IP Settings (Network settings)	V	V	V	E	E
Change Time (Changing date and time)	V	V	V	E	E
Files					
Backup (Saving data)	V	V	V	E	E
Restore (Restoring data)	V	V	V	E	E
Service Menu (Settings in Service Menu)					E
Export Logs (Exporting log files)		V	E	E	E

Controller Board Configuration					
Input channel code (Setting codes for input channels)			V	V	E
Analog Outputs Assign/Adjust (Assigning/changing analogue outputs)			V	V	E
Extended Digital Output Function Code (Setting extended function codes for digital outputs)			V	V	E
Synchronize differing board configuration (Synchronising different configurations of the controller board)			E	E	E
Modbus mapping (Modbus settings)			V	V	E
Digital Output Function Code (Setting function codes for digital outputs)			V	V	E
Balance Settings (Settings for balances)	V	V	V	E	E

TEMPORARY SCREEN LOCK (System / Wipe Screen)	**User Groups**				
	Guests	User	Technician	Admin.	Service
Activating the temporary screen lock	V	E	E	E	E

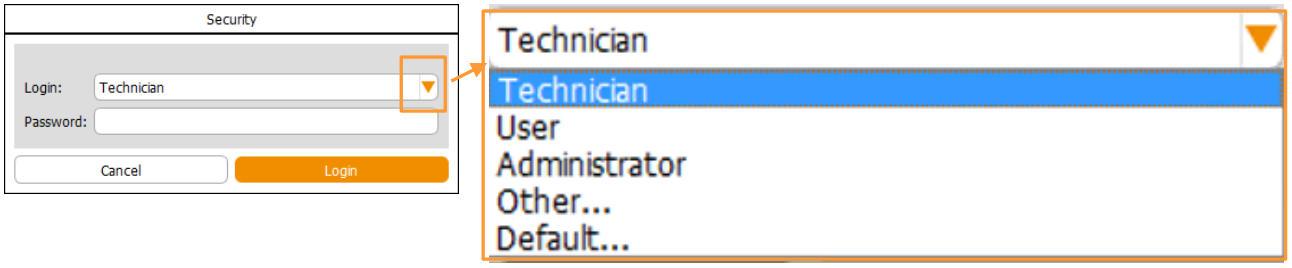
SYSTEM SHUTDOWN	**User Groups**				
	Guests	User	Technician	Admin.	Service
Shutting down the system	V	E	E	E	E

10.3.2.3 Login / Logout – Logging on or off to/from the System

To log on to the system, proceed as follows:

Procedure

1. Call up the main menu *System* and press **Security**.
Submenu *Security* appears.

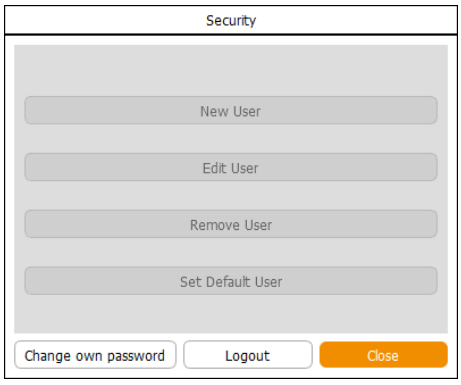


The drop-down list (*Login*) lists all users available by default with factory settings.

- *User*
- *Technician*
- *Administrator*
- *Other*: for use by INFORS HT service employees only
- *Default*: automatic user login without entering a password if previously set using **Set Default User**.

2. Select the desired user, e.g. *Technician.*
3. Enter the password and press **Login**.

   The user is logged in.



The different functions are listed now as buttons in the *Security* menu.
The buttons **Change Password** for password changes**, Logout** for logging off from the system, and **Close** for leaving the menu are enabled on all user levels (except for *Guest*).

INFORMATION

On user level Administrator and above, the password rules can be configured here, too. For details refer to chapter “Password Security – Defining Password Rules”.

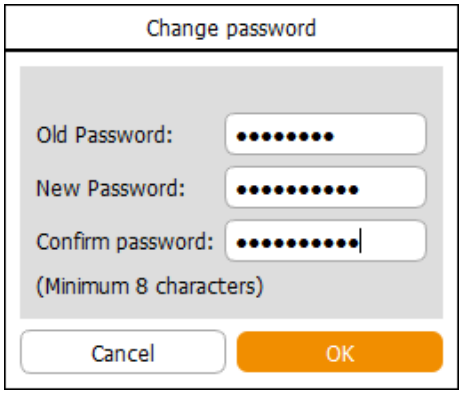
10.3.2.4 Change own Password – Changing the (own) Password

Users of all user groups can change their own password. In order to be able to change the own password, the user must be logged on to the system.

Proceed as follows:

Procedure

1. Call up submenu Security and press **Change own Password**.
   The *Change password* dialogue box appears.



2. Enter the old password.
3. Enter the new password and confirm it by entering it a second time.
   All inputs are displayed as dots.

INFORMATION

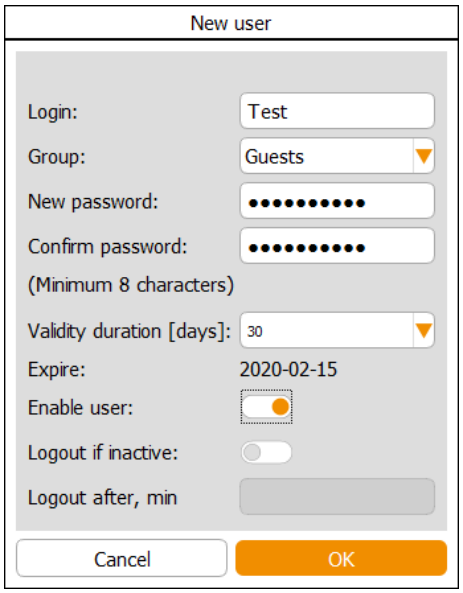
Depending on the password rule settings, the password must meet different conditions. Password rules are configured on user level Administrator and above. For details refer to chapter “Password Security – Defining Password Rules”.

4. Press **OK**.
   The dialogue box disappears; the new password is saved.

10.3.2.5 New User – Adding a New User

To add a new user to the user list, proceed as follows:

Procedure



1. Log on to the system on user level Administrator.
2. Call up the submenu *Security* and press **New User**.
   The *New User* dialogue box appears.
3. Enter a new user in *Login*.
4. Select the desired user group in drop-down list *Group*.
5. Enter the password and confirm it by entering it again in

INFORMATION

Depending on the password rule settings, the password must meet different conditions. Password rules are configured on user level Administrator and above. For details refer to chapter “Password Security – Defining Password Rules”.

6. Select the validity duration of the password in drop-down list *Validity duration [days]*, choose “unlimited”, 30, 100 or 365 days.
   The corresponding expiry date is then displayed in *Expire.*

7. Activate/deactivate access authorisation of the new user in
   This function (enable user) is switched on by default.

INFORMATION

The user has no access rights and no password can be defined, if this function is deactivated.

8. Switch the automatic logout on/off when inactive after a predefined duration and set the expiration time in minutes, if given.

9. Press **OK**
   The dialogue box disappears, the new user is added and shown in the user selection list of submenu *Security*.

10.3.2.6 Edit User – Editing User Settings

In **Edit User** the following settings can be changed for existing users:

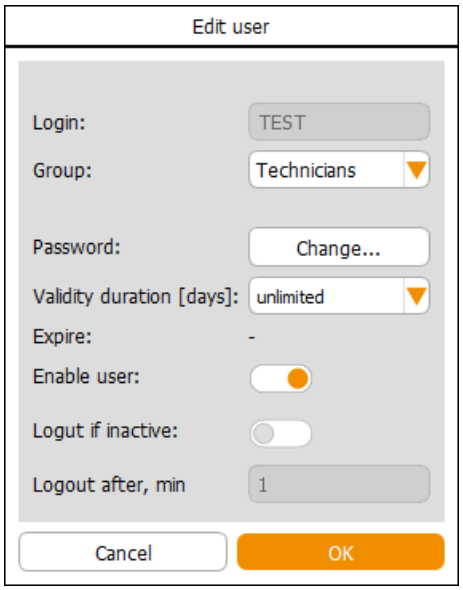
- Assigning a new user group, see chapter “New User – Adding a New User”.
- Changing the password, see chapter “Change Password”.
- Automatic user log-out when screen is inactive after a predefined time in minutes has elapsed. The first user level *Guests* is then set automatically.

To edit user settings, proceed as follows:

Procedure

1. Log on to the system on user level *Administrator* and call up submenu U *Security*.

2. Select the desired user (here: TEST) from the user selection list and press **Edit User**.



The *Edit User* dialogue box appears with nearly identical options as for creating a new user in dialogue box *New User.*

3. Make required settings.
4. Press **OK**

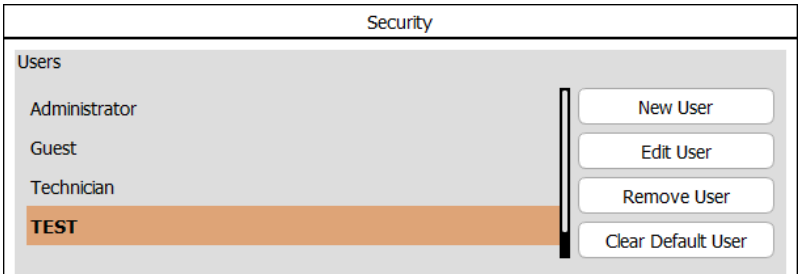
Settings are adopted; the dialogue box disappears.

10.3.2.7 Remove User – Deleting a User

To remove a user from the list, proceed as follows:

Procedure

1. Log on to the system on user level *Administrator* and call up submenu *Security*.



2. Select the user to be deleted (here: *TEST*) in the user selection list.
3. Press **Remove User**.

The *Confirmation* dialogue box appears with information and prompt to confirm deletion of the user from the list.

4. Confirm deletion by pressing **OK.**

The dialogue box disappears, the user *TEST* is deleted from the user selection list.

10.3.2.8 Set / Delete Default User – Setting or Deleting an Automatic User Login

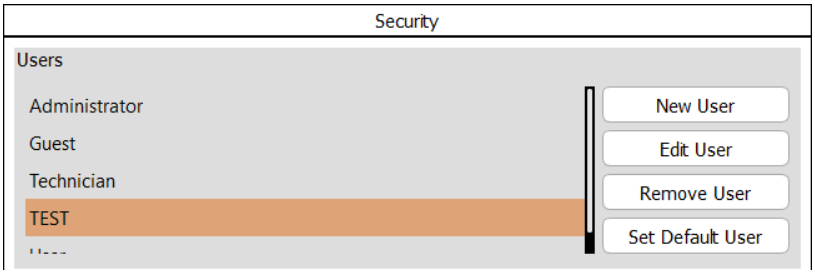
Set Default User is used to set an automatic user login. I.e. a user can be defined who is then automatically logged on to the system the next time it is switched on.

Clear Default User is used to delete the automatic login of a user.

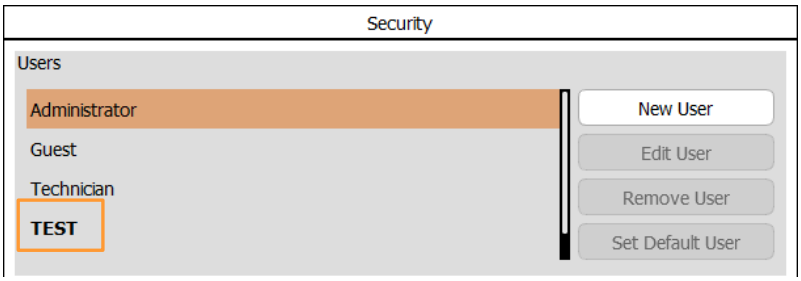
Proceed as follows:

Procedure

1. Log on to the system on user level *Administrator* and call up submenu *Security.*



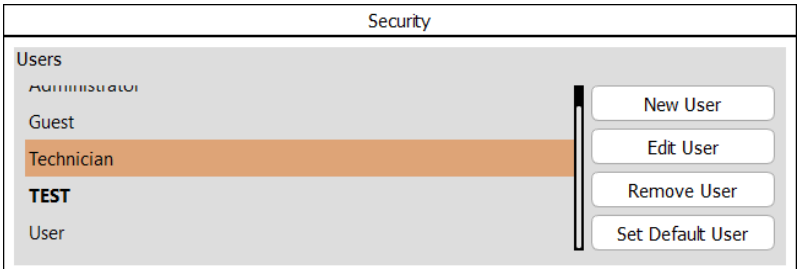
2. Select the desired user (here: *TEST*) in the user selection list.
3. Press **Set Default User**.



The defined user for automatic login is displayed in bold letters, the **Set Default User** button is only visible, but not enabled anymore.

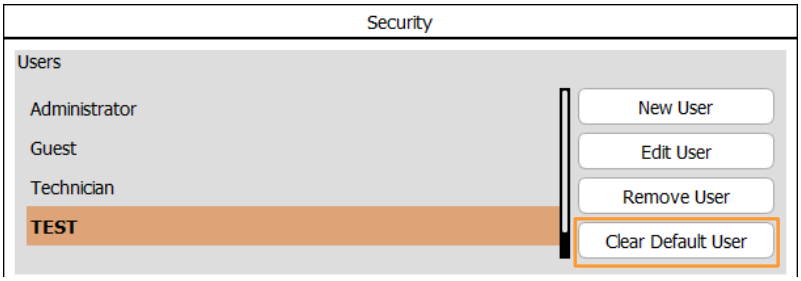
Changing the automatic user login

Another user can be defined here for automatic login, too (here: *Technician*). When selecting tis user, the **Set Default User** button is enabled again.



Deleting automatic user login

When selecting the defined user with the automatic user login setting in the list (here: *TEST*), the **Clear Default User** button is visible and enabled for deleting the automatic user login.



10.3.2.9 Password Security – Configuring Password Rules

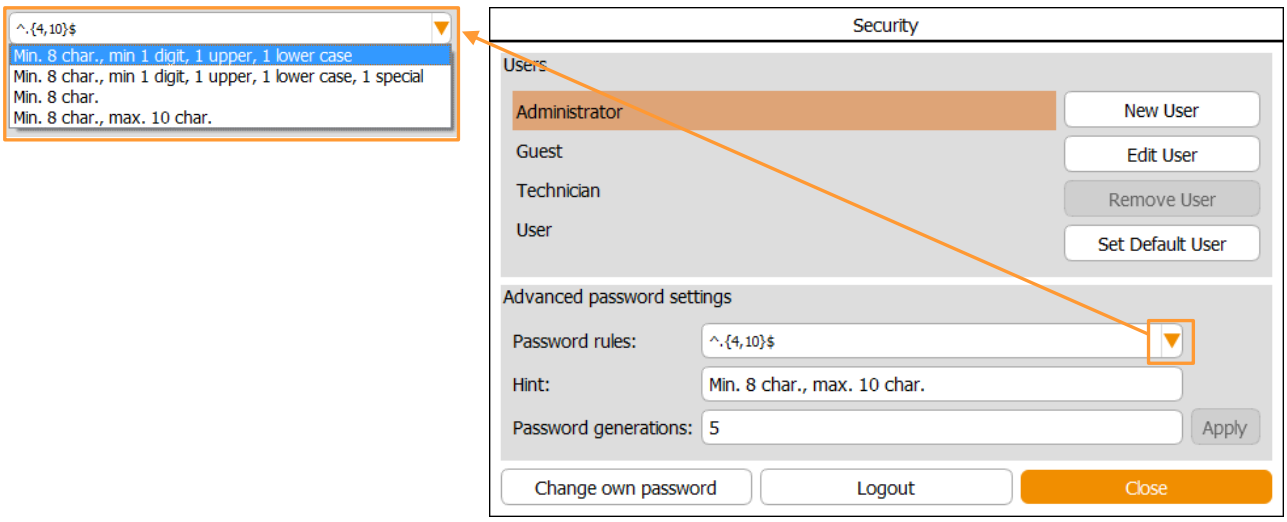
Conditions for creating new user passwords can be configured from user level Administrator on in submenu *Security*

Proceed as follows:

Procedure

1. Login to the system on user level *Administrator* and call up submenu *Security*.

The *Advanced password settings* area is visible and enabled now in the lower part of the menu:



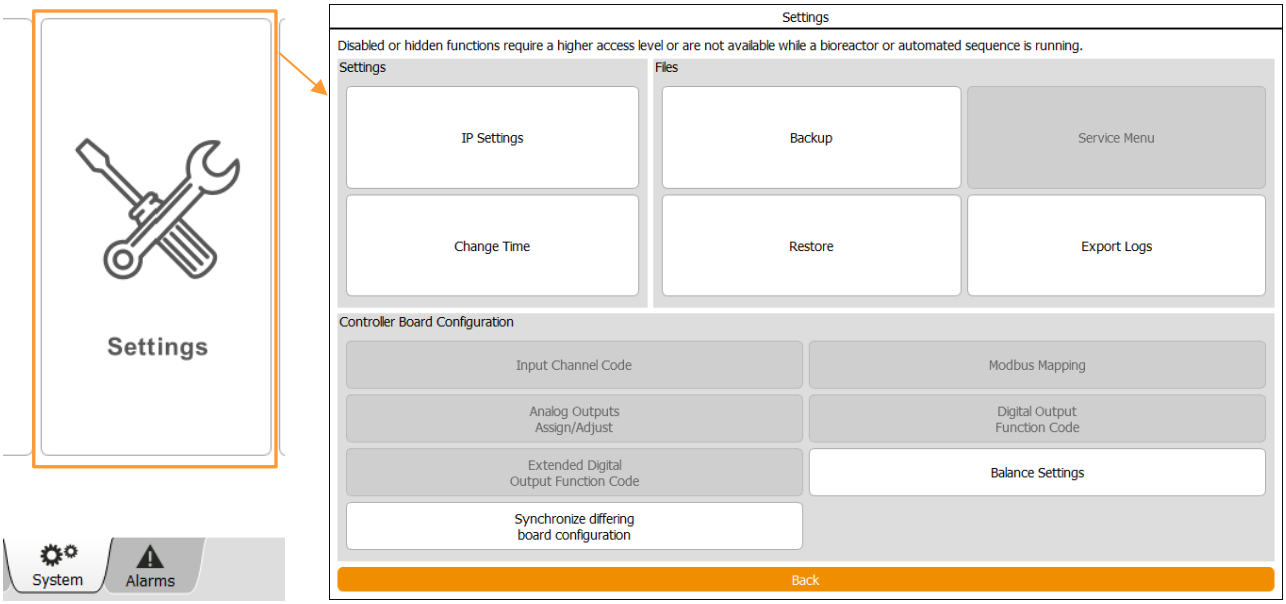
- *Password rules*: drop-down list with choice of four password rules (see figure to the top left). The password must have at least:
  - 8 characters, containing at least 1 number, 1 capital letter and 1 lower case letter.
  - 8 characters, containing at least 1 number, 1 capital letter and 1 lower case letter and 1 special character.
  - 8 characters.
  - 8 up to max. 10 characters.
- *Hint*: shows which rules must be followed during creation of a new password.
- *Password generations*: defines the number of passwords that must be newly created, before a password may be reused.
- **Apply:** to instantly apply the rule when creating a new password. This button is enabled as soon as a rule is changed.

2. Select the desired rule to apply and the number of new passwords that must be created until reuse of an old password is allowed.
3. Press **Apply**.

   The rule is saved and will be shown when creating the next password.
4. Press **Close**.

   Submenu *Security* disappears.

10.3.3 Settings – Basic Settings Device



In the submenu *Settings* basic settings for the device are made. Depending on the access authorisation, more or less buttons are visible and enabled (for details refer to the tables in chapter “Access Authorisations of User Groups”. The figure above shows the menu on user level *Administrator.*

The menu is divided into three areas with the following functions:

Settings

- **IP Settings**: for network settings
- **Change Time**: to set the date and time

Files

- **Backup**: to save data.
- **Restore**: to restore and upload saved data.
- **Service Menu**: access only for qualified INFORS HT service technician or licensed dealer.
- **Export Logs**: to export log files.

Controller Board Configuration

- **Input Channel Code**: to set codes for input channels
- **Analog Outputs Assign/Adjust**: to assign/change analogue outputs.
- **Extended Digital Output Function Code**: to set function codes for extended digital outputs.

- **Synchronize differing board configuration**: to synchronize differing board configurations.

> **INFORMATION**
>
> This button is only visible, if the appropriate alarm (*Difference in board configuration!*) has been triggered and is displayed in main menu *Alarms* after an update of the firmware / change of a control board. For details refer to chapter “System Alarm Difference in board configuration”.

- **Modbus mapping**: for Modbus settings.
- **Digital Output Function Code**: to set function codes for digital outputs.

> **INFORMATION**
>
> None of the functions concerning inputs and outputs, function codes and modbus mappings are described in this manual. These functions are only accessible for INFORS HT service technicians or represantatives.

- **Balance Settings**: for balance settings.

Back directs back to the main menu *System*.

10.3.3.1 IP Settings – Network Settings

IP Settings is used to establish a network connection. This can be performed either automatically or manually.

> **INFORMATION**
>
> This is only possible, if a network cable is connected.

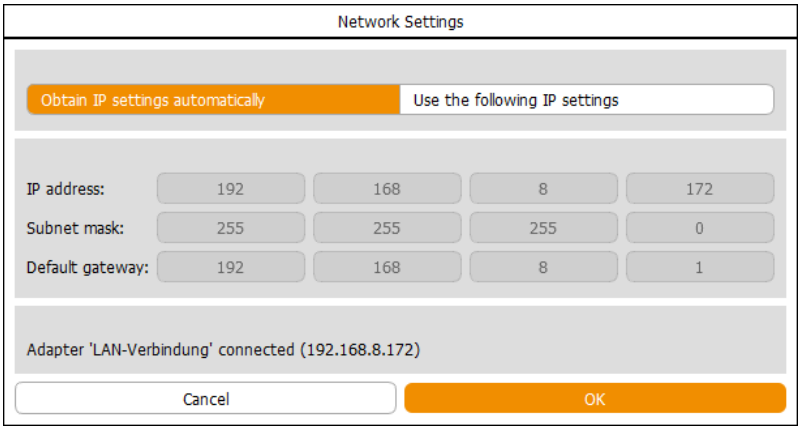
This manual does not describe how to setup a network connection.

To call up the menu to make settings, proceed as follows:

Procedure

1. Log on to the system on user level Administrator and call up submenu *Settings*.
2. Press **IP-Settings**.

The *Network Settings* menu appears with:



- **Obtain IP settings automatically**: to set IP settings automatically (default setting). Condition: a DHCP [1)] server is available in the network.
- **Use the following IP settings**: to use the following IP settings.

  Only after pressing this button, the following fields are enabled.
- *IP address*: shows current IP address or to enter IP address manually.
- *Subnet mask*: displays default gateway or allows manual input.
- *Default gateway*: shows default gateway or allows manual input.

INFORMATION

The status message …*connected* indicates that correct network connection is established. If this is not the case (no signal), the message "*No active LAN connection"* appears.

1) *Dynamic Host Configuration Protocol*

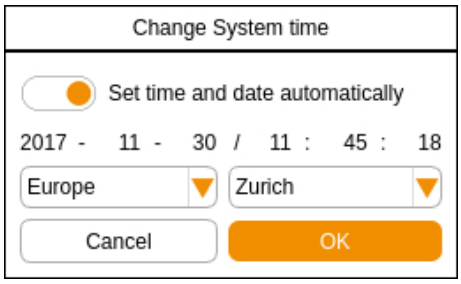
10.3.3.2 Change Time – Changing Date and Time

Change Time enables adjusting the system date and time to the local conditions. The system is set for automatic synchronisation with the time server ex-factory. I.e. the display is corresponding with the selected time zone. Alternatively, these settings can be manually adjusted.

To make settings, proceed as follows:

Procedure

1. Log on to the system on user level *Administrator* and call up submenu *Settings*.
2. Press **Change Time**.



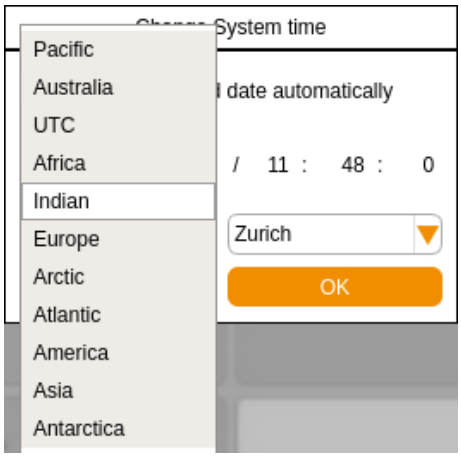
The *Change System time* dialogue box appears with the default configuration ex-factory:

- **ON/OFF** switch *Set time and date automatically* is in position **ON.**
- Display (from left to right) for year, month, day, hours, minutes and seconds.
- Drop-down lists for time zone and city: default = Europe / Zurich

Changes with automatic adjustment

Proceed as follows:

Procedure



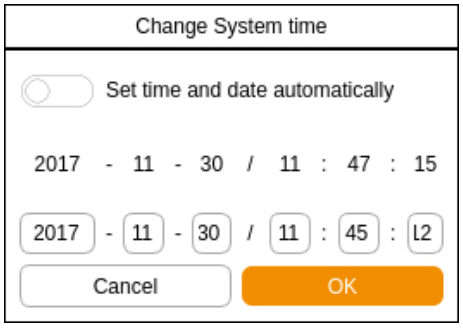
1. Select the time zone and city in the drop-down lists.
2. Press **OK.**

Settings are saved, dialogue box disappears.

Manual changes

Proceed as follows:

Procedure



1. Switch automatic time and date setting **off.**

   Input fields (from left to right) for year, month, day, hours, minutes and seconds appear.
2. Enter desired values.
3. Press **OK.**

   Inputs are saved, dialogue box disappears.

10.3.3.3 Backup – Saving Data

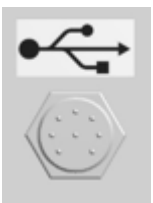
The Backup function is used to save the entire settings of the touch screen software and the control board of the bioreactor. These data can be restored using the Restore function.

Note the following:

- Data can be saved on the internal memory or on a USB stick.
- A data backup is only executable when all running processes are stopped.

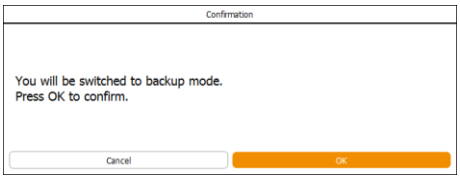
To execute a backup, proceed as follows.

Procedure



Only when using a USB stick, otherwise go to step 2:

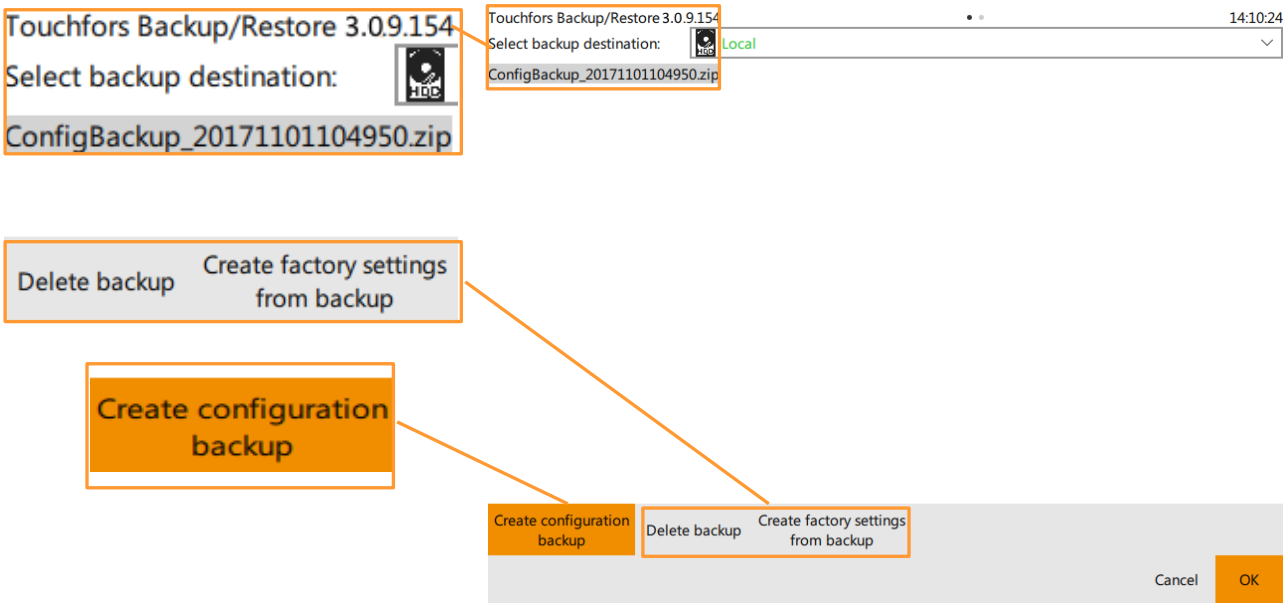
1. Use the special cable provided with the device and connect it to the appropriate connector (see figure on the left) on the rear side of the operating panel and connect the USB stick.
2. Log on to the system on user level *Administrator*, call up main menu *System* and select submenu *Settings*.
3. Press **Backup** in the *Files* area.



The *Confirmation* dialogue box appears with information and prompt to confirm switching to backup mode.

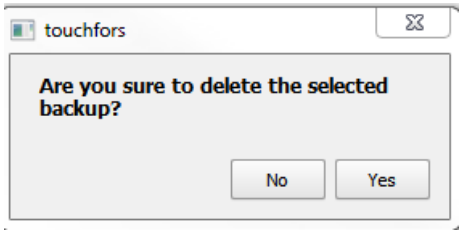
4. Press **OK**.

The menu for data backup opens with:



- *Select backup destination*:
  - *local*: to locally save the backup.
  - *external*: to save the backup externally on a detected and connected USB stick.
- **Create configuration backup**: to create the backup.
- **Delete backup**: to delete the backup.
- **Create factory settings from backup**: to create factory settings from the backup.

5. Select the backup destination and press **Create configuration backup** to create the backup.
6. Press **OK** to save the backup and leave the menu.



Deleting a backup

Pressing **Delete backup** opens a dialogue box with inquiry and prompt to confirm deletion.

If backup on USB stick:

7. Remove the USB stick and the cable.

10.3.3.4 Restore – Restoring Saved Data or Restoring Factory Settings

The Restore function enables to restore data, which have previously been saved using the Backup function. Data will be uploaded to the system again. It is also possible to restore factory settings using this function.

INFORMATION

Factory settings usually represent the settings of the bioreactor in as-delivered condition. In case of retrofitting of the bioreactor, these settings can be updated, too. Both is exclusively carried out by an INFORS HT service technician or a licensed dealer.

Note the following:

- Data are either restored from the internal memory or from a USB stick, see chapter “Backup – Saving Data”.
- The Restore function is only executable when all running processes are stopped.

To execute the Restore function, proceed as follows:

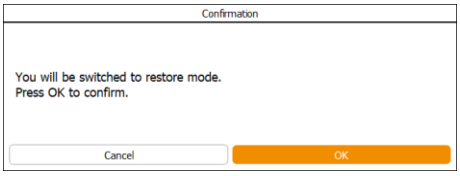
Procedure

Only when using a USB stick, otherwise go to step 2:

1. Use the special cable provided with the device and connect it to the appropriate connector on the rear side of the operating panel and connect the USB stick with the saved date (Backup data).

2. Log on to the system on user level *Administrator*, call up main menu *System* and select submenu *Settings*.

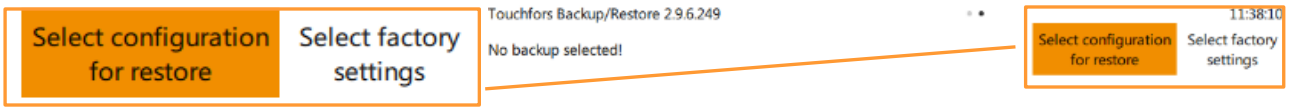
3. Press **Restore**.



The *Confirmation* dialogue box appears with notice and prompt to confirm switching to restore mode.

4. Press **OK**.

The menu for data restoring appears with:

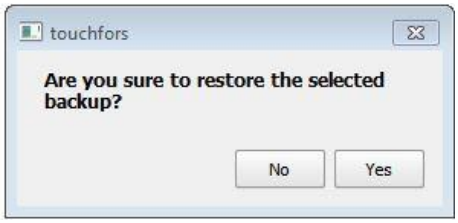


- **Select Configuration for restore**: to select the backup data for restoring.
- **Select factory settings:** to select factory settings.

Executing the backup for data restoring

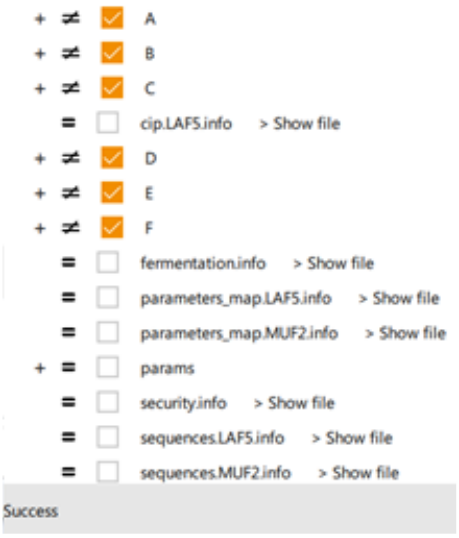
Pressing **Select configuration for restore** changes the menu display and shows with *Select backup source* the choice of the possible data sources:

- local: internal memory
- xy (drive) / external: detected and recognised USB stick
- **OK**: To confirm selection.



After selection of the data source, a dialogue box appears with inquiry and prompt to confirm restoring.

5. Press **Yes**.



The screen changes and lists data for configuration comparison.

- **≠** signifies a difference between Backup and current configuration.
- **=** No difference between Backup and current configuration.
- **+/-** To open/close tree
- Show file / Show difference: To display file / difference

INFORMATION

This view for showing the difference within a file is for information purposes and mainly foreseen for Infors service or licensed Infors dealers. It shows the differences between the settings of the file to restore and the currently used version in unified format (also *unidiff*).

- **Cancel**: to cancel the backup process and leave the menu.
- **OK**: to execute the backup for restoring data.

10.3.3.5 Export Logs – Exporting Log Files

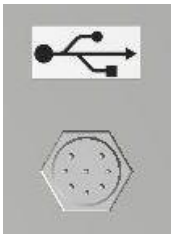
The Export Log functions enables to save all log files (protocol files) as well as alarms and error messages on a USB stick.

Note the following:

- A USB stick is needed for the export.
- Export is only executable when all running processes are stopped.

Proceed as follows:

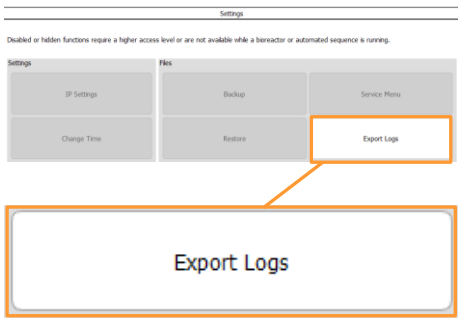
Procedure



1. Use the special cable provided with the device and connect it to the appropriate connector (see figure on the left) on the rear side of the operating panel.

2. Connect the USB stick.

3. Log on to the system on user level *Technician* or *Administrator*.
4. In main menu *System*, call up submenu *Settings*.



5. Press **Export Logs**.

   Data export is started.

   Once the export is finished, the *Information* dialogue box appears with message *Log files successfully exported to: xxxxx*

6. Press **OK**.

   The dialogue box disappears. The Zip file is stored on the USB stick now.

10.3.3.6 Balance Settings

This function is used to set up to a maximum of 7 connectable balances (via the switchbox of the device manufacturer).

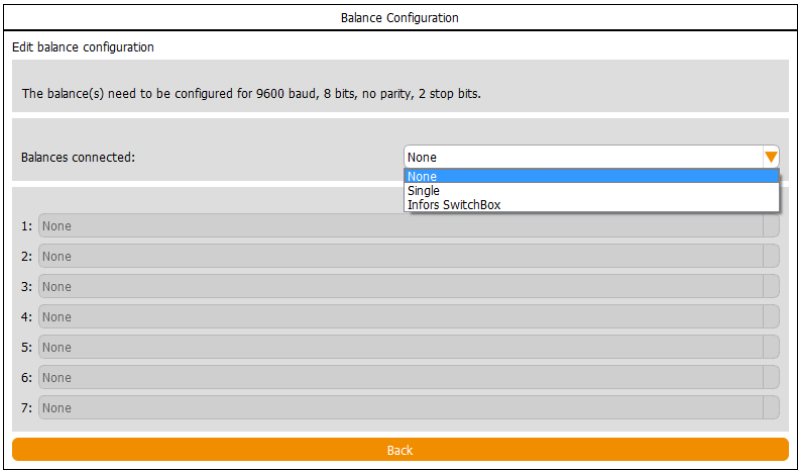
Balances must be configured with the following values: Baud rate 9600, 8 bits, no parity, 2 stop bits.

Proceed as follows:

Procedure

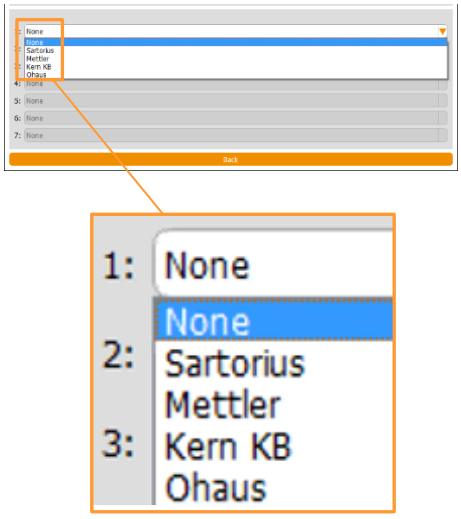
1. Connect the balance(s) or switchbox
2. Log on to the system on user level *Administrator*.
3. In main menu *System*, call up submenu *Settings*.
4. Press **Balance Settings.**

The menu *Balance Configuration* appears with:



- Information with the above-mentioned configuration values for balances.
- Drop-down list *balances connected*: to select number of connected balance(s).
  - *None*: no balance
  - *Single*: one balance (without Switchbox)
  - *Infors SwitchBox*
- 7 drop-down lists, of which one or all are enabled, once one option has been selected.

5. Select the number of balance(s).



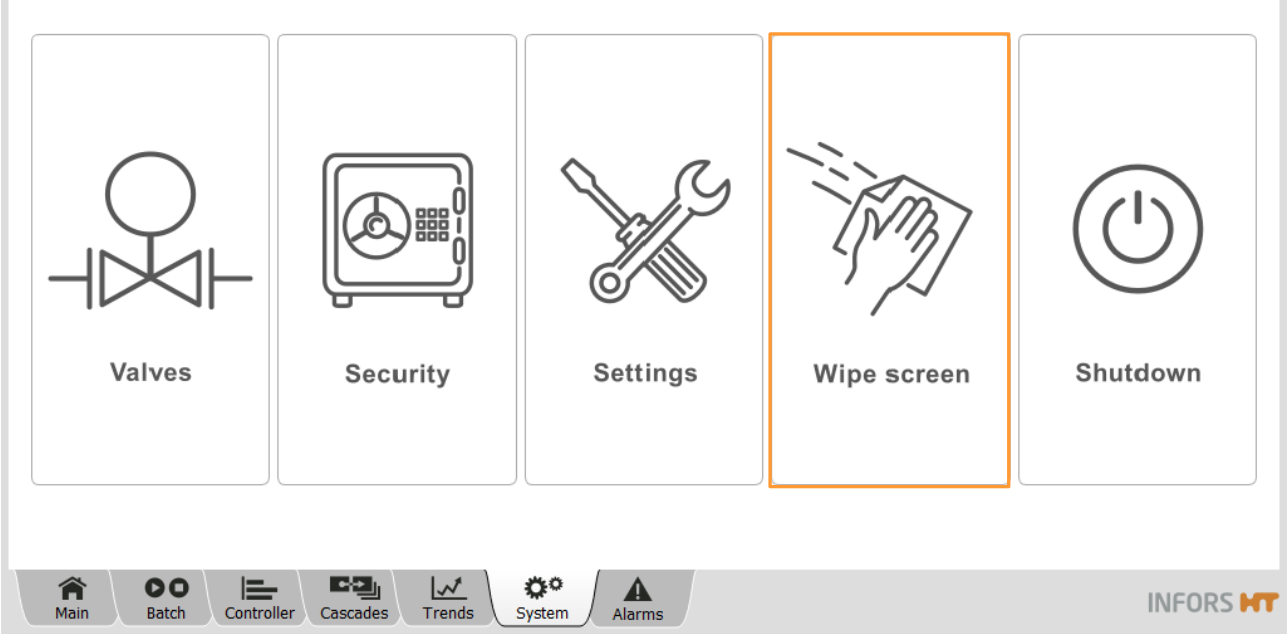
Drop-down list(s) for selection of the balance type(s) connected appear(s). The choice contains the following types: none (no balance), Sartorius, Mettler, Kern KB und Ohaus.

6. Select the balance type(s).

7. Press **Back**.

Settings are adopted, submenu Settings reappears.

10.3.4 Wipe Screen – (Temporarily) Locking the Screen



The submenu Wipe Screen has one function only: It locks the screen to prevent any inputs on the screen for 20 seconds. This allows e.g. cleaning the screen for 20 seconds if required.

To activate the temporary screen lock, proceed as follows:

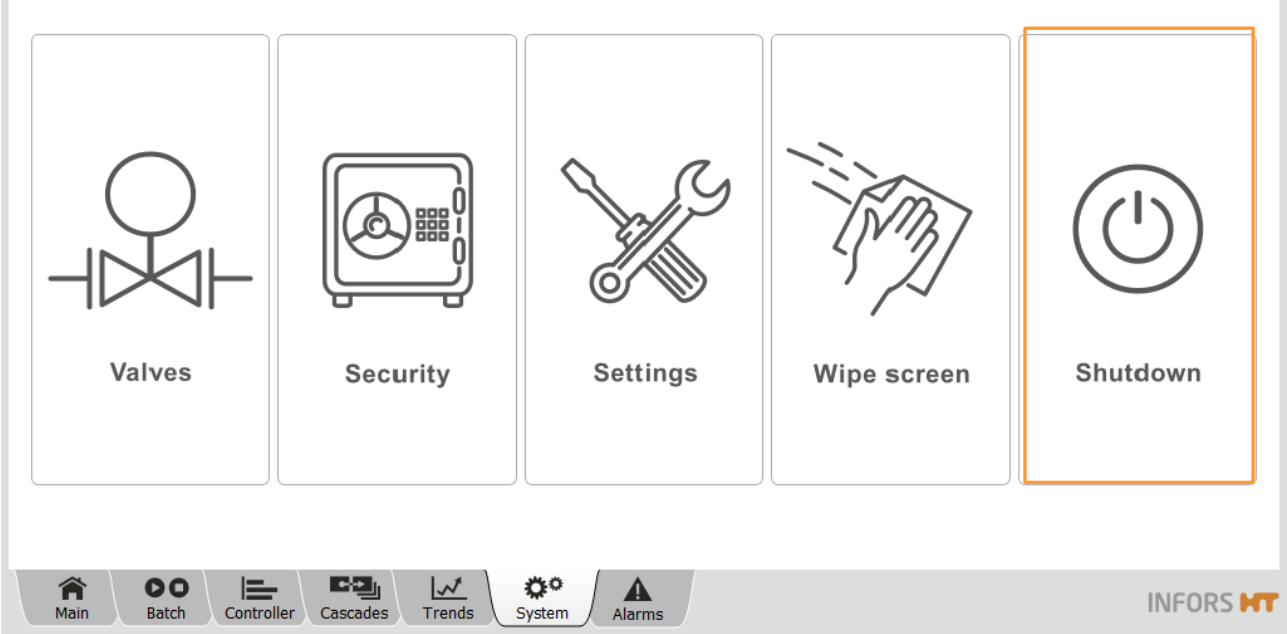
Procedure

1. In main menu *System*, press **Wipe Screen**.

The screen turns white, the remaining time is displayed in seconds.

Once the time has elapsed, the last screen reappears automatically.

10.3.5 Shutdown – Shutting Down the System



The submenu *Shutdown* has one function only: it shuts down the system. The system can only shut down and switch off if all bioreactors have been stopped.

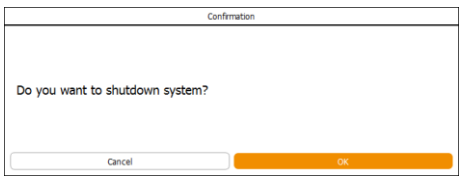
INFORMATION

ALWAYS shut down the system first, only then switch the device off at the main switch.

Proceed as follows:

Procedure

1. Stop any running process by pressing **Stop** in the main menu *Batch*, if necessary.
2. Call up the main menu *System* and press **Shutdown**.



The *Confirmation* dialogue box appears to confirm the shutdown.

3. Press **OK**.

The system shuts down.

10.4 Recipes

The various buttons for the Recipes function in main menu *Batch* can be used to load and start, save or delete what are referred to as recipes. This means all parameter settings (including cascade settings) for a cultivation process can be saved and re-used for re-curring operating processes later.

INFORMATION

All parameter settings, cascade settings and calibration data of sensors are saved. Pump calibration data are not saved. Calibration data of sensors are not uploaded.

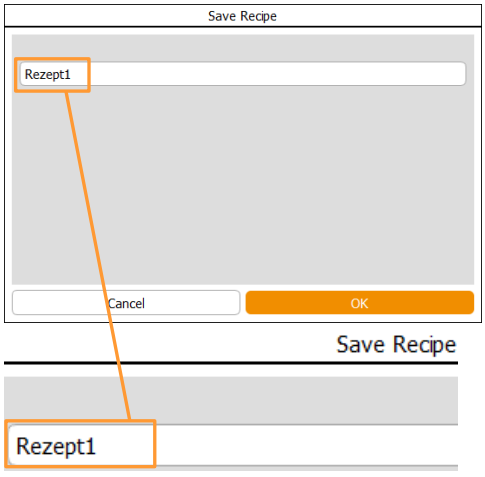
10.4.1 Save Recipe – Saving a Recipe

Recipes can be saved when the bioreactor is running or stopped.

To save a recipe, proceed as follows:

Procedure

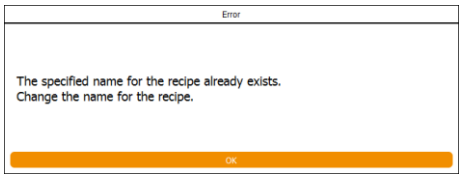
1. Log on to the system on user level *Technician* or above.
2. Call up main menu *Batch* and press **Save Recipe**.



The *Save Recipe* dialogue box appears.

3. Enter the desired file name.
4. Press **OK**.

The dialogue box disappears, the recipe is saved.



Recipe file name used twice

If the file name for a recipe has been used twice, an *Error* dialogue box appears with the appropriate information and instruction.

10.4.2 Load/Start Recipe – Loading and a Recipe

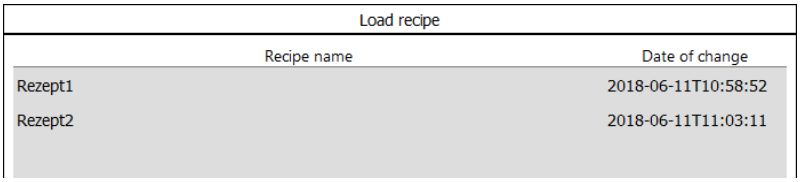
All preparations for a cultivation process should be made before loading and starting a recipe.

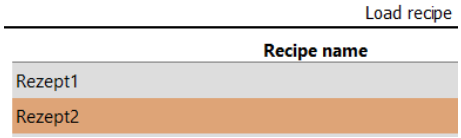
To load a recipe, proceed as follows:

Procedure

1. Call up main menu *Batch* and press **Load/Start Recipe**.

   The *Load recipe* dialogue box appears, listing all the saved recipes with save date and time.



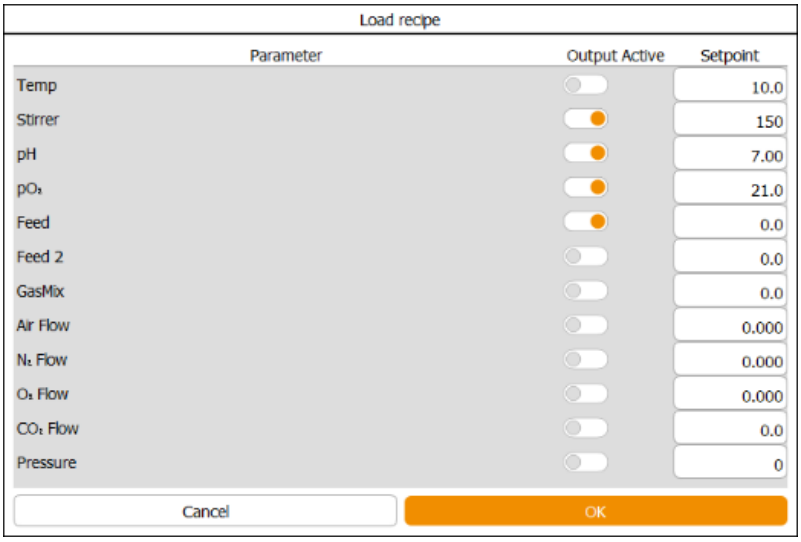


2. Select the desired recipe.

   The selected recipe is displayed with an orange background.

3. Press **Next**.

The *Load recipe* dialogue box changes views.



All parameters used in the recipe are listed here. Setpoints can be subsequently changed here and parameters switched on or off. The bioreactor is started with **OK**.

4. If applicable, change setpoints and/or switch parameters on/off.
5. Press **OK**.

   The dialogue box disappears, the bioreactor starts.

10.4.3 Delete Recipe – Deleting a Recipe

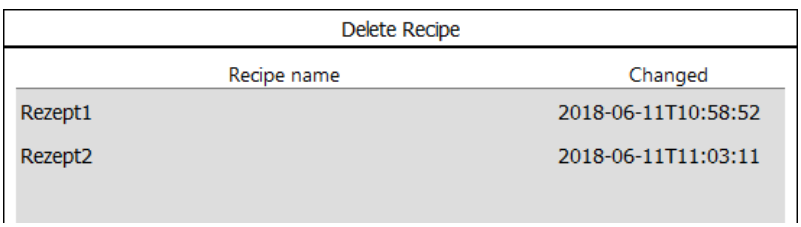
Recipes can only be deleted one by one. Recipes can also be deleted during a running cultivation process.

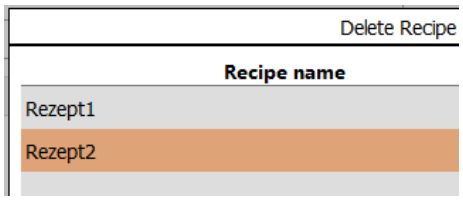
To delete a recipe, proceed as follows:

Procedure

1. Log on to the system on user level *Technician* or above.
2. Call up main menu *Batch* and press **Delete Recipe**.

   The *Delete Recipe* dialogue box appears and lists all saved recipes.

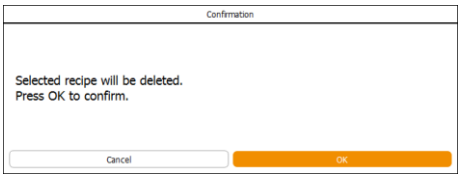




3. Select the desired recipe.

The selected recipe is displayed highlighted in orange.

4. Press **OK**.



The *Confirmation* dialogue box appears with information and prompt to confirm the deletion of the recipe.

5. Press **OK**.

The dialogue box disappears; the recipe is deleted.

10.5 Parameters

The following chapter contains short descriptions of all pa-rameters. In addition to all the parameters that are available as standard in every device configuration, this also includes those parameters that are only configured if the device option is available.

10.5.1 Temperature

Measures and controls the temperature in the vessel. The measured values are recorded by a platinum resistance thermometer (Pt100 sensor).

10.5.2 Stirrer

Measures and controls the rotation speed of the stirrer shaft. The speed range depends on factors such as vessel volume, number of impellers and viscosity of the culture. For details see main chapter “Technical Data”, chapter “Specifications”, “Stirrer”.

10.5.3 pH

Measures and controls the pH. The range of control is from pH 2 to 12. Depending on the selected variant, the measurement system is analogue or digital.

The pH is controlled by adding acid and base via the two peristaltic pumps *Acid* and *Base*. The activity of the pumps is time dependent. This means that they always operate in start/stop mode at the

same speed. Control is made by a PID loop. A dead band can be used to prevent unwanted rapid dosing.

Temperature compensation is a special function of the pH parameter when using the analogue pH sensor from the manufacturer METTLER. This function must be switched on during cultivation so that the temperature dependency of the measurement principle is corrected.

INFORMATION

pH of liquids is also temperature dependent which is why the pH also reacts on temperature changes when temperature compensation is switched on.

For the digital pH sensors, this function is integrated in the sensor.

10.5.4 pO_2

Measures and controls the saturation of dissolved oxygen. Depending on the selected variant, the measurement system is analogue or digital.

In comparison, for example, with pH measurement, which is calibrated to absolute measurements, calibrating the oxygen measurement is always performed to a relative reference point. To do this the calibration is to 100 % relative oxygen saturation, generally determined with air to a max. stirrer speed and maximum gassing rate. The absolute concentration of dissolved oxygen in mmol/l can therefore differ for 100 % saturation depending on the process.

The PID controller output from pO_2 is generally cascaded to other parameters such as *Stirrer*, *Flow*, *Feed* or *GasMix*.

10.5.5 Antifoam

Measures the foam formation and regulates the addition of antifoam agent. The antifoam pump is activated as soon as the antifoam sensor comes into contact with foam.

The activity of the pump is time dependent. This means that it always operates in start/stop mode at the same speed.

- The *Dose time* must be set in seconds instead of the setpoint.
- The *Wait time* must be set in seconds instead of setting an alarm limit.

10.5.6 Level

Measures the level in the vessel by means of the level sensor. A signal is generated (*Output* of parameter *Level* = 100 %), as soon as the level sensor detects liquid. To regulate the level in the vessel, a pump can be assigned to parameter *Level* using a simple cascade.

10.5.7 Feed

Regulates the analogue peristaltic pump *Feed* for addition of the nutrient solution. The pump speed is adjustable and can be set in steps of 0.1 % within a range of 0 % to 100 %.

10.5.8 Feed 2 and Feed 3

Regulate the optional analogue peristaltic pumps *Feed 2* and *Feed 3*. The pump speed is adjustable and can be set in steps of 0.1 % within a range of 0 % to 100 %.

10.5.9 Flow

Measures and regulates the volume flow of two or more process gases in the culture vessel via a single mass flow controller (thermal mass meter with integrated control valve). The measurement system is entirely electronic, and the measurement is displayed according to the present configuration in L min^{-1}.

If the parameter *Flow* is available this means that the individual process gas lines are equipped with solenoid valves, which are switched using the *Gasmix* parameter.

10.5.10 Air Flow, O_2 Flow, N_2 Flow

All these flow parameters measure and control the volume flow of the appropriate process gas in the vessel via an individual mass flow controller (thermal mass meter with integrated control valve) per gas. The measurement system is entirely electronic, and the measurement is displayed in L min^{-1}.

10.5.11 GasMix

Controls the oxygen concentration in the inlet air. This is achieved by switching between air and oxygen or air and nitrogen for a 2-gas-mix system or air, oxygen and nitrogen for a 3-gas-mix system.

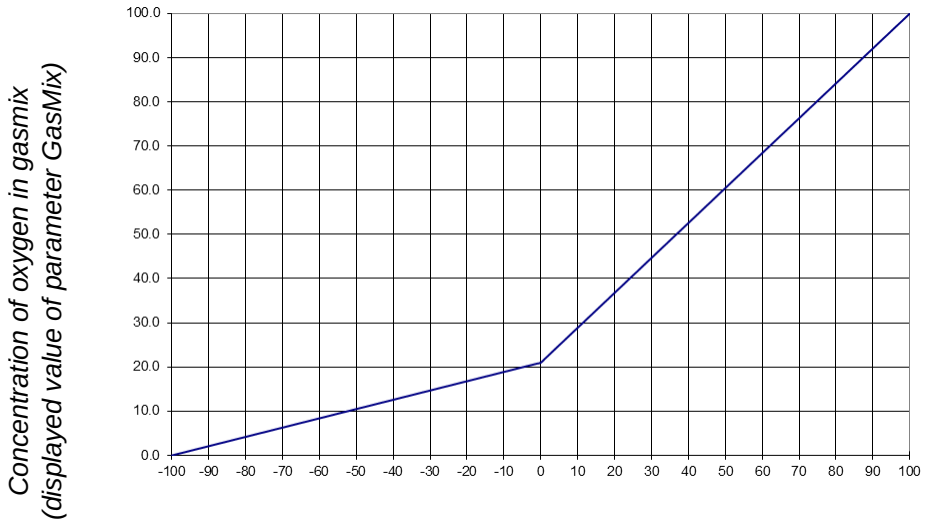
Depending on the existing configuration this means that the relevant solenoid valve is switched on or the individual gas flow parameters are controlled.

INFORMATION

If the parameter *GasMix* combined with the parameter *GM Flow* and the parameters *Air Flow*, *O_2 Flow* and/or *N_2 Flow* is installed and configured, the specified parameters are preconfigured by the device manufacturer in an advanced cascade for pO_2 control.

The following applies to the setpoint input and value display in the touch screen software:

Setpoint GasMix	Meaning	Value display
-100 %	Nitrogen only	0 % O_2
0 %	Air only	21 % O_2
100 %	Oxygen only	100 % O_2



Setpoint Parameter GasMix

Example

2-gas-mix system with air and oxygen, supplied via a magnetic valve.

The solenoid valves are switched according to the pre-set cycle duration in parameter option *PID* of the *GasMix* parameter.

Settings

- cycle duration: 10 seconds (*Eval. Time (s)* in option *PID*)
- setpoint *GasMix*: 20

This means that:

- the solenoid valve for oxygen opens for 2 seconds
- the solenoid valve for process air opens for 8 seconds

Setpoint 100 ≙ 10 seconds

Setpoint 20 ≙ 2 seconds

INFORMATION

For this described configuration of the 2-gas-mix system with air + oxygen with two solenoid valves, the oxygen portion of the gas mixture cannot fall below 20.95 %.

10.5.12 GM Flow

Sets the gassing rate of the gas mixture (GasMix parameter). This parameter can only be used and set in conjunction with the parameters *GasMix*, *Air Flow* and O_2 *Flow* and/or N_2 *Flow*.

From the gassing rate of the gas mixture (*GM Flow*) and the setpoints of the GasMix parameters the device calculates the volume flow rates of the individual gases (e.g. *Air Flow*, O_2 *Flow* etc.)

Only a setpoint input for the *GM Flow* parameter is required, the values of the parameters specified above are automatically determined and controlled.

10.5.13 Pressure

Measures and controls the pressure in the vessel. The measurement is performed by a piezoresistive pressure sensor and controlled by the control valve in the exit gas line.

10.5.14 Weight

Measures the weight of the vessel and its contents via the three load cells. The weight display is tared via *Tare Weight* function.

10.5.15 Turbidity

Is used to determine the turbidity of the culture. Turbidity can be used to draw conclusions regarding the biomass concentration in

the culture. The measurement system comprises a sensor with integrated transmitter. Measurement range of absorption: 0 to 4 CU. The parameter *Turbidity* is set to this measurement, too.

10.5.16 Exit CO_2 and Exit O_2

Measure the gas concentration of carbon dioxide (CO_2) and oxygen (O_2) in the exit gas of the bioreactor via a combined gas sensor and are used for exit gas analysis. Depending on the selected variant of the measurement system, the measurement ranges and application areas of the gas sensors are different.

10.5.17 pCO_2

Measures the saturation of dissolved carbon dioxide (CO_2) in the culture by means of a digital CO_2 sensor with integrated temperature sensor. Measured values are displayed on the associated transmitter and in the touchscreen software. The measurement display of parameter *pCO_2* is set to a range from 0 to 1000 hPa, analogous to the measurement display of the transmitter.

10.5.18 Redox

Measures the reduction/oxidation potential (redox) in the medium in mV. Depending on the selected variant, the measurement system is analogue or digital. The measurement range is -2000 mV to +2000 mV (analogue system) or -1500 mV to +1500 mV (digital system).

10.5.19 Conductivity

If the bioreactor is equipped with an ABER FUTURA biomass sensor, this can also be used to measure conductivity. In this case the measurement range is: 0 to 40 mS cm^{-1}.

Sensors of the ABER Futura systems measure the permittivity (also: *capacitance*) and conductivity of the culture. This measured data can be used to determine a correlation with the live biomass concentration, for example, using the soft sensor in eve® or data evaluation.

INFORMATION

The sensor with the corresponding transmitters must be purchased directly from the manufacturer ABER. INFORS HT offers a connection to the transmitter on the basic unit.

10.5.20 Capacitance

Measures the capacity that correlates to the live biomass. This is measured using an ABER FUTURA biomass sensor. The measurement range is 0 pF cm^{-1} to 400 pF cm^{-1}.

Sensors of the ABER Futura systems measure the permittivity (also: *capacitance*) and conductivity of the culture. This measured data can be used to determine a correlation with the live biomass concentration, for example, using the soft sensor in eve® or data evaluation.

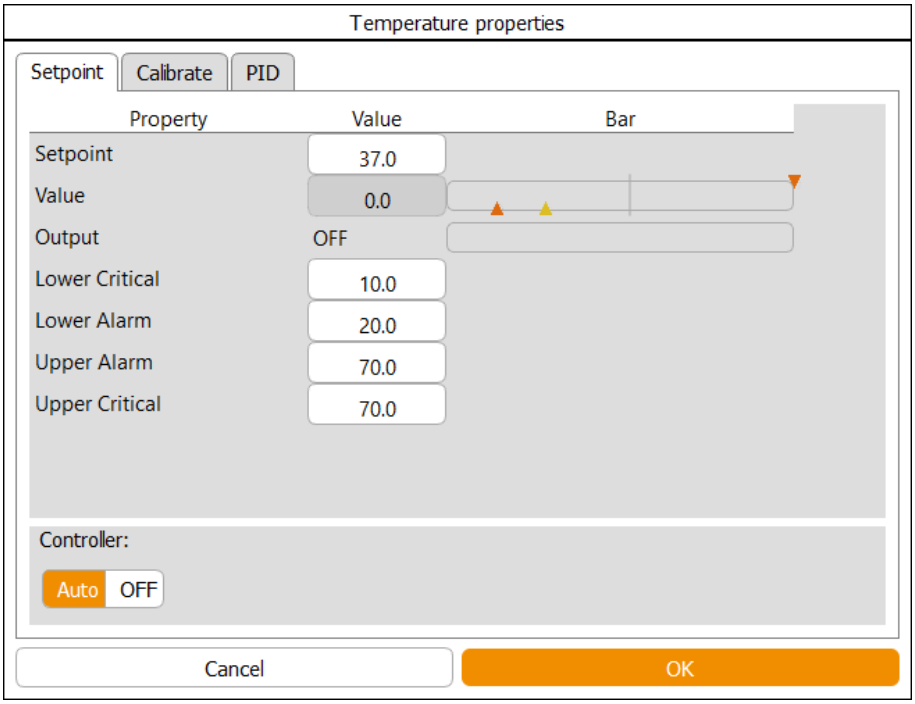
INFORMATION

The sensor with the corresponding transmitters must be purchased directly from the manufacturer ABER. INFORS HT offers a connection to the transmitter on the basic unit.

10.5.21 Ext. Pump

Regulates the external peristaltic pump of the type 120U/DV from the manufacturer Watson Marlow. The pump speed is adjustable and can be set in steps of 0.1 % within a range of 0 % to 100 %.

10.6 Parameter Options



Parameter options are setting menus for the parameters. They are shown as tab pages in the *Properties* dialogue box for the selected parameter. The figure above shows the example of the *Temp properties* dialogue box (temperature parameter).

The parameters and their options (setting menus) are called up in main menu *Controller*.

INFORMATION

If a load cell is available, the weight display can be tared via the **Tare Weight** button in main menu *Batch*. This function can only be performed there and is not available as an option in the *Weight* parameter.

Depending on the access authorisation and the type of the parameter, more or less options may be available.

Every *properties* dialogue box for each parameter has two buttons:

- **OK**: to save inputs and close the dialogue box
- **Cancel**: to close the dialogue box without changes

Most parameters have the following options:

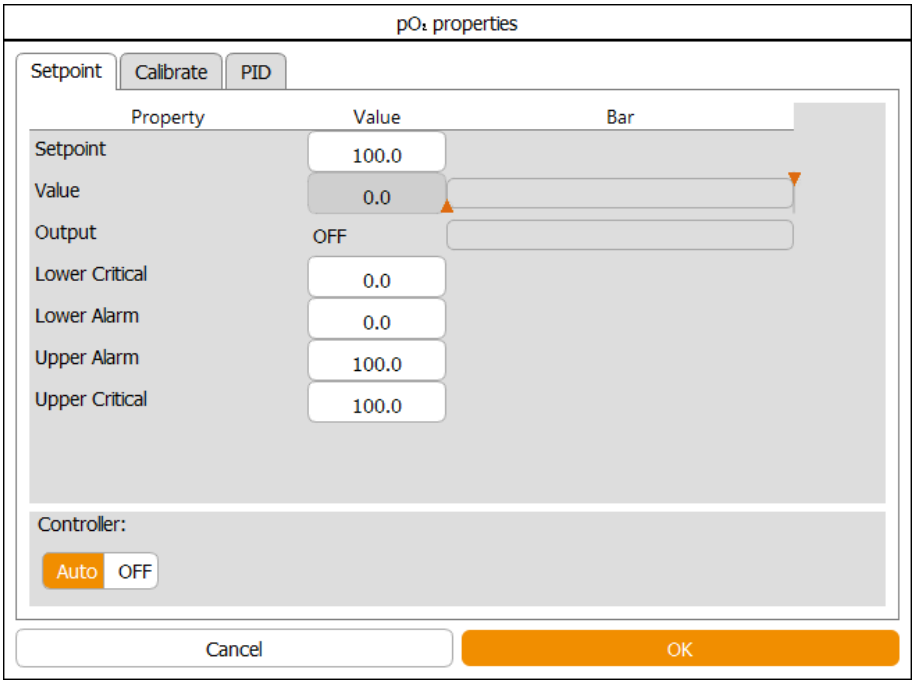
- *Setpoint*: this is where setpoint values, alarm values and critical values can be set and where parameters can be switched on and off.
- *Calibrate*: this is where the sensors' measured values are calibrated.

  This option is only available for calibration of the measured values of the pH, pO_2 and turbidity sensors (OPTEK system) on user levels *User* and *Technician*. All other calibration menus are only accessible on user level Administrator and above.
- *PID*: This is where controller settings are made.
- *Options*: This is where the basic parameter settings are made.

  This option is only accessible to the manufacturer's qualified personnel. This option is not visible or enabled at any other user level.

The following chapters describe the content and function of the individual tab pages, i.e. parameter menus. Each menu description is followed by either detailed setting instructions or a cross reference to the respective corresponding in these operating instructions.

10.6.1 Setpoint



The tab page for the *Setpoint* option is divided up into a three-column main area with input fields and view boxes and a *Controller* area.

Columns

- *Property*: designation of the input fields and view boxes
- *Value*: values of the input fields and view boxes
- *Bar*: graphic display of the values as in main menu Controller. For details refer to chapter “Main Menus”, “Controller – Value Display”.

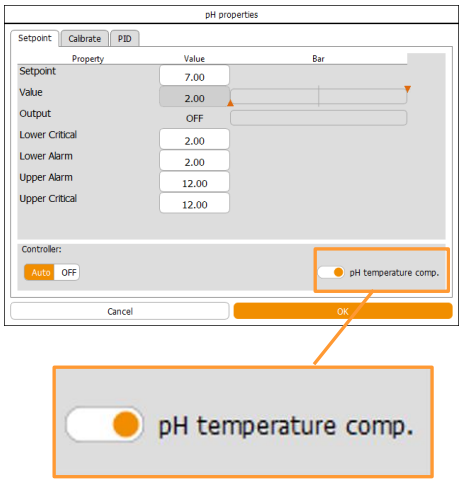
Input fields and view boxes

- *Setpoint*: to enter the setpoint
- *Value*: displays the current value
- *Output*: shows the controller output as a percentage.
- *Lower Critical* and *Upper Critical*: to enter the lower critical and upper critical value
- *Lower Alarm*: to enter the lower alarm value
- *Upper Alarm* and *Lower Alarm*: to enter the upper alarm and lower alarm value

Controller

- **Auto**: to switch on the parameter into automatic mode. In this mode, it is possible to switch the parameter on or off by touching the controller output (displayed value *OFF* or %) in main menu *Controller* during a running cultivation.
- **OFF**: to switch off the parameter. This mode deactivates the controller output in main menu *Controller*, too.

pH temperature compensation



If the pH measurement system with analogue pH sensors from the manufacturer METTLER is present, parameter pH has the additional function *pH temperature comp*. (pH temperature compensation). With digital pH measurement systems, this function is integrated into the pH sensor.

pH temperature compensation must be switched on during cultivation so that temperature-compensated values can be generated. That means, the temperature dependency of the measuring principle will be corrected.

INFORMATION

pH of liquids is temperature-dependent, too. Therefore, pH will still be responsive to temperature variation, although temperature compensation is switched on.

This function must also be switched on to calibrate the pH sensor whilst simultaneously measuring the temperature of the pH buffer solution or manually entering the temperature of the buffer solution.

10.6.1.1 Setting Setpoint Values, Switching Parameters ON / OFF

Parameter setpoint values are basically set in the configuration dialogue for the bioreactor. Once the bioreactor is running, setpoint values can be changed then via main menu *Controller*.

Parameters can be switched on or off in the configuration dialogue or via main menu *Controller* once the bioreactor is running, if their controller output is set to automatic mode (*Auto*) in the *Setpoint* option of the parameter.

In stopped state of the bioreactor, all its parameters are automatically switched off and cannot be switched on.

INFORMATION

The bioreactor is always started with the settings in the configuration dialogue. Changes to these settings are saved and transferred to the next configuration dialogue. If setpoint values are changed or parameters are switched on/off whilst the bioreactor is running, these settings are only adopted for the current cultivation process.

Note the following when setting setpoints:

When using a lightly foaming medium, set the setpoints in parameters *Stirrer* (stirrer speed) and the different *Flow* parameter(s) as low as possible if this does not have a negative effect on the oxygen supply to the culture. If there is still heavy foaming, a chemical antifoaming agent will need to be used. In this case the *Dose time* and *Wait time* in the parameter *Antifoam* must be set accordingly.

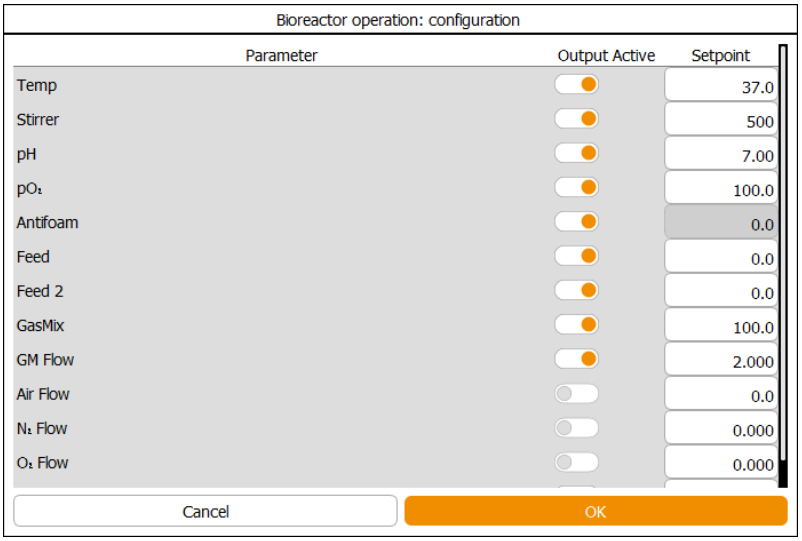
Settings in the configuration dialogue

To make the settings in the configuration dialogue, proceed as follows:

Procedure

1. Call up main menu *Batch* and press **Start**.

The configuration dialogue box appears.



- **The left side** lists all controlled parameters (number and kind depends on device configuration).

- **On the right side** are the switches for switching the parameters on or off and the starting setpoints. The setpoints can be changed here.

INFORMATION

The on/off switches are present if the *Controller* is in automatic (*Auto*) mode in the *Setpoint* option of the parameter.

2. If necessary, change the setpoints of the parameters individually via ***Setpoint***.
3. Switch on/off parameters as required.
4. Press **OK**.

   The dialogue box disappears, the settings are saved, and the bioreactor is started.

   Changed settings are transferred to the next configuration dialogue.

Settings on the running bioreactor

To make the settings on the running bioreactor, the following two options are available:

a) Directly via the *Setpoint* input field/view boxes and the controller output buttons in the *Output* column of the main menu *Controller*.

b) In the *Setpoint* menu of the selected parameter in the *Parameter* column of the main menu *Controller*.

INFORMATION

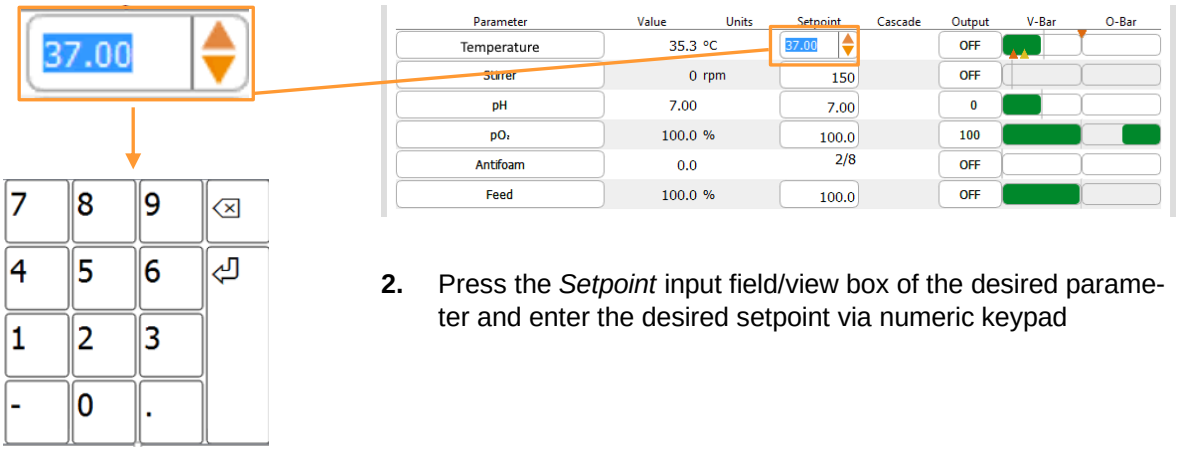
Changed settings are adopted for the cultivation process in progress only.

Proceed as follows:

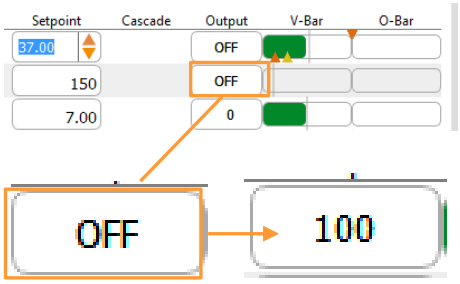
Variant a)

Procedure

1. Call up main menu *Controller*.



2. Press the *Setpoint* input field/view box of the desired parameter and enter the desired setpoint via numeric keypad



3. Switch the parameter on via controller output button **OFF**.

The parameter is switched on, the controller output changes from *OFF* to the display of the corresponding numeric value in %.

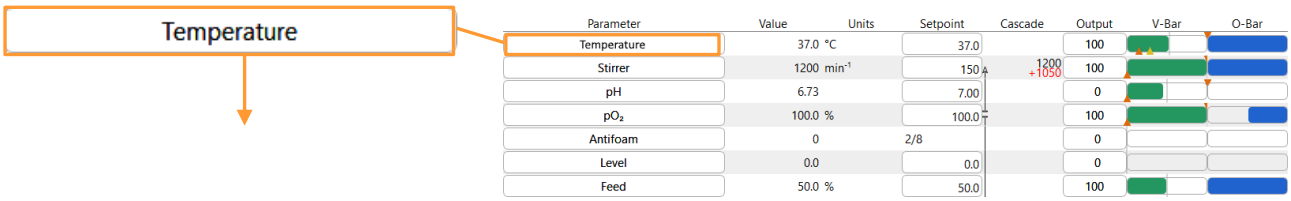
INFORMATION

To switch the parameter i.e. controller output on or off here, is only possible, if the controller of the parameter is set to automatic (Auto) mode in its *Setpoint* option. See also next procedure in variant b).

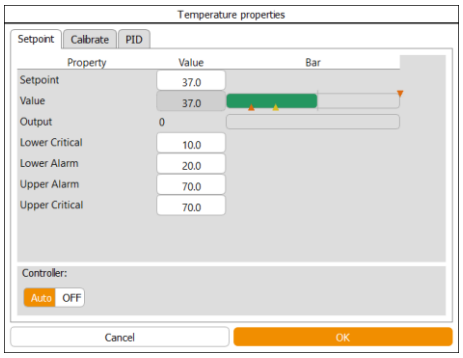
Variant b)

Procedure

1. Call up main menu *Controller*.



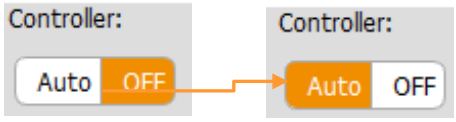
2. Press the desired parameter button.



The tab page *Setpoint* appears.

3. Enter the desired setpoint via ***Setpoint***.
4. Change alarm values and critical values as required.

   For details about alarm value and critical value settings refer to chapter „Setting Alarm Values and Critical Values".



5. Ensure the controller output is switched to automatic mode (**Auto)**, change setting as necessary.

   The parameter is set switched on now.

6. Press **OK**.

   The dialogue box disappears, the settings are saved.

10.6.1.2 Setting Alarm Values and Critical Values

Alarm values and critical values can be set symmetrically or asymmetrically.

- Symmetrically: The difference between the setpoint value and the upper alarm value or the upper critical value = the difference between the setpoint value and the lower alarm value or the lower critical value.
- Asymmetrically: The difference between the setpoint value and the upper alarm value or the upper critical value ≠ the difference between the setpoint value and the lower alarm value or the lower critical value.

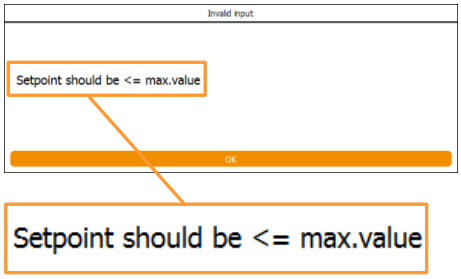
Upper alarm values can be set ≤ upper critical values. Lower alarm values can be set ≥ lower critical values.

A parameter alarm is triggered as soon as a value drops below the lower alarm value or exceeds the upper alarm value. For details see the chapter "Alarms – Parameter Alarms, User Alarms, System Alarms", "Parameter Alarms".

INFORMATION

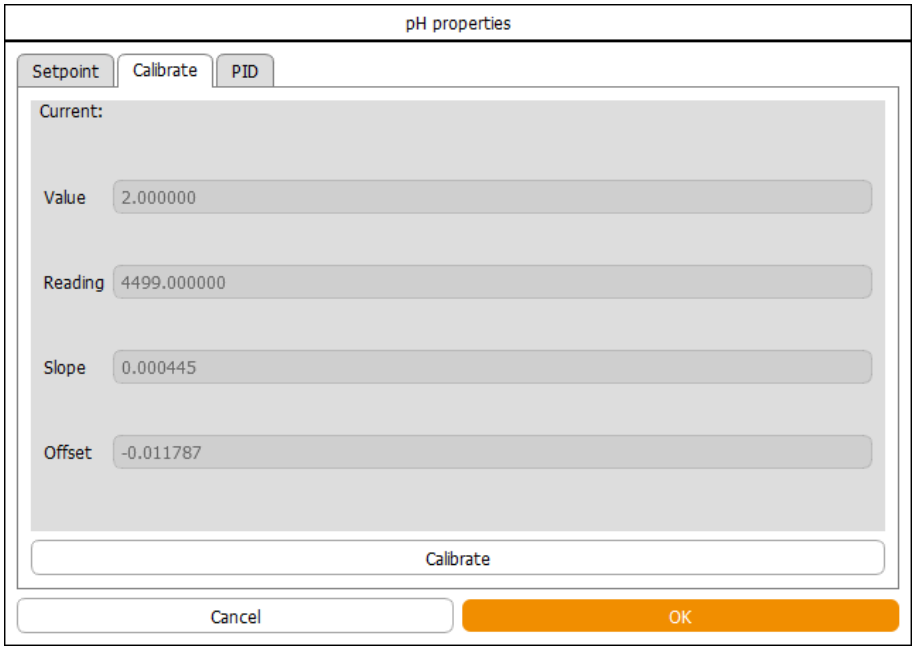
Alarm values and critical values have to be set by selecting the desired parameter in the main menu Controller and calling up its *Setpoint* option menu. The setting procedure remains the same as for setpoint values. The bioreactor can be in stopped or running state while entering these values.

Invalid setpoint value or alarm limit input



When an invalid setpoint, alarm or critical alarm value is entered, a corresponding *Invalid input* dialogue box appears with the appropriate notice.

10.6.2 Calibrate - Calibration



The tab page for the *Calibrate* option contains four view boxes and a button:

- *Value*: shows the current measured value depending on the last calibration
- *Reading*: shows the current measured value in digital units
- *Slope*: shows the digital value of the calculated slope of the calibration line
- *Offset*: describes the intersection point of the calibration line with the X axis
- **Calibrate**: to open the calibration menu

Reading, *Slope* and *Offset* are not relevant for measurement systems of the digital pH and pO_2 sensors. These values are stored directly in the integrated electronics of the respective sensor.

INFORMATION

The calibration menus for pH and pO_2 can also be called up directly via **Calibrate pH** and **Calibrate pO_2** in the main menu *Batch*.

General Information on calibration

Sensors for measurement of pH, pO_2 and turbidity (variant OPTEK only) are usually recalibrated before each cultivation. Depending on the sensor and measurement system, either a 2-point calibration or a 1-point calibration or a zero adjustment is sufficient. Detailed information on calibration can be found in the separate documentation provided by the sensor manufacturers.

The various calibrations are described in the following chapters.

10.6.2.1 pH Sensor Calibration

The calibration must be carried out before sterilisation, i.e. before mounting the pH sensor in the culture vessel.

Depending on the version selected, the device is equipped and configured with a digital or analogue pH measurement system.

Digital sensors

The pH buffers and their temperature dependencies are stored in these pH sensors and are automatically detected during calibration. It is therefore not necessary to carry out a separate temperature measurement of the buffer solution.

INFORMATION

If a digital pH sensor has already been calibrated externally, the bioreactor will use this data and the calibration procedure in the touch screen software is not necessary.

Analogue sensors

If very exact calibration values are required, the exact temperature of the buffer solutions should be determined. The measurement can be made directly with the temperature sensor of the device during calibration. Another possibility is to measure the temperature exactly and enter the value manually in the touch screen software. In both cases, temperature compensation must be switched on in the SETPOINT option of the pH parameter. This corrects the temperature dependence of the measurement principle. Without temperature measurement or input, a puffer temperature of 20 C is assumed.

Detailed information on calibration, general use, service and maintenance can be found in the separate documentation provided by the sensor manufacturers.

10.6.2.2 pH Sensor (Digital) Calibration

To calibrate a digital pH sensor in the touch screen software, proceed as follows:

Procedure

1. Connect the sensor cable.
2. Carefully remove the watering cap from the pH sensor and rinse the pH sensor with distilled water, do not rub!

ATTENTION

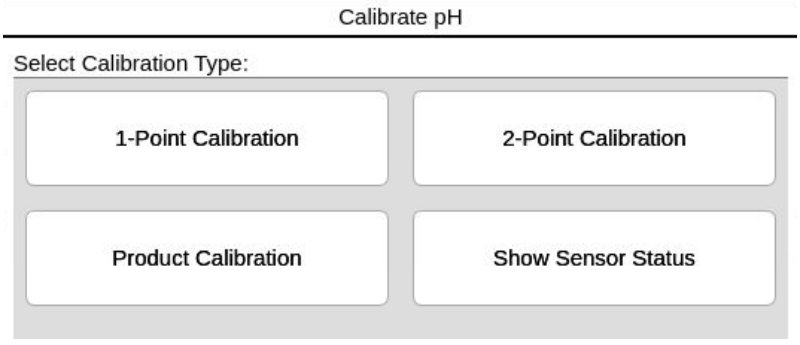
Dry wiping or rubbing a pH sensor after rinsing can cause electrostatic charge. This can greatly increase the response time and generate incorrect measurements. At most, gently dab a pH sensor after rinsing, **NEVER** rub or wipe it!

INFORMATION

Only sensor type Easyferm Plus ARC: the ERROR Glass resistance too high which may appear after initialization can be ignored. It may occur if the sensor is in contact with air or nonconductive liquid such as distilled water.

3. Call up main menu *Batch* and press **Calibrate pH**.

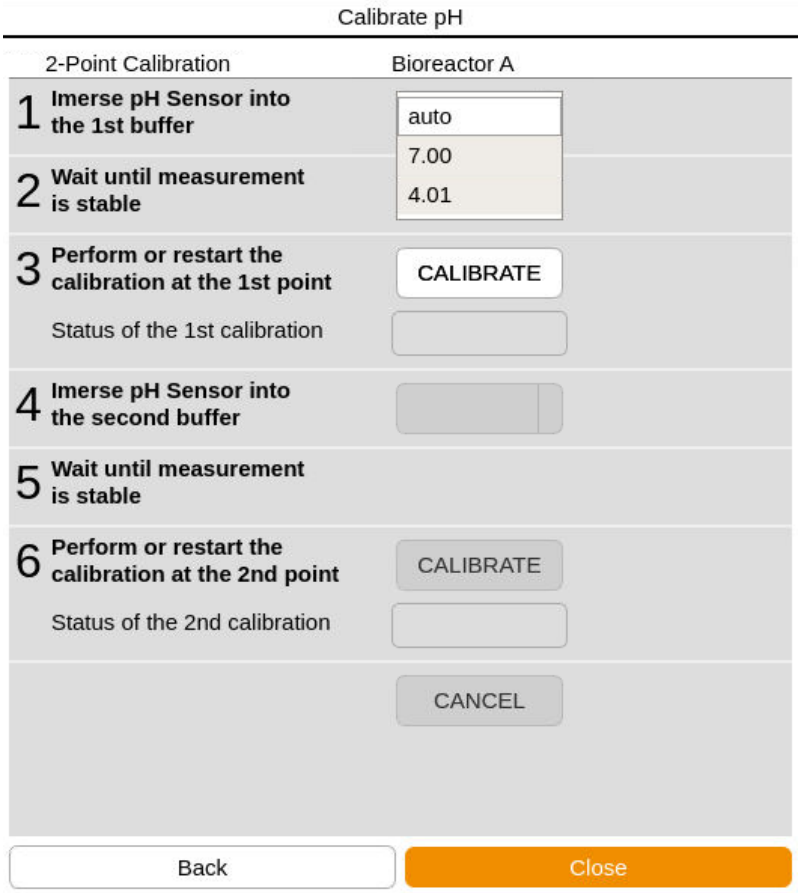
   The calibration menu opens with four options:



- **1-Point Calibration** and **2-Point Calibration**: to select 1-point or 2-point calibration.
- **Product Calibration**: to select product calibration. For details see chapter “pH Sensor (Digital) Product Calibration”.
- **Show Sensor Status**: shows data and values produced by the firmware of the sensor manufacturer that is integrated in the sensor. For more details see section “Sensor Status”.

4. Select 2-point calibration.

The menu opens and leads step by step (1 to 6) through the calibration:



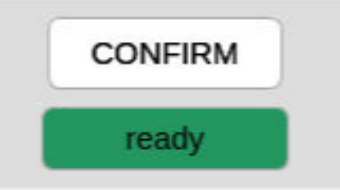
- **Drop-down list**s (step 1 and 4) for selection of the 1st, respectively the 2nd reference value. If the connected sensor allows the use of different calibration buffers or an automatic recognition of the calibration buffer (“auto”), it can be selected. Otherwise, the calibration buffer to be used is displayed.
- Measured value display (step 2 and 5)
- **CALIBRATE** and status display (step 3 and 6): to start the calibration procedure.

  As soon as the bar of the status display is filled up and shows *Ready*, the button changes to **CONFIRM** to save the calibration point. **CANCE**L for possible abortion of the calibration process becomes available.

INFORMATION

The calibration process can be continued at any time from the last stored point if the menu has been left via **Close**. This does not apply, however, if another calibration process is started

5. Hold the pH sensor into the appropriate buffer solution of the first calibration point and if possible, select reference value or automatic buffer recognition in the drop-down list (step 1).
6. Wait until the measurement is stable (step 2).
7. Press **CALIBRATE** (step 3a).



The calibration process begins. The **CALIBRATE** button changes to **CONFIRM**.
The status display slowly turns green, indicating the ideal waiting time until a stable measured value is reached.

INFORMATION

If the measured value is assumed to be already stable, the waiting time can be skipped by pressing **CONFIRM** to continue with the second calibration point.

8. Press **CONFIRM** (step 3b).

   The calibration point is stored.

INFORMATION

If the calibration process fails, an error message is displayed with a corresponding note. Restart calibration in this case.

If the calibration is successful, the drop-down list for selection of the second reference value and the **CALIBRATE** button become available to calibrate the second point.

The calibration procedure for the second point remains the same as for the first point. After rinsing the pH sensor with distilled water, the same *ERROR* may occur. This can also be ignored here.

After successfully storing the 2nd calibration point via **CONFIRM** the calibration is finished and the menu can be left via **Close**.

Sensor Status

Show Sensor Status is used to call up data and values that are output by the firmware of the sensor manufacturer integrated in the sensor. In addition to sensor type and calibration information, the following two values are displayed for METTLER ISM sensors:

- **ACT** (Adaptive Calibration Timer in days): determines the time of the next calibration to ensure optimum measurement performance. It is reset to its initial value after successful calibration.
- **DLI** (Dynamic Lifetime Indicator in days): displays the number of days remaining and is preset by the sensor manufacturer.

10.6.2.3 pH Sensor (Digital) Product Calibration

Adapting the calibration curve to the current process conditions is possible by performing a product calibration. This could be necessary if there is a possibility of drift of the displayed pH during a long-term cultivation, for example.

INFORMATION

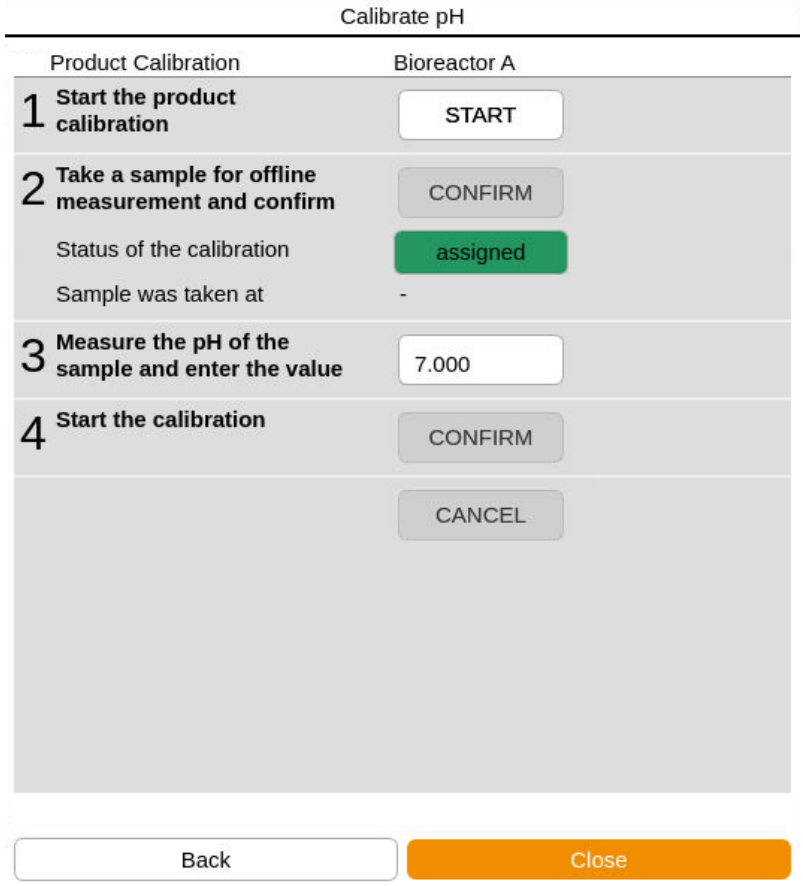
Product calibration can only be carried out and is only effective if the externally measured and entered pH value does not deviate from the original pH value by more than 2 pH units.

Proceed as follows for product calibration:

Procedure

1. Call up the calibration menu of the pH sensor and press **Product Calibration**.

The product calibration menu opens and guides step by step (1 to 4) through the product calibration:



- Step 1 +2: start product calibration via **START** and confirm sampling via **CONFIRM** to generate a time stamp (*Sample was taken at*).

  Status display of the calibration with the following possible displays:
  - *ready*: time stamp for sampling can be generated via **CONFIRM**.
  - *measured*: time stamp was generated.
  - *assigned*: last product calibration was successful and is active. Performing a new product calibration is possible.
  - *aborted:* last product calibration was aborted via **CANCEL** or was not successful, restart product calibration.
- Step 3 + 4: enter external measured value and confirm entry via **CONFIRM** to start calibration.

INFORMATION

The calibration process can be continued at any time from the last stored point if the menu has been exited via **Close**. This does not apply, however, if another calibration process is started.

2. Press **START**.

3. Take a sample from the process (culture in the vessel).

There are two possible approaches:

a) Confirm the sampling (generate a time stamp), carry out a laboratory measurement of the pH value for the sample, enter the measured value and carry out product calibration.

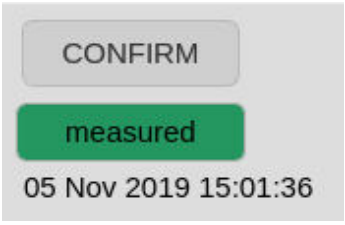
OR:

b) Confirm the sampling (generate a time stamp), leave the calibration menu via **Close** and carry out the product calibration with an external measured value at a later time.

Variant a)

Procedure

1. Press **CONFIRM**.



Status display changes to *measured.*
Date and time of sampling are now displayed below.

2. Carry out a laboratory measurement of the pH value for the sample.

3. Enter the measured pH value of the sample, in the example to the left, pH 7.0.

4. Press **CONFIRM** to start calibration.

5. Wait until the calibration is complete.

This means that the status display changes to *assigned*. This status allows to perform a new product calibration or to exit the menu.

6. Leave the menu via **Close**.

> **INFORMATION**
>
> A new product calibration or a 1-point or 2-point calibration cancels the active product calibration.

Variant b)

Procedure

1. Press **CONFIRM**.

   As in variant a), the status display changes to *measured* and the date and time of sampling are displayed below.

   This indicates that sampling is successful, but product calibration is not yet active. If a sample is lost, step 1 can be performed again.
2. Exit calibration menu via **Close** and perform laboratory measurement of the pH value for the sample at a later time.
3. To perform the product calibration, proceed as described in variant a) from step 2.

10.6.2.4 pH Sensor (Analogue) Calibration

To calibrate an analogue pH sensor in the touch screen software, proceed as follows:

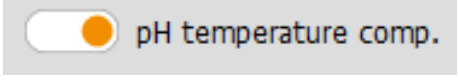
Procedure

1. Connect the sensor cable.

   Ensure the cable is not buckled or twisted.

> **ATTENTION**
>
> The integrity of the sensor cable can be damaged by buckling or twisting. This may lead to faulty measurements.

If the externally measured temperature of the pH buffer solutions is to be entered or if their temperature is to be measured with the temperature sensor:



2. Switch pH temperature compensation on in *Setpoint* option of parameter *pH*.

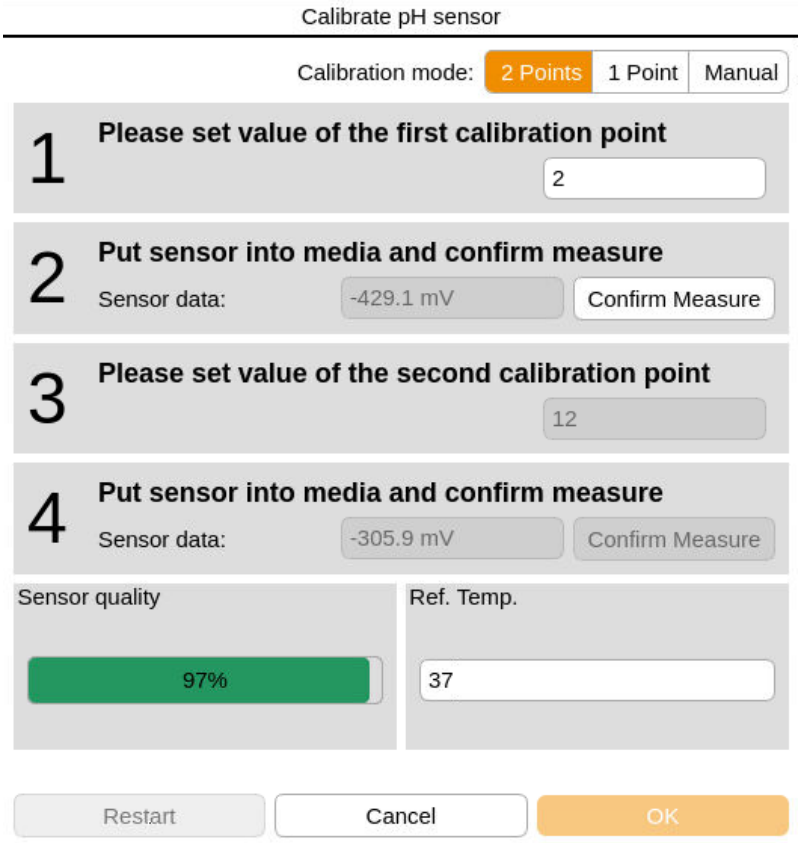
3. Carefully remove the watering cap from the pH sensor and rinse the pH sensor with distilled water, do not rub!

ATTENTION

Dry wiping or rubbing a pH sensor after rinsing can cause electrostatic charge. This can greatly increase the response time and generate incorrect measurements. At most, gently dab a pH sensor after rinsing, **NEVER** rub or wipe it!

4. Call up main menu *Batch* and press **Calibrate pH**.

The calibration menu *Calibrate pH sensor* appears and leads step by step (1 to 4) through the calibration.



The 2-point calibration mode is automatically selected. The *Ref. Temp* input field/view box is displayed.

INFORMATION

Without switching pH temperature compensation on before, this field is not visible.

The *Sensor quality* display bar charts the quality of the sensor in a scale from 0 to 100 %.

5. Enter the value of the low (or high) reference buffer in the input field on line 1.

INFORMATION

The order in which the reference points are calibrated is irrelevant.

With activated temperature compensation:

6. Enter the temperature of the buffer solution in the *Ref. Temp*. view box/input field or hold the temperature sensor together with the pH sensor into the relevant buffer solution at step 7.
7. Hold the pH sensor into the relevant buffer solution.

   The measurement (in mV) is displayed in line 2 in *Sensor data*.

   As soon as the measurement is stable:
8. Press **Confirm Measure** in line 2.

   The calibration value is accepted. The input fields and buttons in line 3 and 4 are available now.

INFORMATION

The signal characteristics are asymmetric. In other words, the closer the signal comes to the real value, the slower the change. The calibration is inaccurate, if the measurement is confirmed with **OK** before the sensor signal has completely stabilised. Wait a few minutes before confirming with **OK** and check the reading again, if in doubt.

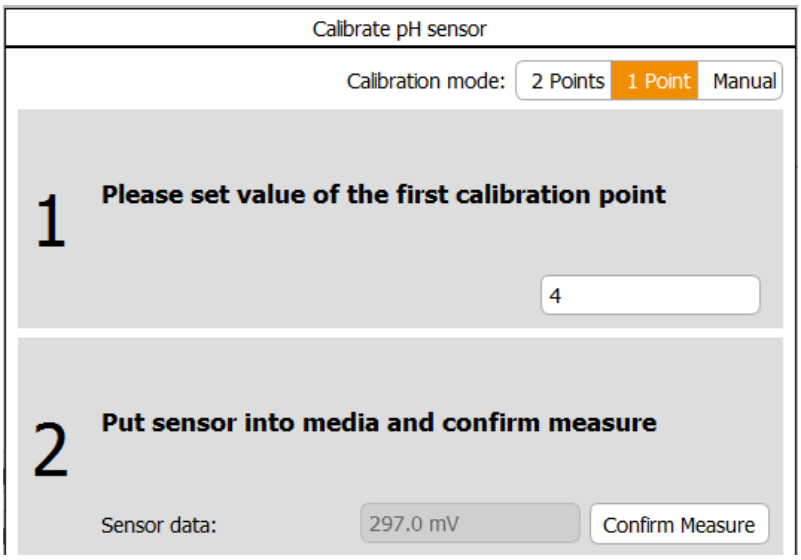
9. Rinse the pH sensor with distilled water, do not rub!
10. Repeat the same steps for the second point like for the first point.

    Once the second calibration value is accepted:
11. Press **OK**.

    The dialogue box disappears, the calibration values are stored.
12. Rinse the pH sensor with distilled water, do not rub!

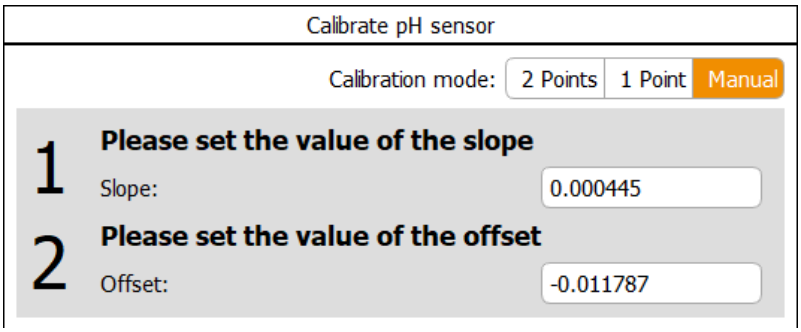
10.6.2.5 pH Sensor (Analogue) Recalibration

To compensate for a deviation (drift) in the measurement of an analogue pH sensor over a long-term cultivation, it is possible and sufficient to recalibrate with a 1-point calibration.



This means that the pH of a sample measured using an external measurement device is accepted as the new reference value in 1-point calibration mode.

The same effect is achieved by manually correcting the offset (deviation). In other words, the difference between the externally determined measurement and the displayed measurement in the culture needs to be added to or subtracted from the last calculated offset value depending on the result.



The correction is made in manual calibration mode.

10.6.2.6 pO_2 Sensor Calibration

A 1-point calibration to 100 % is usually sufficient for exact measurement and should be carried out before each cultivation. If requirede, a 2-point calibration to 100 % and 0 % is also possible.

INFORMATION

The prerequisites for exact calibration results can be found in the separate documentation of the sensor manufacturer. The calibration conditions and how they are achieved are defined by the operator and are not the subject of this operating manual.

Depending on the version selected, the device is equipped and configured with a digital or analogue pO_2 measurement system.

Digital sensors

The 2-point calibration can only be carried out in the correct sequence: 1st calibration point = 100 %, 2nd calibration point = 0 %.

INFORMATION

Digital pO_2 sensors are preconfigured by the device manufacturer to the measurement value %-sat.

Analogue sensors

A 2-point calibration of the analogue pO_2 sensors can be performed in the 2-point calibration mode or successively in the 1-point calibration mode.

The 2-point calibration **must** be carried out in the correct sequence: 1st calibration point = 0 %, 2nd calibration point = 100.

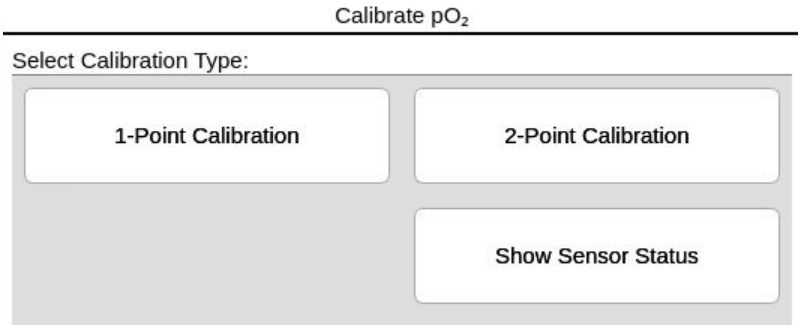
10.6.2.7 pO_2 Sensor (Digital) Calibration

The following example describes a 2-point calibration of a digital pO_2 sensor. Here the first calibration point is 100 %, the second calibration point is 0 %.

Proceed as follows, once desired calibration conditions for 100 % calibration are achieved:

Procedure

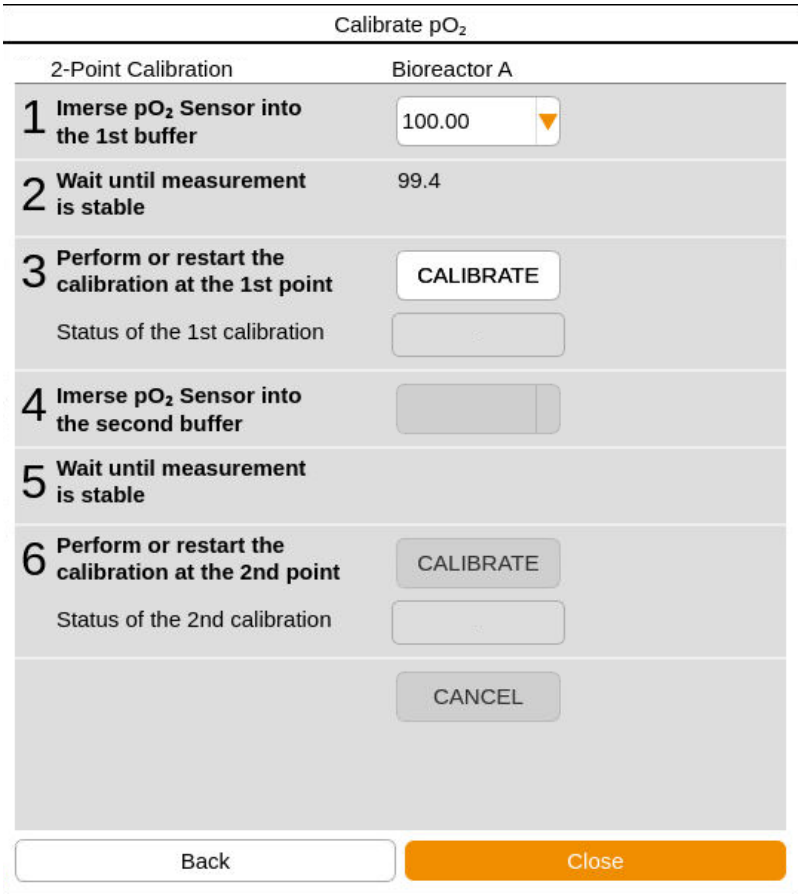
1. Call up main menu *Batch* and press **Calibrate pO_2**.
The calibration menu appears with three options:



- **1-Point Calibration** and **2-Point Calibration**: to select 1-point or 2-point calibration.
- **Show Sensor Status**: shows data and values produced by the firmware of the sensor manufacturer that is integrated in the sensor. For more details see chapter “pH Sensor (Digital) Calibration”, section “Sensor Status”.

2. Select 2-point calibration.

The menu opens and leads step by step through the 2-point calibration.



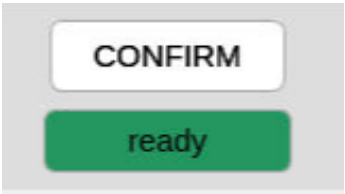
- **Drop-down lists** (step 1 and 4) for selection of the 1st, respectively the 2nd reference value. If the connected sensor allows the use of different reference values or an automatic recognition of the reference value (“auto”), it can be selected. Otherwise, the reference value to be used is displayed.
- Measured value display (step 2 and 5)
- **CALIBRATE** and status display (step 3 and 6): to start the calibration procedure.

  As soon as the bar of the status display is filled up and shows *Ready*, the button changes to **CONFIRM** to save the calibration point. **CANCEL** for possible abortion of the calibration process becomes available.

INFORMATION

The calibration process can be continued at any time from the last stored point if the menu has been left via **Close**. This does not apply, however, if another calibration process is started.

3. If possible, select reference value **100** (= 100 %) in drop-down list (step 1)
4. Wait until the measurement is stable (step 2).
5. Press **CALIBRATE** (step 3a).



The calibration process begins. The **CALIBRATE** button changes to **CONFIRM**.
The status display slowly turns green, indicating the ideal waiting time until a stable measured value is reached.

INFORMATION

If the measured value is assumed to be already stable, the waiting time can be skipped by pressing **CONFIRM** to continue with the second calibration point.

6. Press **CONFIRM** (step 3b).

   The calibration point is stored.

INFORMATION

If the calibration process fails, an error message is displayed with a corresponding note. Restart calibration in this case.

If the calibration is successful, the drop-down list for selection of the second reference value and the **CALIBRATE** button become available to calibrate the second point.

7. Create correct calibration conditions for 0 % calibration.

   Once achieved:

8. Proceed the same way as described from step 4 on for the second calibration point with 0 %.

   After successfully storing the 2nd calibration point via **CONFIRM** the calibration is finished and the menu can be left via **Close**.

10.6.2.8 pO_2 Sensor (Analogue, Polarographic) Polarisation

Polarographic pO_2 sensors must be polarised at initial operation or after disconnection from the voltage source. Correct calibration is not possible otherwise.

For polarisation, the sensor cable must simply be connected to the pO_2 sensor and the device must be switched on at the main switch.

Duration of polarisation (= polarisation time) depends on how long the pO_2 sensor has been disconnected from the voltage source (= depolarisation time)

As a general rule: if depolarisation time > 30 minutes, the minimum polarisation time is 360 minutes.

More details about polarisation can be found in the separate documentation from the sensor manufacturer.

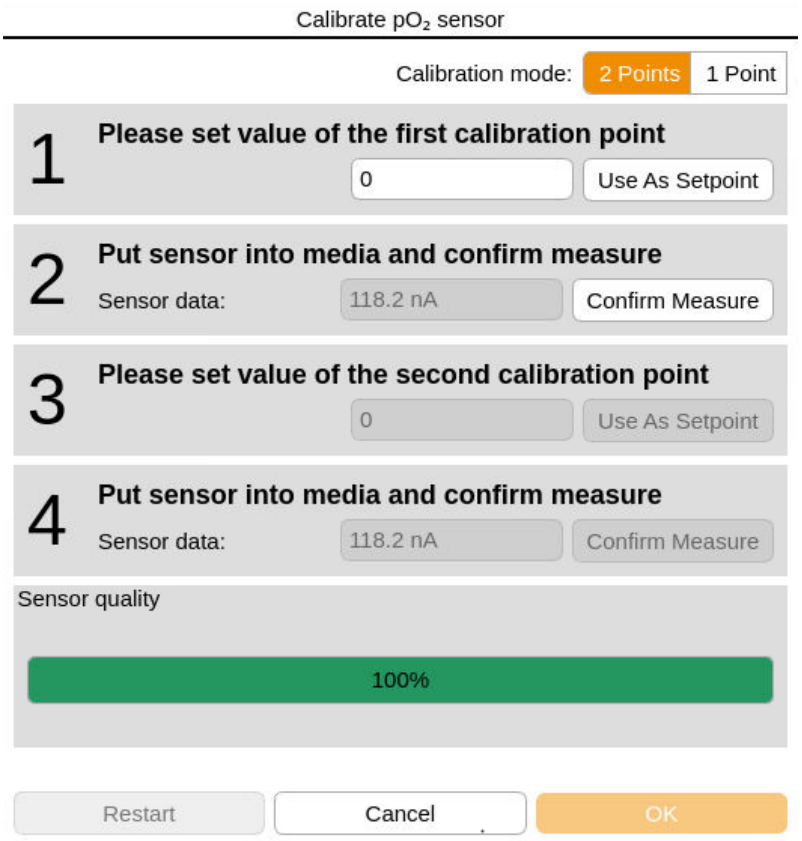
10.6.2.9 pO_2 Sensor (Analogue) Calibration

The following example describes a 2-point calibration of an analogue (amperometric/polarographic) pO_2 sensor. This must be done in the correct order. This means that the first calibration point is 0 % (zero point), the second calibration point is 100 %.

Proceed as follows, once desired calibration conditions for 0 % calibration are achieved:

Procedure

1. Call up main menu *Batch* and press **Calibrate pO_2**.
   The calibration menu appears.



   The 2-point calibration mode is automatically selected. The menu leads step by step (1 to 4) through the calibration.

INFORMATION

The **Use As Setpoint** button is only usable and relevant under certain circumstances, see next section “Function Use As Setpoint analogue pO_2 sensors”.

2. If not preset: enter value **0** (zero = 0 %) for the first calibration point in line 1
3. Wait until the measured value (*Sensor data*, line 2) is stable.
4. Press **Confirm Measure** in line 2.
   Value is accepted as 0 % oxygen.

5. Create correct calibration conditions for 100 % calibration.

   Once achieved:

6. Enter value **100** (= 100 %) for the second calibration point in line 3.
7. Wait until the measured value (*Sensor data,* line 4) is stable.
8. Press **Confirm Measure**.

   The value is accepted as 100 % oxygen saturation.

9. Press **OK**.

   The dialogue box disappears, the calibration values are stored.

Use As Setpoint function analogue pO_2 sensors

The **Use As Setpoint** buttons in the calibration menu of the analogue pO_2 sensors can only be used by the operator under the following circumstances:

- Gasmix configuration with air/O_2/N_2 is present
- Parameter *Gasmix* is configured in a cascade for the pO_2 control.

INFORMATION

For all other parameters the Use As Setpoint button is only relevant to INFORS HT service technicians.

How it works

In the calibration menu of the *pO_2* parameter (METTLER sensors):

- 0 % calibration: The input ***0*** (%) in the input field of the first calibration point and pressing the **Use As Setpoint** button causes the *Gasmix* parameter to switch to nitrogen for this value.
- 100 % calibration: (2nd point), before entering the ***100*** value: The input ***21*** (%) in the input field of the second calibration point and touching the **Use As Setpoint** button causes the *Gasmix* parameter to switch to air for this value. The value can then be changed to ***100*** (%) in the input field and the calibration completed.

10.6.3 Turbidity Sensor Calibration

Optek turbidity sensors are pre-calibrated in the factory. Inserts are available for reference measurement.

Due to the different light absorption of different media, zero point calibration of the turbidity sensor should be performed before each cultivation process. This can be done either **before or after** sterilising, depending on the application in question.

Conditions for zero point calibration of the sensor

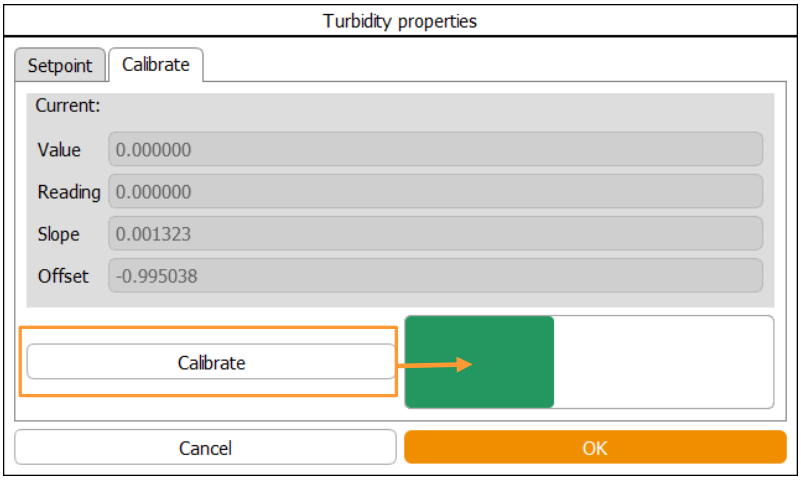
The sapphire windows of the optical density sensor must be clean and free of air or gas bubbles.

The light absorption of the medium before activation of the gassing and before inoculation can be used as a reference value for the zero point.

To calibrate the zero point of the turbidity sensor, proceed as follows:

Procedure

1. Call up the main menu *Controller* and wait until the measured value (parameter *Turbidity*) is stable
2. Call up the *Calibration* menu of the parameter and press **Calibrate.**

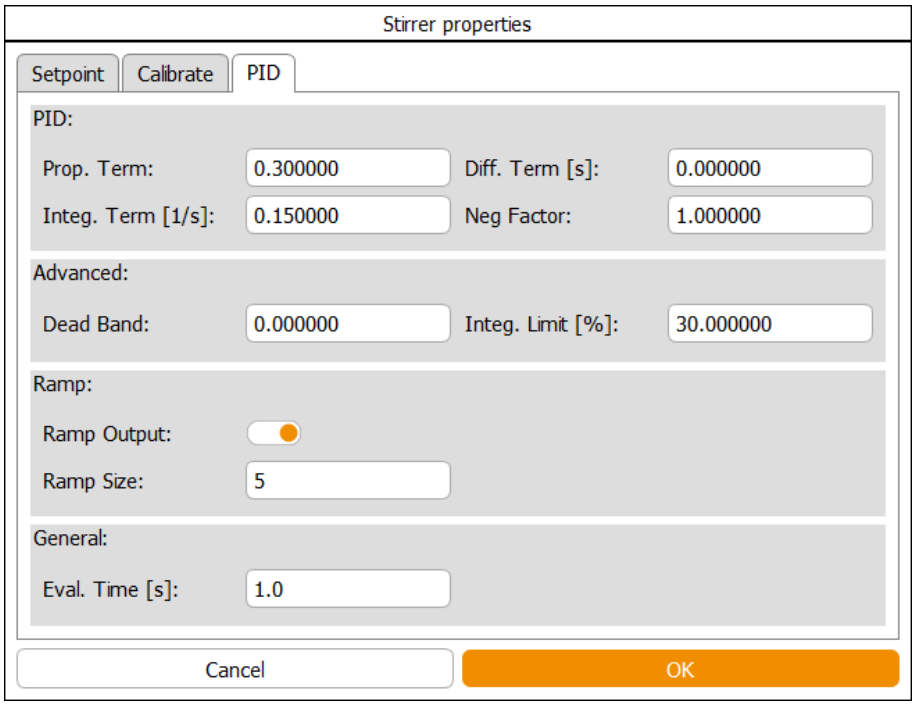


Calibration is started and a view bar appears to the right side of the **Calibrate** button which charts the course of the calibration. The progress is shown by a green colour. If the view bar disappears after a few seconds, the calibration is completed.

3. Press **OK.**

   Calibration is saved, menu disappears.

10.6.4 PID (Control)



The *PID* tab page is split into four horizontal areas and contains input fields for PID (Proportional Integral Derivative) control settings. The table in the following chapter explains the function of the individual setting values in more detail.

Note the following:

- If the ramp output is switched off, the value in the Ramp Size-input field is not relevant.
- In the case of parameters which are not controlled but only measured, only the value in the Eval Time (s) input field is relevant. This value is always > 0.

10.6.4.1 Table with Setting Values for PID Control

Setting value	Description
Prop. Term	Proportional factor: The greater the discrepancy between the set-point value and the actual value the greater the controller output.
Integ. Term [1/s]	The integral factor aggregates all errors over the time. If the setpoint is not achieved using the proportional factor, the integral factor adjusts the output successively until the setpoint value is achieved. An integral factor set too high will lead to oscillation of the control loop.
Diff Term [s]	The differential quotient calculates the change in the actual value over the time and counteracts this change to limit any overshoot.
Neg. Factor	The negative factor can be used to add weighting to two-sided control (+100 to -100 %) (e.g. heavy acid, light alkali). In the process 1 is the balance and 0.5 or 2 equate to the half or double the controller output accordingly. Example: Nitrogen influences the pO_2 value less than oxygen, thus a negative factor of 2 can compensate for the reaction of the controller.
Dead Band	If a dead band is entered, no control is implemented within this value at either side of the setpoint value (symmetrically, + / -). I.e. the controller output is = 0. The dead band is used for pH control.
Integ. Limit [%]	The integral influence is used to ensure that the integral factor cannot increase over an indefinite period. This limits erroneous accumulation. The integral influence is set between 0 and 100 % of the controller output.
Ramp output	In order to perform changes slowly or step-by-step, a ramp can be introduced. This is useful above all for the stirrer speed or a mass flow valve.
Ramp Size	Period of time during which the controller set point is gradually brought up to the newly entered set point.
Eval Time [s]	The evaluation time determines the intervals in seconds at which the PID value is recalculated. The controller speed is defined this way. A scanning time of 10 seconds is a good average value.

10.6.4.2 Explanations of PID Control

The PID function is based on a generic formula provided as example:

$$Error_n = \frac{Set - Act}{Max.Value - Min.Value}$$

$$Output_n = P.Term * \left\{ Error_n + I.Term \cdot \int_{i=0}^{n} Error_i + D.Term \cdot (Error_n - Error_{n-1}) \right\}$$

Explanation of the formula

- Error = deviation between setpoint value and actual value.
- P = proportional factor, proportional response to an error, used to reach a setpoint.
  The bigger the value, the sharper the control.
- I = integral factor, integration of the error in 1/second.
  A typical integral factor is < 0.05.
- D = differential quotient, derivative of the error, set in seconds (mostly to 0).

Be aware of the following relating to the individual factors:

Proportional factor

The change of the proportional factor has a considerable effect on a running process.

If the proportional factor is increased excessively, this causes oscillations in the control loop around the setpoint value.

Example, the pH parameter

To achieve the setpoint value, a little acid, then a little base, acid again, then base etc. is added.

If the proportional factor is reduced excessively, the controller hardly reacts to the deviations and never achieves the setpoint value.

Integral factor

The integral factor should have a low value and only be changed a little in small steps with long pauses.

The ideal approach is to switch off the device briefly after changing the integral factor in order to delete the pending error calculation.

A typical integral factor is < 0.05. It should equate to the reciprocal value of double to quadruple the system's cycle duration. The higher the entered value, the less the time (in seconds) remains for control.

A higher value than 0.05 is generally of no use as it exceeds the time minimum for which the control is required. This causes fluctuations in the control circuit.

Example of calculation of the integral factor

The cycle duration of system oscillations is measured at 50 seconds from amplitude to amplitude. The integral factor is thus calculated as follows:

$1 / (50 \text{ s} \times 2) = 0.01 \text{ s}^{-1}$

$1 / (50 \text{ s} \times 4) = 0.005 \text{ s}^{-1}$

Integral factor	Seconds
0.1	10
0.05	20
0.001	100
0.005	200

Differential quotient

The differential quotient is rarely required. It is set to 0 (zero) at the beginning.

A high value is only necessary if major changes are made in quick succession. In all circumstances it causes the controller output to react stronger.

10.6.4.3 Changing the PID Controller Settings

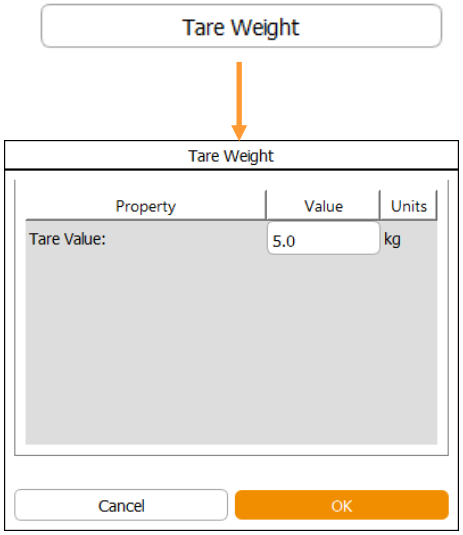
When making changes to the PID controller settings proceed as follows:

Procedure

1. Make a note of the factory settings, i.e. make sure they can be restored, if necessary.
2. For readjustment of a PID controller, start with the setting for the proportional factor. Select a proportional band width as large as possible.
3. Reset the integral factor and the differential quotient to zero.
4. Increase the proportional factor until the controller causes the actual value to oscillate.

5. Measure the oscillation duration, e.g. with eve®, the bioprocess platform software from the device manufacturer.
6. Halve the proportional factor and vary the integral factor between the reciprocal value of the doubled and quadrupled oscillation duration.

10.6.5 Tare Weight Function – Taring the Weight Display



The zero point of the vessel weighing system is defined using the **Tare Weight** button in main menu *Batch*, generally. Hereby, the vessel weight is set to zero (tared) to only measure the weight of the vessel content.

INFORMATION

If required, e.g. for specific applications, instead of 0 (zero) any numerical value can be entered as a tare weight.

Before taring, note the following:

The vessel must be fully equipped and all hoses (e.g. reagent bottle/vessel hoses) must be filled with liquid, before setting the weight display to zero. Otherwise, the displayed weight in parameter *Weight* will not correspond to the liquid mass in the vessel.

After taring, any change to the vessel, e.g. by removing components, emptying hoses, etc., also means a change to the weight. This has the consequence that the weight measurement is falsified.

10.7 Cascade Control

The main menu *Cascade* provides the option of setting up a cascade control of a process parameter – mostly pO_2. This means that the controller output parameter (=Output) of the master controller (e.g. pO_2) is used as a master parameter for the slave controller(s).

INFORMATION

The master controller and slave controllers are also called master and slave.

Serial cascade

A deviation of the setpoint of the parameter to be controlled (master controller) influences the setpoint of the first parameter (slave controller) in the cascade.

If the first parameter in the cascade reaches its maximum or minimum setpoint and the setpoint of the parameter being controlled is not yet achieved, the next parameter in the serial cascade is activated and so it continues.

In the example of the left-hand figure:
The parameter *Stirrer,* the 1st slave controller, is activated first in the cascade, to control the pO_2 parameter, the master controller.
The parameter *AirFlow,* the 2nd slave controller, is only activated when the setpoint of parameter pO_2 has not been achieved by the *Stirrer* parameter.

Parallel cascade

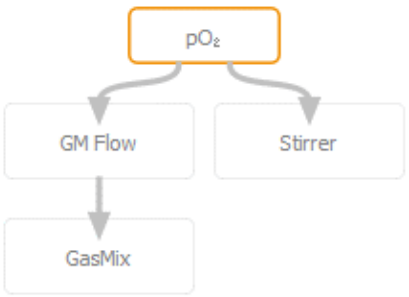
A deviation of the setpoint of the parameter to be controlled (master controller) influences the setpoint of all parameters (slave controllers) that are in the cascade.

In the example of the left-hand figure:
The parameters *Stirrer* and *Air Flow*, both slave controllers, are activated at the same time to control the pO_2 parameter, the master controller.

Parallel serial cascade

A deviation of the setpoint of the parameter to be controlled (master controller) influences the setpoint of all parameters (slave controllers) that are parallel and the first element in the cascade.

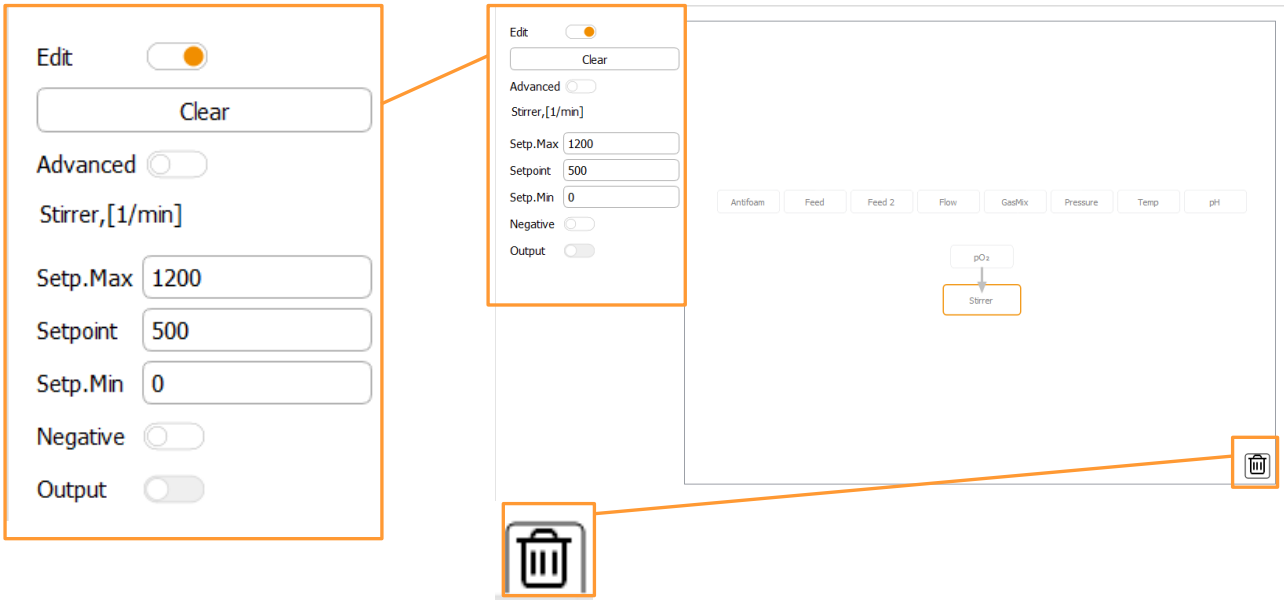
If the parameters that are connected in parallel reach their maximum or minimum setpoint and the setpoint of the parameter being controlled is not yet achieved, the next parameter(s) in the cascade is/are activated.



In the example of the left-hand figure:
The parameters *Stirrer* and *Air Flow* (master controller) are activated at the same time to control the pO_2 parameter.
The parameter *GasMix* (slave controller) is only activated when the setpoint of parameter *pO_2* has not been achieved by the *Stirrer* and *AirFlow* parameters.

10.7.1 Setting a Cascade

The different cascade settings are made in the left-hand side of the main menu *Cascade*. The process parameters can be merged to a cascade in the main area of the menu using drag & drop.



Cascade elements (parameters) can be removed and dropped off in the recycle bin using drag&drop.

- *Edit*: to switch on/off the edit function of the cascade.
  Switching off this function will also deactivate the display of the present process parameters in the main area of the menu.
  Once the edit function is switched on, all parameters can be merged to one or even several cascades using drag&drop.
  Each parameter can only be used once and in one cascade only.
- **Clear**: to call up warning dialogue and delete cascade after confirmation.

- *Advanced*: to switch on/off the setting mode for advanced cascade.

INFORMATION

Advanced cascades are used for customised device configurations. They are only set from the device manufacturer at the factory. Their settings and possible adjustments are device-specific saved at the factory. If required, they may be obtained upon request from the manufacturer.

- Parameter name, (e.g. *Stirrer*): selected parameter with unit.

  The selected parameter visually stands out from the other parameters in the main screen area. The input fields for min./ max. and setpoint values are visible and enabled at the same time to the left-hand side.
- *Setp. Max*. und *Setp. Min*.: factory settings for min. and max. setpoint values which define the adjustable value range of the selected parameter in which the cascade can change the setpoint of the cascaded parameter to control the setpoint of the master controller. These values are adjustable within this predefined value range.
- *Setpoint*: setpoint of the parameter.
  - Master controller: the setpoint to be controlled.
  - Slave controller: the starting setpoint of the parameter from which the setpoint of the parameter of the cascade can be varied within the value range of *Setp. Min. up to Setp. Max.*

INFORMATION

In most cases, it is recommended to set the setpoint for the slave controller to the lower end of the value range (Setp. Min.)

- *Negative*: to switch on/off the negative function of a cascade. Can be used for slave controller, if an increase of the setpoint of the slave controller leads to a decrease of the current value of the slave controller.
- *Output*: to switch on/off the cascade and all used parameters in the cascade hereby.

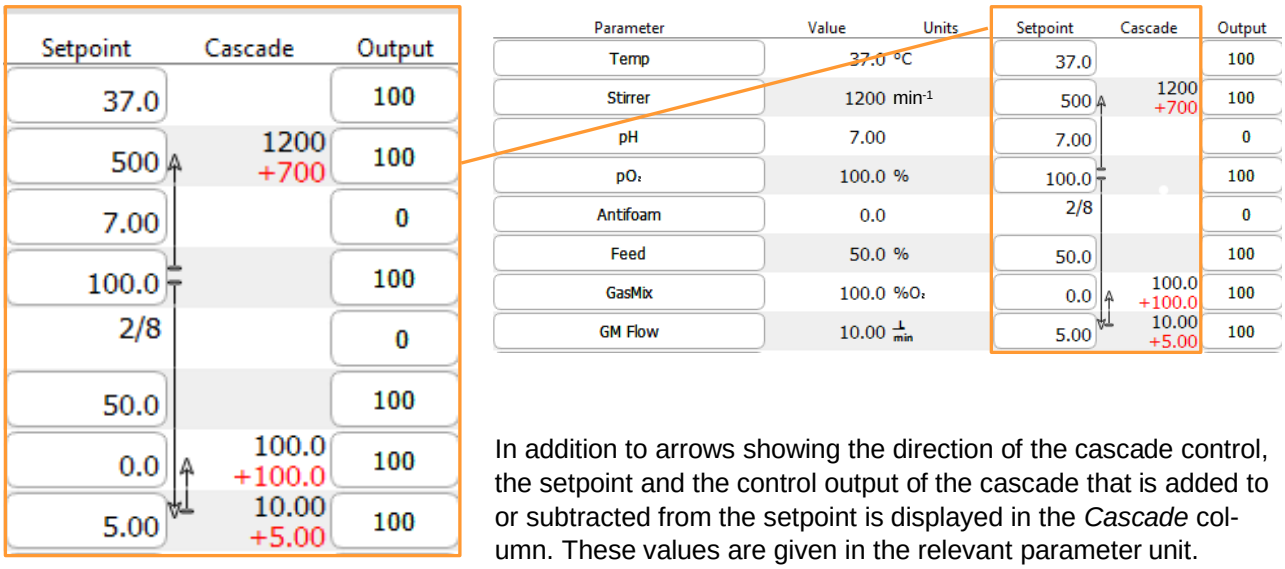
  Each parameter in the cascade must be switched on (*Output ON*) for the cascade to function.

  The parameters can also be switched on and off in the *Controller* main menu.

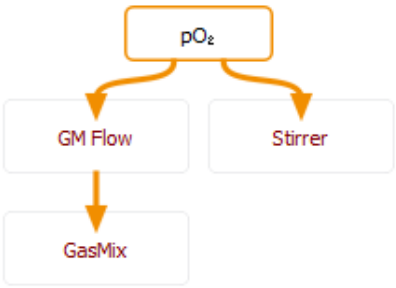
  If a parameter is switched off (*Output OFF*), all of the following parameters are uncoupled from the cascade.

Cascade progress display

A cascade and its progress can be seen in the *Controller* main menu.



In addition to arrows showing the direction of the cascade control, the setpoint and the control output of the cascade that is added to or subtracted from the setpoint is displayed in the *Cascade* column. These values are given in the relevant parameter unit.



The colour of the added/subtracted setpoint in the *Controller* menu and the name of the parameter in the *Cascade* menu indicates the progress of the cascade and the remaining scope of the cascade within the value range of a slave controller to control the master controller according to the following scheme:

Colour	Utilisation of value range
Grey	Inactive
Green	0 – 90 %
Yellow	90 – 99 %
Red	100 %
Blue	0 %

Example of calculation

Stirrer, e.g. for slave controller from setpoint to max. setpoint.

- Setpoint: 500
- Setpoint max. 1200
- Value range: 1200 – 500 = 700

700 = 100 % / 630 = 90 %

500 + 630 = 1130 = setpoint, from which 90 % of the value range are reached.

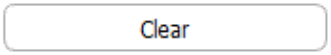
This means for the display according the colour scheme mentioned:

- Green: up to 1130
- Yellow: up to 1193
- Red: at 1200

10.7.2 Deleting a Cascade

To delete all settings of a cascade (does not apply to advanced cascade), proceed as follows:

Procedure



1. In main menu *Cascade*, press **Clear**.

A dialogue box appears with the warning that all entries that have NOT been made in advanced cascade mode will be deleted.

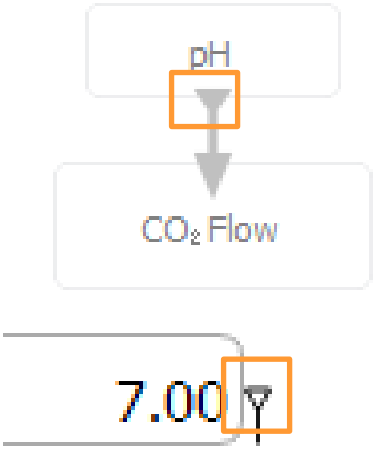
2. Press **OK**.

Cascade is deleted.

10.7.3 Negative Function of a Cascade

The *Negative* function causes a change in sign of the controller output. This means, a negative controller output causes the addition of a positive value for the set point of the cascaded parameter and vice versa.

The pH control with base and CO_2 instead of acid is a classic example of this: to reduce the pH, the CO_2 flow rate (*CO_2 Flow* parameter) needs to increase.



The fact that the *Negative* function has been switched on is illustrated by the triangle symbol on the arrow that indicates the direction of the cascade control.

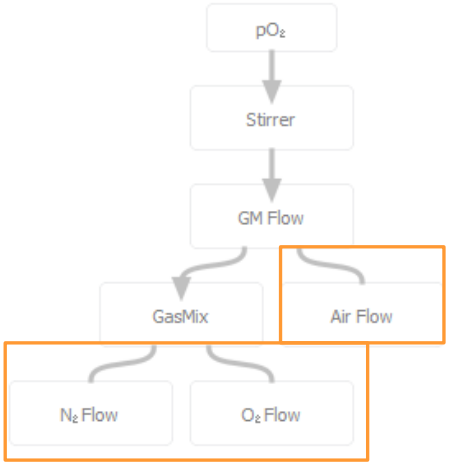
This arrow shape can be seen both in the *Cascade* menu as well as in the *Controller* menu.

10.7.4 Special Configurations

For bioreactors with gassing strategy “High End” (configuration with several mass flow controllers for flow control and gas mix) the gases to be used e.g. *Air Flow*, *N_2 Flow* and *O_2 Flow*, must be assigned to both parameters that control the gas mixture, i.e. parameters *GasMix* and *GM Flow*, in the cascade configuration.

For this purpose, setup the following cascades additionally to the desired cascade configuration, if the appropriate parameters are present:

- Parameter *Air Flow* as slave controller to parameter *GM Flow*
- Parameter *O_2 Flow* as slave controller to parameter *GasMix*
- Parameter *N_2 Flow* as slave controller parameter *GasMix*



If parameters *O_2 Flow* and *N_2 Flow* are present, then they are setup as a parallel cascade below parameter *GasMix*.

To make a distinction between the allocation of these parameters and regular cascade elements, the connections are shown without arrow.

10.8 Pumps and Settings

The pumps are controlled in accordance with the corresponding parameters:

Standard

- *Acid* pump (digital): in accordance with the *pH* parameter
- *Base* pump (digital): in accordance with the *pH* parameter
- *Antifoam* pump (digital): in accordance with the *Antifoam* parameter
- *Feed* pump (analogue): in accordance with the *Feed* parameter

Optional

- *Feed 2* and *Feed 3* pumps (analogue): in accordance with the *Feed 2* and *Feed 3* parameters.

Digital pumps have a set speed and are time controlled. I.e., they always run at the same speed in start/stop mode. The pump speed of analogue pumps is adjustable and can be set in steps of 0.1 % within a range of 0 % to 100 %. Both digital and analogue pumps are controlled within a range of 0 % to 100 %.

Example

- Analogue: 50 % of the maximum feed rate = pump runs at half speed.
- Digital: 50 % of the maximum feed rate = pump runs during half the time

The following pump settings are possible:

- Setting the pump speed for feed pump(s) and dosing/waiting time for the antifoam pump
- Calibrating the pumps
- Resetting the delivery rate manually to zero
- Filling or emptying the pump hoses manually or time controlled

For details on how to change the settings for the feed pump(s) and the antifoam pump refer to the appropriate chapters in chapter “Parameters”. Calibration, pump counter and automatic filling and emptying is described in detail in the following chapters.

10.8.1 Calibrating the Pumps

Calibrating a pump makes it possible to display and record the actual delivered volume. The delivery rate is indicated in millilitres.

Note the following points:

- Always use hoses of the same kind with the same dimensions for calibration and pumping media.
- Pump calibration must be executed before sterilisation.

Aid

- Graduated measuring cylinder/jug or scale/balance and an empty vessel
- Reagent bottle equipped with silicone hose, filled with the reagent to be delivered, the nutrient solution or a liquid which has the same viscosity

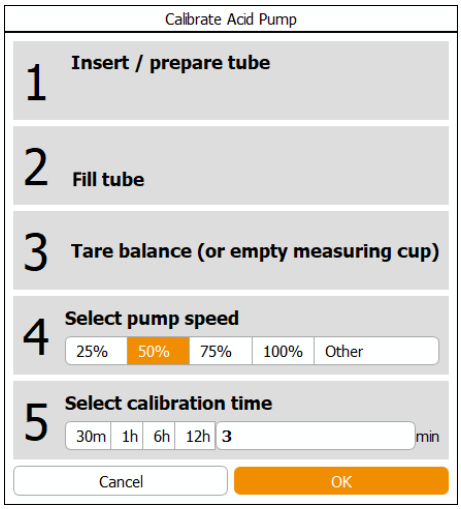
INFORMATION

To obtain precise results, the reagent bottle should be put on a scale which is linked to the bioreactor or to the bioprocess platform software eve® installed on a PC or laptop.

To calibrate a pump, e.g. the acid pump, proceed as follows:

Procedure

1. Connect the reagent bottle to the pump.
2. Place the output end of the hose in a measuring cylinder/jug. Or: Place the reagent bottle on a scale and tare to zero, place the output end of the hose in an empty vessel
3. Completely fill the hose.
4. Call up the main menu *Batch* and press **Calibrate Acid**.



The *Calibrate Acid Pump* dialogue box appears and leads step by step through the calibration.

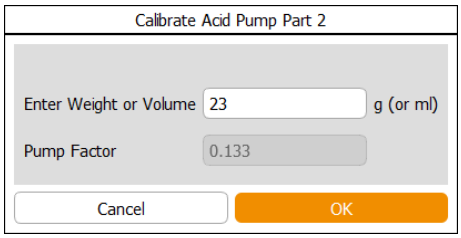
5. At step 4, select the pump speed in percent or enter another value in % after pressing **Other**.

> **INFORMATION**
>
> To obtain most accurate results, the pump should be calibrated at the same speed as it is to be expected to run during cultivation.

6. At step 5, select calibration duration or enter it manually.
7. Press **OK**.

Calibration is started.

The remaining time in h/min/s is shown next to the **Stop**-button.



Once the time has elapsed, the dialogue box with part 2 appears.

8. Enter the delivered liquid in mL or g.

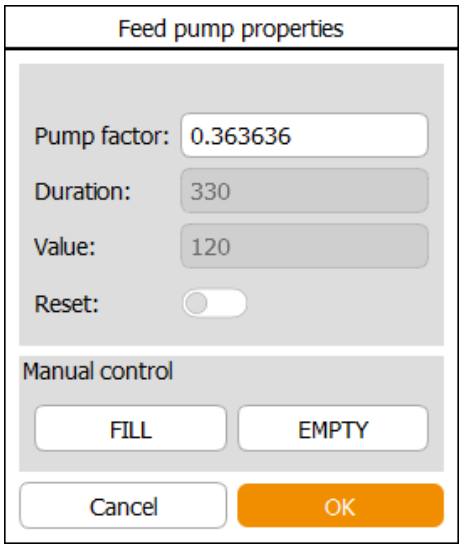
   After entering the pumped quantity, the automatically calculated pump factor is displayed.
   The pump factor is always ≠ 1 with a calibrated pump.
9. Press **OK**.

The dialogue box disappears; the calibration value is saved.

Completed at with date and time next to the **Stop** button indicates that and when the pump was calibrated.

10.8.2 Resetting the Pump Counter to Zero

The number of pump revolutions and the delivered quantity (in mL) of calibrated pumps are displayed constantly during a running cultivation process. The display remains in place after completion of the process (when the bioreactor is stopped) until a new cultivation process is started again (when the bioreactor is started). The counter can also be reset to zero manually, proceed as follows:



Pressing one of the pump buttons in the main menu *Main* opens the pump properties dialogue box, e.g. of the Feed pump, as shown to the left.
The displayed number of pump revolutions (*Duration*) and the delivered quantity in mL (*Value*) can be reset by switching the Reset-function on.

INFORMATION

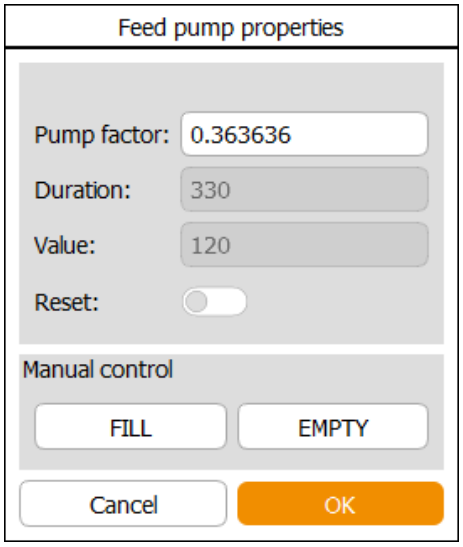
Manual change of the pump factor leads to rejection of the previous calibration value. The pump factor is always ≠ 1 with a calibrated pump.

For details about FILL and EMPTY see chapter “Filling and Emptying Pump Hoses”

10.8.3 Filling and Emptying Pump Hoses

The pump hoses can be manually or time controlled filled and emptied in the touch screen software.

Manual filling and emptying

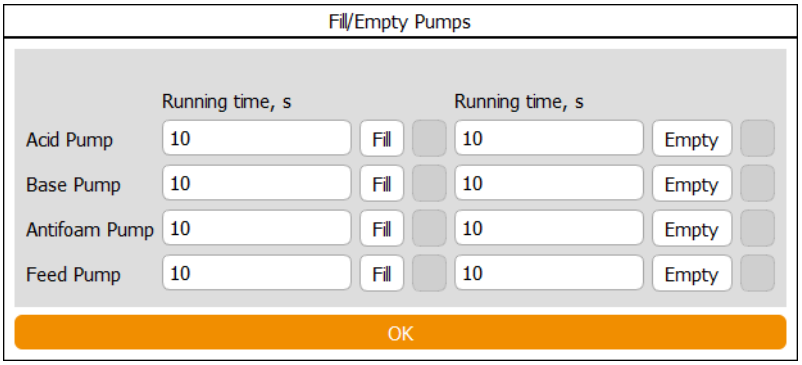


Pressing one of the pump buttons in the main menu *Main* opens the pump dialogue box with the **FILL** and **EMPTY** buttons for filling and emptying. The pump runs as long as the corresponding button is pressed.
The picture on the left shows the pump dialogue box of the feed pump

Time controlled filling and emptying

Fill/Empty Pumps in main menu *Batch* allows the automatic filling or emptying of the pump hoses when the bioreactor is in idle state.

The figure below shows the *Fill/Empty Pumps* dialogue box.



For each pump, an individual filling/emptying duration in seconds can be defined. The filling or emptying procedure is started via **Fill** and **Empty**. Stop buttons are provided next to each of these buttons for immediately stopping the filling or emptying process.

INFORMATION

If a filling or emptying procedure is active, the remaining filling or emptying duration is displayed. The menu cannot be closed while at least one filling or emptying procedure is active.

Note the following:

- The pump duration of a pump should preferably be tested with the liquid which has the same or similar viscosity as the liquid to be pumped.
- Observe hose lengths and hose sizes of the pumps and, if necessary, test the pump duration of each pump considering the same conditions mentioned above.

10.9 SIP – Sterilisation in Place

Sterilisation is always carried out according to the application and user specifications.

General information about in situ sterilisation and possible methods are described in main chapter “Before Cultivation”, chapter “In situ Sterilisation – General Information”.

The following chapters describe the SIP processes (Sterilisation in Place) which are started on the touch screen software.

⚠ WARNING

The vessel is under pressure during sterilisation!

Removing built-in parts or the vessel top plate lead to spurting out of liquids and/or rapid exhausting of gasses. This may cause severe chemical burns, burns or intoxication.

Always ensure the vessel is unpressurised before manipulating on built-in parts or the vessel top plate.

⚠ CAUTION

Danger of scalding and burns due to contact with hot surfaces!

The vessel, the pipework and their components can get hot during sterilisation. Touching these parts can lead to burns!

For details about the process sequences, see also document “Process Sequences” in the separate technical documentation of the device.

10.9.1 Full Sterilisation – Vessel Sterilisation

The water in the vessel jacket is heated up by steam injection for full sterilisation of the vessel. The steam generated by the liquid in the vessel sterilises the filters for inlet air and exit gas at the same time.

The harvest/sample valve **05.12.01** (bottom valve) is separately sterilised, see chapter “SIP Harvest / Sample Valve - Sterilisation of the Harvest / Sample Valve”.

The optional sample valve **17.13.01** (situated on the vessel side) is separately sterilised, see chapter “SIP Sample Valve – Sterilisation of the Sample Valve”.

The optional resterilisable feed line is separately sterilised, see chapter “SIP Feed Line – Sterilisation of the Feed Line”.

10.9.1.1 Process Sequence

In the following table, the individual process steps with corresponding status messages and dialogue boxes are listed on the left. These appear alongside the running process (*Full sterilisation*) in the touch screen software.

Process steps	**D = Dialogue box, user interaction required** **S = Status message, no user interaction**	
Configuration	D	*configuration* for process configuration
	See next chapter for details about configuration.	
User interaction	D	*user interaction required* with instructions.
Start inhibitor	S	*Starting inhibitor* + *time left* in h:min:s
	Sequence is skipped if function is switched off.	
Heat up to degassing temperature	S	*heating up to degassing temperature* + setpoint temperature in °C + current temperature
	Sequence is skipped if value for degassing duration = 0.	
Degas at degassing temperature	S	*degassing at degassing temperature* + setpoint temperature in °C + *time left* in h:min:s
	Sequence is skipped, if value for degassing duration = 0. (see next section for details about degassing)	
Heat up to sterilisation temperature	S	*heating up to sterilisation temperature*+ setpoint temperature in °C + current temperature
Sterilisation at sterilisation temperature	S	*sterilising at sterilisation temperature* + setpoint temperature in °C + *time left* in h:min:s
User interaction required	D	*user interaction required* with user interaction
	Dialogue box only appears, if resterilisable feed line is present.	
Cool down to 95 °C	S	*cooling down to 95 °C* + current temperature
Cool down to 70 °C	S	*cooling down to 70 °C* + current temperature
	Immediate process abortion is possible at temperature < 70 °C.	
Cool down to “Holding phase temperature” +10 °C	S	*cooling down to holding phase temperature +10 °C* + setpoint temperature in °C + current temperature
Cool down to “Holding phase temperature”	S	*cooling down to holding phase temperature* + setpoint temperature in °C + current temperature
Holding phase	S	*holding phase* + setpoint temperature in °C
	Holds holding phase temperature until bioreactor is started or full sterilisation is stopped.	
Full sterilisation completed	S	*completed at* with date and time in h:min:s

Degassing

If the medium is heated too quickly, foaming can occur due to escaping gases. During the "degassing" phase, a certain temperature is therefore maintained for a defined time to allow gases to escape

in a controlled manner. The time and temperature settings are made in the configuration dialogue.

10.9.1.2 Process Configuration

Input field	Value range	Unit
Stirrer	20 to 1000	min[1]
Degassing temperature	to 95	°C
Degassing time	0 to 120	min
Sterilisation temperature	110 to 125	°C
Sterilisation time	10 to 120	min
Cooling flow *(Only with mass flow controller, otherwise manual flow control via rotameter)* Air flow during cooling phase to prevent vacuum in the vessel.	10.0 to 20.0 (TV 15 L) 20.0 to 40.0 (TV 30 L) 30.0 to 60.0 (TV 42 L)	L/min
Holding phase temperature	up to 79	°C
Holding phase flow *(Only with mass flow controller)* Air flow during holding phase	0 / 0.2 to 20.0 (TV 15 L) 0 / 0.4 to 40.0 (TV 30 L) 0 / 0.6 to 60.0 (TV 42 L)	L/min
Holding phase pressure *(Only with optional pressure control)*	0 to 1.5	bar
Heating up time max.	90 to 300	min
Start inhibitor Switching process start inhibitor on or off	No / Yes	
Hours	0 to 99	h
Minutes	0 to 59	min
(Starting process in … hours … minutes)		

10.9.1.3 Starting the Process

Before starting the process, check and ensure that:

- All required services are available and activated.
- All services have the correct connection pressure.
- The mechanical seal is lubricated.

ATTENTION

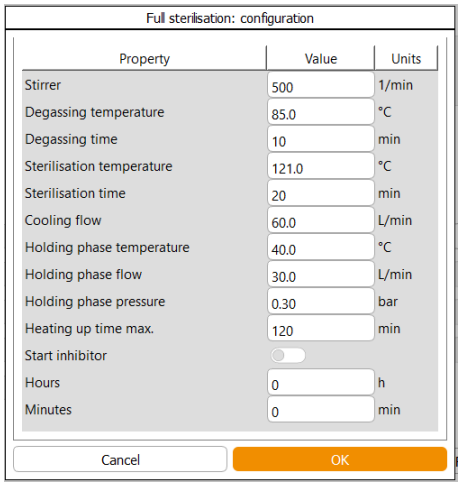
A mechanical seal, which has not been adequately lubricated is destroyed when running dry.

- Antifoam sensor is removed.
- If present: inoculation needles are removed.
- If present: push valves are closed.

To start the process, proceed as follows:

Procedure

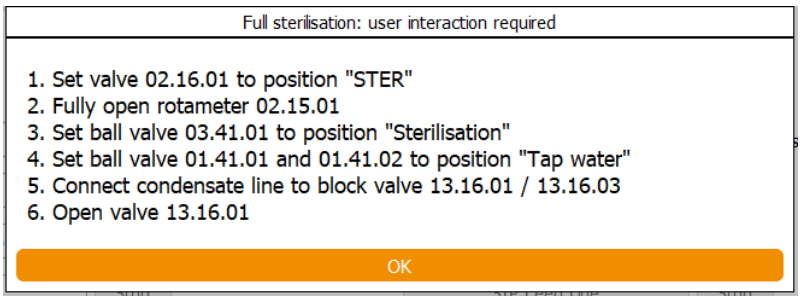
1. Call up main menu *Batch* and press **Full Sterilisation**.



The configuration dialogue appears, containing more or less input fields depending on the device configuration.

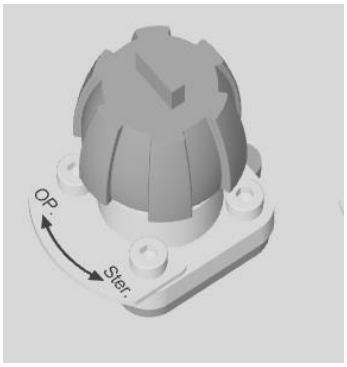
2. Enter the setpoint values.
3. Press **OK**.

The dialogue box for user interaction appears with more or less instructions depending on the device configuration.



The figure shows as an example the dialogue box of a device with rotameter, gas sensors for exit gas analysis, ball valves for switchover tap water/chilled water and a resterilisable feed line.

4. Carry out all listed steps one after the other:

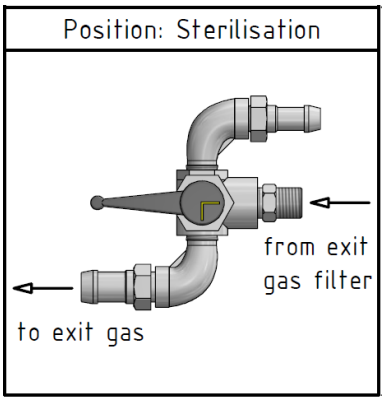


a) Turn valve **02.16.01** in position *STER* (sterilisation).

If a rotameter is present (depending on chosen gassing strategy):

b) Slowly fully open rotameter **02.15.01** (*Gas inlet*).

If gas sensors for exit gas analysis are present:

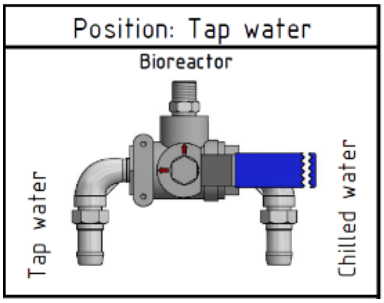


c) Set 3-way ball valve **03.41.01** (*Exit gas*) to position *Sterilisation*.

ATTENTION

Entry/intrusion of humidity (e.g. condensate from the exit gas cooler) into the gas sensors may damage them or lead to erroneous measuring results!

The exit gas line in direction of the gas sensors must be closed during sterilisation.

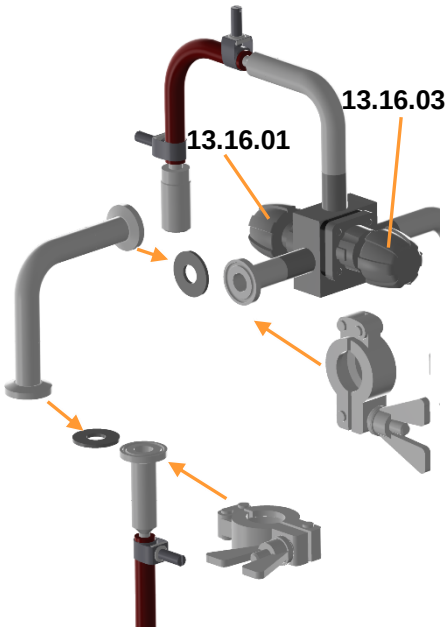


If the switchover from tap water/chilled water is present:

d) Set 3-way ball valves **01.41.01** (inlet) and **01.41.02** (outlet) in position *Tap Water* (Cooling circuit with tap water).

ATTENTION

Wrong position of the manual 3-way ball valves for tap water/chilled water may lead to overfilling or overflow of the house cooling circuit!



If a resterilisable feed line is present:

e) Connect the condensate line to block valve **13.16.01 / 13.16.03** (*vessel feed line/ steam feed line*) by means of the condensate elbow.

f) Open valve **13.16.01** (*vessel feed line*).

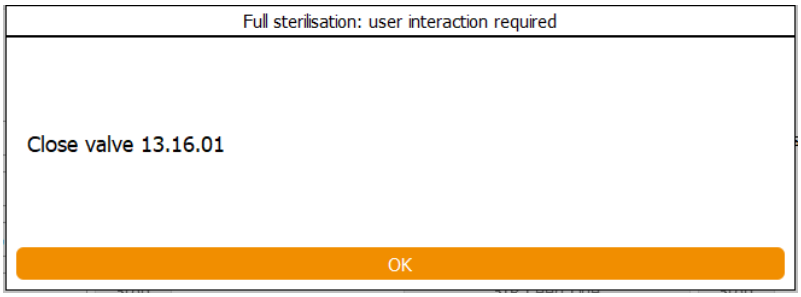
5. Press **OK**.

The program automatically runs through the different process sequences until the holding phase at the configured holding phase temperature.

INFORMATION

Should the sterilisation temperature fall below the set point, the message *temperature is low* will appear. The countdown stops until the temperature has reached the set point again to proceed with the process.

With resterilisable feed line, the second dialogue box appears after the set sterilisation time has elapsed with the instruction to close valve **13.16.01** (*vessel feed line*).



6. If applicable, close valve **13.16.01** (*vessel feed line*) and press **OK**.

10.9.1.4 End of Process

Holding phase temperature is held until the bioreactor (cultivation) is started via **Start** or by stopping the process by pressing **Stop** next to the **Full Sterilisation** button. The end of process is always indicated by *completed at* with date and time.

10.9.1.5 Aborting the Process

The process can be aborted by pressing **Stop** next to **Full Sterilisation**.

For safety reasons, the process can only be aborted immediately at a temperature < 70 °C. This means, if the temperature is ≥ 70 °C, the cooling sequence will start first and be indicated appropriately. Process abortion is indicated by *aborted at* with date and time.

10.9.2 SIP Harvest / Sample Valve – Sterilisation of the Harvest/Sample Valve

The harvest/sample valve **05.12.01** can be sterilised as often as required with clean steam. This procedure is independent of the full sterilisation process.

After sterilisation, the harvest/sample valve should cool down before sampling.

The process is started and ended in the touch screen software and the sterilisation duration is entered in the configuration dialogue. But steam inlet is manually regulated via valve **05.10.01**, which is located on the steam hose line of the harvest/sample valve.

10.9.2.1 Process Sequence and Process Configuration

In the following table, the individual process steps with corresponding status messages and dialogue boxes are listed on the left. These appear alongside the running process (*Sterilisation harvest / sample valve*) in the touch screen software.

Process steps	D = Dialogue box, user interaction required S = Status message, no user interaction	
Configuration	D	*configuration* for process configuration
User interaction required	D	*user interaction required* with instruction.
Sterilisation	S	*sterilisation* + *time left* in h:min:s
User interaction required	D	*user interaction required* with instruction.
Sterilisation harvest / sample valve completed	S	*completed* at with date and time in h:min:s

Duration of sterilisation is set in the configuration dialogue box:

Input field	Value range	Unit
Sterilisation time	10 to 60	min

10.9.2.2 Starting the Process and End of Process

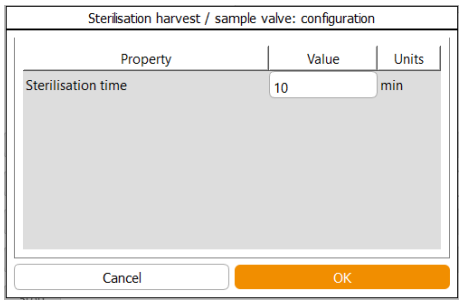
Before starting the process, check and ensure that:

- All required services are available and activated.
- All services have the correct connection pressure.
- Harvest/sample valve **05.12.01** is closed.
- Steam hose is connected
- Container/hose for draining the condensate is prepared.

To start the process, proceed as follows:

Procedure

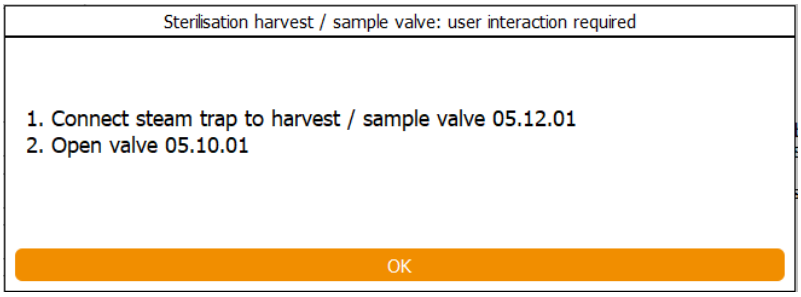
1. Call up main menu *Batch* and press **SIP Harvest / Sample Valve**.



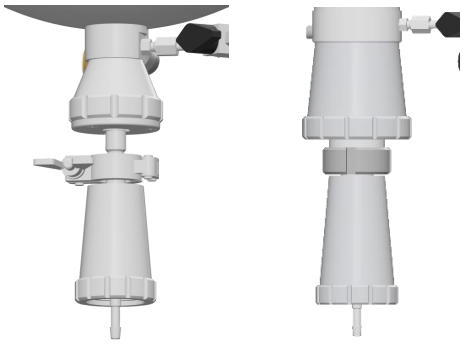
The configuration dialogue appears.

2. Enter desired sterilisation duration.
3. Press **OK**.

The dialogue box for user interaction appears with instructions.



4. Carry out the listed steps one after the other:

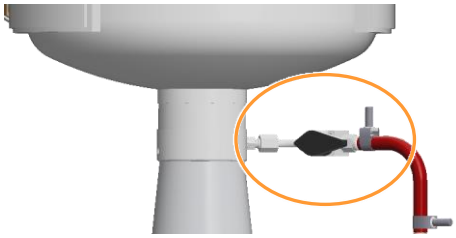


a) Connect the steam trap to harvest/sample valve **05.12.01**:

- Left valve type of 15 L and 30 L vessel: connect steam trap with clamp.
- Right valve type of 42 L vessel: screw on the steam trap.

INFORMATION

Ensure that a container is provided under the steam trap or a hose is connected to drain the condensate.

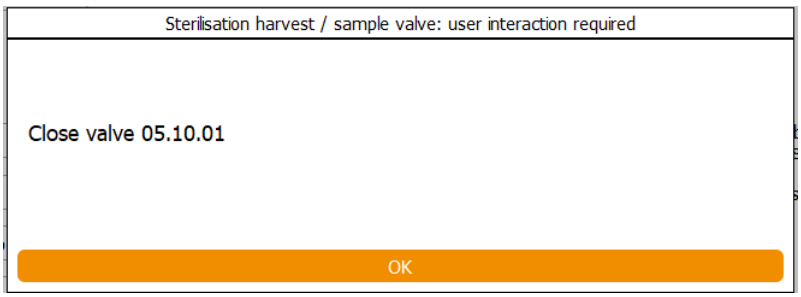


b) Open valve **05.10.01** (*steam harvest/sample valve*).

5. Press **OK**.

The sterilisation sequence begins.

Once sterilisation time has elapsed, the second dialogue box appears with instruction.



6. Close valve **05.10.01** (*steam harvest/sample valve*).
7. Press **OK**.

   The process is finished.

10.9.2.3 Aborting the Process

The process can be aborted any time by pressing **Stop** next to **SIP Harvest / Sample Valve**. The same dialogue box like at the end of the process appears. Process abortion is indicated with *aborted at* with date and time.

10.9.3 SIP Sample Valve – Sterilisation of the Sample Valve

The optional sample valve **17.13.01** can be sterilised as often as required with clean steam. This procedure is independent of the full sterilisation process.

After sterilisation, the sample valve should cool down before sampling.

The process is started and ended in the touch screen software and the sterilisation duration is entered in the configuration dialogue. But steam inlet is manually regulated via valve **17.10.01**, which is located on the steam hose line of the sample valve.

10.9.3.1 Process Sequence and Process Configuration

In the following table, the individual process steps with corresponding status messages and dialogue boxes are listed on the left. These appear alongside the running process (*Sterilisation sample valve*) in the touch screen software.

Process steps	D = Dialogue box, user interaction required S = Status message, no user interaction	
Configuration	D	Configuration
User interaction required	D	User interaction required
Sterilisation	S	*sterilisation* + *time left* in h:min:s
User interaction required	D	User interaction required
Sterilisation sample valve completed	S	*completed* at with date and time in h:min:s

Duration of sterilisation is entered in the configuration dialogue box:

Input field	Value range	Unit
Sterilisation time	10 to 60	min

10.9.3.2 Starting the Process and End of Process

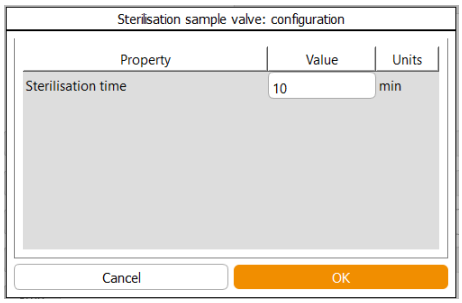
Before starting the process, check and ensure that:

- All required services are available and activated.
- All services have the correct connection pressure.
- Sample valve **17.13.01** is closed.
- Steam hose is connected
- Container/hose for draining the condensate is prepared.

To start the process, proceed as follows:

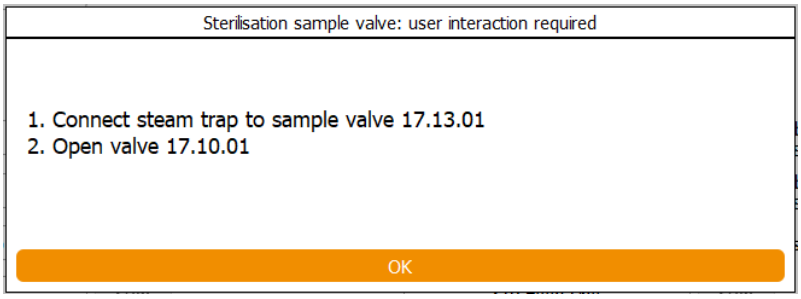
Procedure

1. Call up main menu *Batch* and press **SIP Sample Valve**.

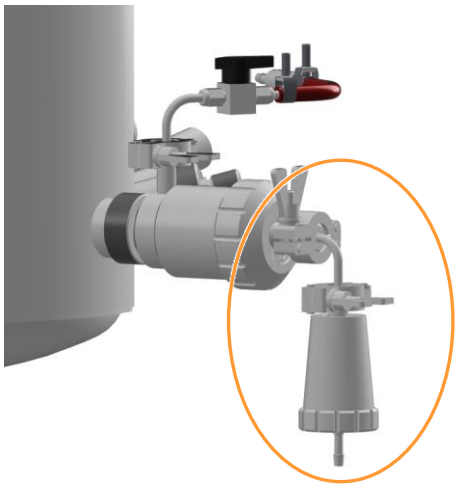


   The configuration dialogue appears.
2. Enter desired sterilisation duration.
3. Press **OK**.

The dialogue box for user interaction appears with instructions.



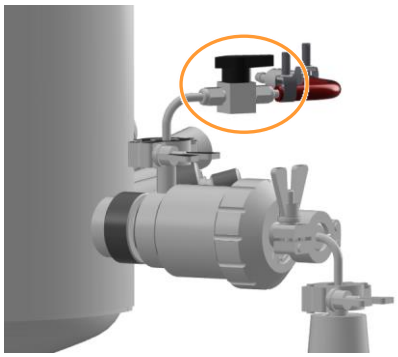
4. Carry out the listed steps one after the other:



a) Connect the steam trap to sample valve **17.13.01** by means of the condensate elbow and clamp.

INFORMATION

Ensure that a container is provided under the steam trap or a hose is connected to drain the condensate.

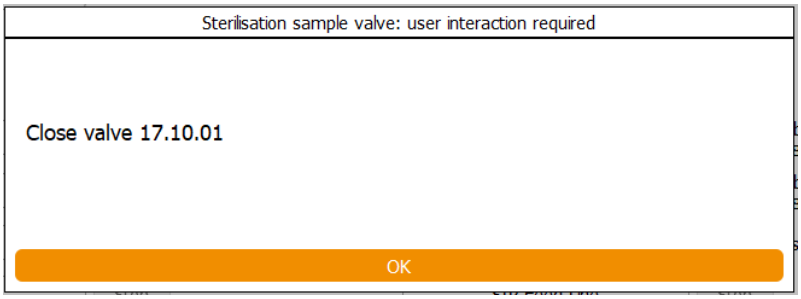


b) Open valve **17.10.01** (*steam sample valve*).

5. Press **OK**.

The sterilisation sequence begins.

Once sterilisation time has elapsed, the second dialogue box appears with instruction.



6. Close valve **17.10.01** (*steam sample valve*).
7. Press **OK**.

   The process is finished.

10.9.3.3 Aborting the Process

The process can be aborted any time by pressing **Stop** next to **SIP Sample Valve**. The same dialogue box like for the process end appears. Process abortion is indicated with *aborted at* with date and time.

10.9.4 SIP Feed Line – Sterilisation of the Feed Line

The optional resterilisable feed line is autoclaved and sterilised in further partial steps beforehand. For a detailed description see the main chapter “Options”, chapter “Resterilisable Feed Line”.

The process is started and ended in the touch screen software and the sterilisation and ventilation duration are entered in the configuration dialogue. However, all valves of the feed line are opened and closed manually.

10.9.4.1 Process Sequence and Process Configuration

In the following table, the individual process steps with corresponding status messages and dialogue boxes are listed on the left. These appear alongside the running process (*Sterilisation feed valve*) in the touch screen software.

Process steps	D = Dialogue box, user interaction required S = Status message, no user interaction	
Configuration	D	*configuration*
User interaction required	D	*user interaction required* with instruction.
Sterilisation	S	*sterilisation* + *time left* in h:min:s
User interaction required	D	*user interaction required* with instruction.
Ventilation	S	*ventilation* + *time left* in h:min:s
	Sequence is skipped, if value for ventilation duration = 0.	
User interaction required	D	*user interaction required* with instruction.
Sterilisation feed line completed	S	*completed* at with date and time in h:min:s

Duration of sterilisation and ventilation are entered in the configuration dialogue box:

Input field	Value range	Unit
Sterilisation time	10 to 60	min
Ventilation time	0 to 60	min

10.9.4.2 Starting the Process and End of Process

Before starting the process, check and ensure that:

- All required services are available and activated.
- All services have the correct connection pressure.
- Block valve **13.16.02** / **13.16.04** is connected.
- Steam hose is connected

INFORMATION

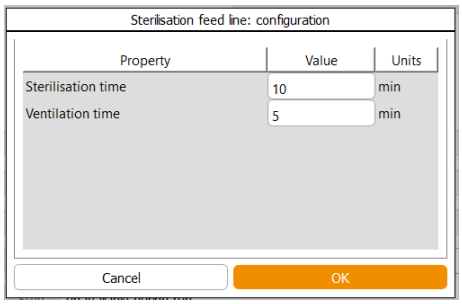
To be able to carry out the process during an active cultivation process, the parameter Feed must be switched off.

To start the process, proceed as follows:

Procedure

1. Call up main menu *Batch* and press **SIP Feed Line**.

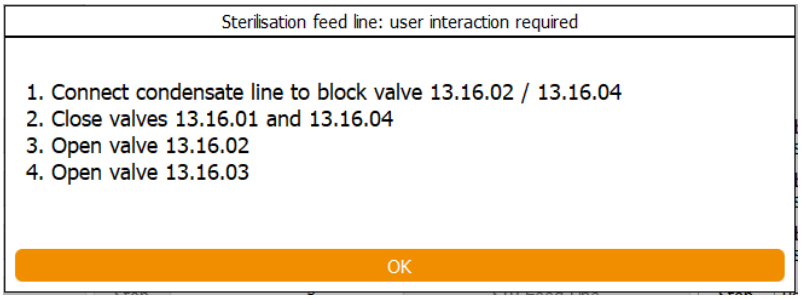
Operation Touch Screen Software



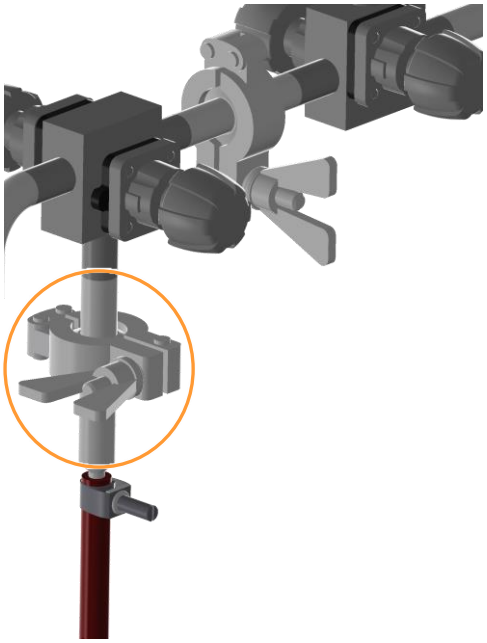
The configuration dialogue appears.

2. Enter desired sterilisation duration and ventilation duration.
3. Press **OK**.

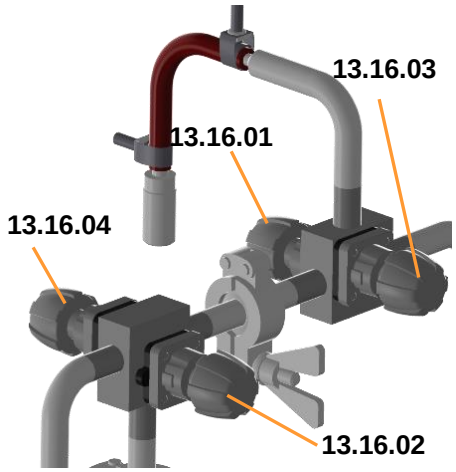
The first dialogue box for user interaction appears with instructions.



4. Carry out the listed steps one after the other:



a) Connect the condensate line to block valve **13.16.02 / 13.16.04** (condensate feed line / reagent bottle feed line)

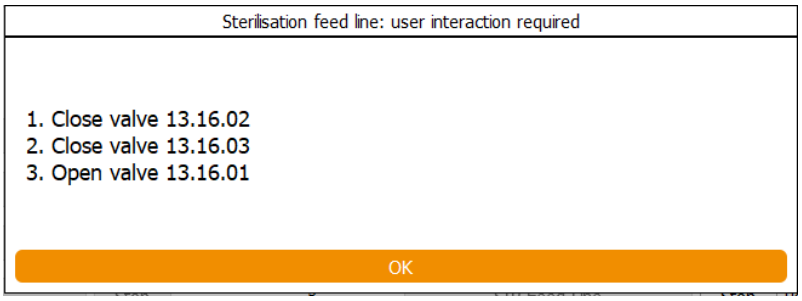


b) Close valve **13.16.01** (*vessel feed line*) and valve **13.16.04** (*reagent bottle feed line*).
c) Open valve **13.16.02** (*condensate feed line*).
d) Open valve **13.16.03** (*steam feed line*).

5. Press **OK**.

The sterilisation sequence begins.

Once sterilisation time has elapsed, the second dialogue box appears with instructions.



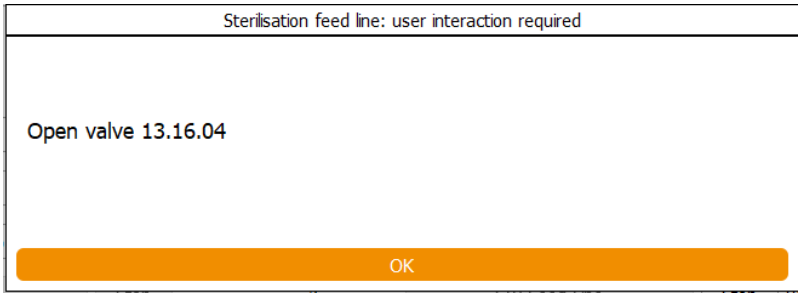
6. Carry out the listed steps one after the other:

a) Close valve **13.16.02** (*condensate feed line*).
b) Close valve **13.16.03** (*steam feed line*).
c) Open valve **13.16.01** (*vessel feed line*).

7. Press **OK**.

The ventilation sequence begins.

Once ventilation time has elapsed, the third dialogue box appears with instruction.



8. Open valve **13.16.04** (*reagent bottle feed line*).
9. Press **OK**.

   The process is finished.

10.9.4.3 Aborting the Process

The process can be aborted any time by pressing **Stop** next to **SIP Feed Line**. Please note that the valves of the feed line must be returned to their initial position as instructed in the appropriate dialogue boxes. Process abortion is indicated with *aborted at* with date and time.

10.10 Starting and Stopping the Bioreactor

10.10.1 Process Configuration

Input field	Value range	Unit
Temperature	0 / 10 to 79	°C
Stirrer	0 / 20 to 1500 (TV 15 L) 0 / 20 to 1200 (TV 30 L + 42 L)	min[1]
pH	2 to 12	pH
pO_2	0 to 100	%
Antifoam	OFF/ON	
Feed	0 to 100	%
Feed 2 / Feed 3 [1)]	0 to 100	%
GasMix [2)]	-100 to +100	%
Flow / GM Flow / Air Flow / O_2 Flow / CO_2 Flow [3)]	0 / 0.1 to 20.0 (TV 15 L) 0 / 0.2 bis 40.0 (TV 30 L) 0 / 0.3 bis 60.0 (TV 42 L)	L/min
Pressure [1)]	0 to 1.5	bar

1) *Option*

2) *The setting range of the GasMix depends on the number and kind of gasses used (air, O_2, N_2).*

3) *Depending on the selected gassing strategy and number of gases, different and more or less flow parameters are available and configured.*

10.10.2 Starting the Process

Before starting the process, check and ensure that:

- All required services are available and activated.
- All services have the correct connection pressure.
- The mechanical seal is lubricated.

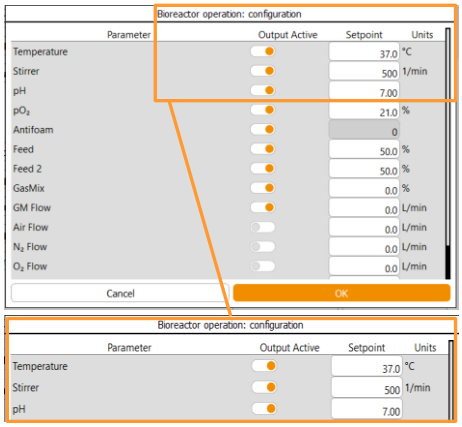
ATTENTION

A mechanical seal, which has not been adequately lubricated is destroyed when running dry.

Operation Touch Screen Software

To start the bioreactor, proceed as follows:

Procedure



1. Call up main menu *Batch* and press **Start**.

The configuration dialogue box appears containing more or less controlled parameters, depending on the device configuration.

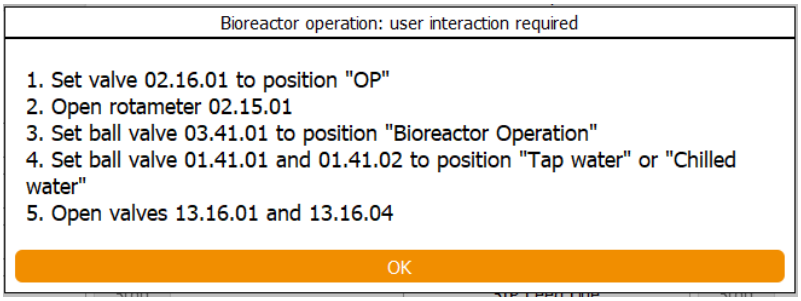
Setpoint settings of the previous cultivation are visible here.

INFORMATION

The bioreactor is started with the settings in the configuration dialogue box. Changes to these settings are saved and transferred to the next configuration dialogue box. If setpoint values are changed or parameters are switched on /off whilst the bioreactor is running, these settings are only adopted for the current cultivation process.

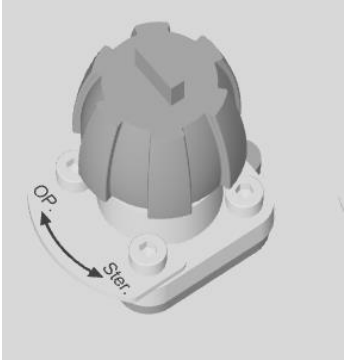
2. Make settings as necessary and press **OK**.

The dialogue box for user interaction appears with more or less instructions, depending on the device configuration.



The figure shows as an example the dialogue box of a device with rotameter and optional gas sensors for exit gas analysis, ball valves for switchover tap water/chilled water and a resterilisable feed line.

3. Carry out all listed steps one after the other:

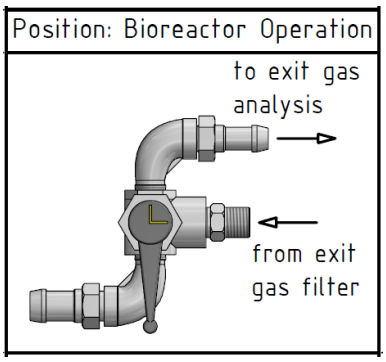


a) Turn valve **02.16.01** in position *OP* (= operation).

If a rotameter is present (depending from chosen gassing strategy):

b) Slowly open rotameter **02.15.01** (*Gas inlet*).

If gas sensors for exit gas analysis are present:



c) Set 3-way ball valve **03.41.01** (*Exit Gas*) in position *Bioreactor Operation*.

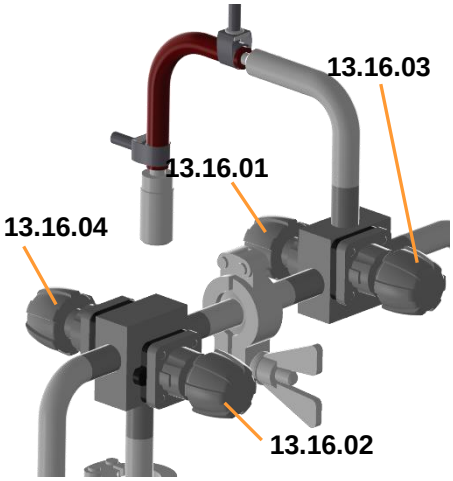
If switchover from tap water/chilled water is present:

d) Set 3-way ball valves **01.41.01** and **01.41.02** in position *Tap Water* (Cooling circuit with tap water) or position *Chilled Water* (cooling circuit with chilled water).

ATTENTION

Wrong position of the 3-way ball valves for tap water/chilled water may lead to overfilling or overflow of the cooling circuit!

If a resterilisable feed line is present:



e) Open valve **13.16.01** (*vessel feed line*) and valve **13.16.04** (*reagent bottle feed line*).

4. Press **OK**.

Once the bioreactor (cultivation) is started, the status message *in progress since* indicates that and since when (in d/h/min/s) the process is running.

All buttons for starting processes that cannot be simultaneously running are deactivated.

CAUTION

Danger of scalding and burns due to contact with hot surfaces!

The vessel, the pipework and their components can get hot during cultivation and may lead to burns when touched!

- Current values and controller outputs are visible in the main menu *Controller*.
- A recording of the current values and a diagram are visible in the main menu *Trends.*

⚠ WARNING

The vessel may be under pressure during operation!

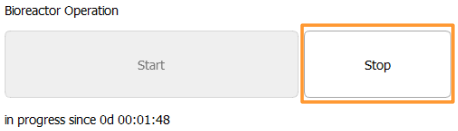
Removing built-in-parts or the vessel top plate lead to spurting out of liquids and/or rapid exhausting of gasses. This may cause severe chemical burns, burns or intoxication.

Always ensure the vessel is unpressurised before manipulating on built-in-parts or on the vessel top plate.

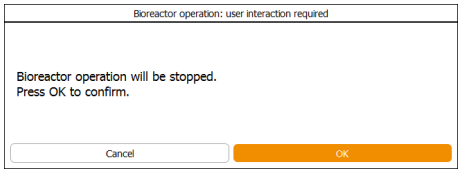
10.10.3 Stopping the Process

To stop the bioreactor, proceed as follows:

Procedure



1. In main menu *Batch,* press **Stop** next to **Start**.



A dialogue box for user interaction appears with the instruction to confirm the bioreactor stop.

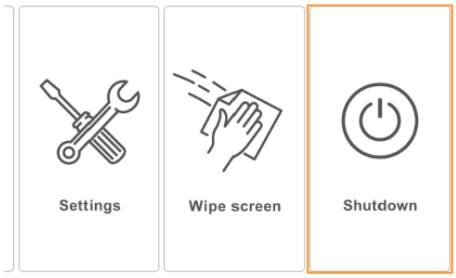
2. Press **OK**.

The bioreactor is stopped. *Stopped after* with display of d:h:min:s below **Start** indicates after how much running time the bioreactor was stopped.

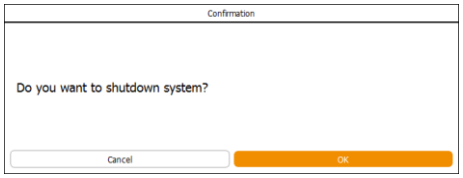
10.11 Shutting Down the System, Switching Off the Device

To shut down the system and to switch off the device, proceed as follows:

Procedure



1. In main menu *System*, press **Shutdown**.



Dialogue box *Confirmation* appears with question/prompt to confirm shutdown.

2. Press **OK**.

The system is shut down.

ATTENTION

Switching off at the main switch without previously stopping the bioreactor and shutting down the system on the operating panel may lead to damage of the operating panel!

When the screen is dark:

3. Turn the main switch in position **0/OFF**.
4. Close/shut off supply lines and ensure they are pressure-free.

WARNING

The vessel may be still pressurised after switching off at the main switched due to stored energy!

Check the vessel pressure on the manometer and, if required, put the vessel into non-pressurised condition before every manipulation on the vessel and its components

11 Cleaning and Maintenance

The following chapters describe in detail how the vessel, the top plate and accessories are cleaned and as required, stored.

Furthermore, the chapter contains a maintenance plan and corresponding descriptions for the procedures to be performed by the operator.

11.1 Cleaning Agent and Disinfectant

Intended use	Allowed products/tools
For vessel with slight contamination	Water
Cleaning agent for denaturation of proteins	0.1 N NaOH
Cleaning agent for smaller component parts	Ultrasonic bath
Cleaning agent for surfaces	Water
Disinfectant for surfaces	Ethanol, 70 %

⚠ CAUTION

Explosive mists can be generated when using spray bottles with ethanol!

All cleaning operations with ethanol must be carried out in an environment that is separate from the appliance, well ventilated and in accordance with internal safety regulations.

11.2 Cleaning the Vessel

After ending cultivation followed by in situ sterilisation for decontamination (depending on user specifications), the vessel should be cleaned.

Depending on the degree and kind of contamination, rinsing with water can be sufficient. If remains of foam or protein are adhering to the inside of the vessel, then the following procedure will ensure sufficient cleaning:

Procedure

1. Carefully remove sensors from the ports and put aside in order to clean them separately according to the manufacturer's specifications.
2. Fill the vessel with 0.1 N NaOH.
3. Close all vessel ports and fit the vessel top plate.
4. Start the bioreactor and stir strongly for 2 hours by using the stirrer function.

   Temperatures of e.g. 40 up to 60 °C improve the cleaning action, prolong stirring duration as necessary.
5. Stop the bioreactor, shut down the system and switch off the device.
6. Empty the vessel.
7. Thoroughly rinse the vessel with water.

   Repeat the procedure, if necessary.

If the vessel is not used again for the next cultivation right after, sufficient air circulation in the vessel should be ensured.

11.3 Cleaning the Vessel Top Plate

Depending on the application, separate cleaning of the vessel top plate may be necessary. To clean the vessel top plate thoroughly, proceed as follows:

Procedure

1. Lift up, swivel, lower and remove the vessel top plate and place it with the inside of the top plate facing upwards on a suitable support.

INFORMATION

A detailed description how to remove the vessel top plate can be found in chapter "Removing the Vessel Top Plate" of the main chapter "Before Cultivation". Observe the safety advice and follow the instructions stated in there.

2. If necessary, remove the baffles:
   a) To do so, loosen the four cap nuts (M8) on the outside of the vessel top plate and remove them together with the washers.
   b) Pull off the baffles from the inside of the vessel top plate.

INFORMATION

The ring sparger is firmly welded to one of the four baffles and is therefore automatically removed, too.

3. If necessary, remove the spacers from the baffles and store them safely for later use.
4. Carefully rinse the baffles and sparger with water.

   Use 0.1 N caustic soda solution as necessary.
5. Carefully rinse the vessel to plate with water or wipe it with a damp cloth or sponge.

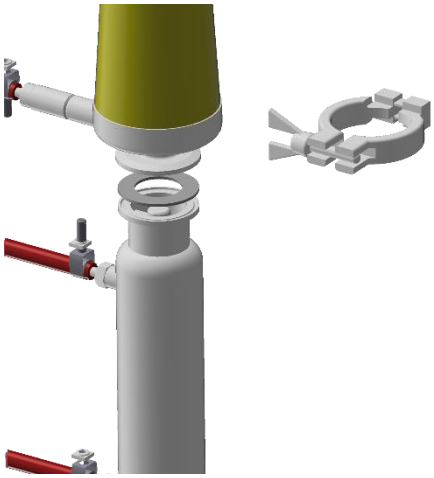
   Use 0.1 N caustic soda solution as necessary.
6. Check vessel top plate sealing (O-ring) and O-rings of all built-in parts on damages and replace them as necessary.
7. Leave the vessel top plate and all built-in-parts to dry or dry wipe them.
8. Mount the clean and dry baffles and sparger into the also clean and dry vessel top plate.
9. Store the vessel top plate clean and dry in a location where it is secure and unable to fall or be damaged in passing, if not used right after for next cultivation.

11.4 Cleaning the Exit Gas Cooler

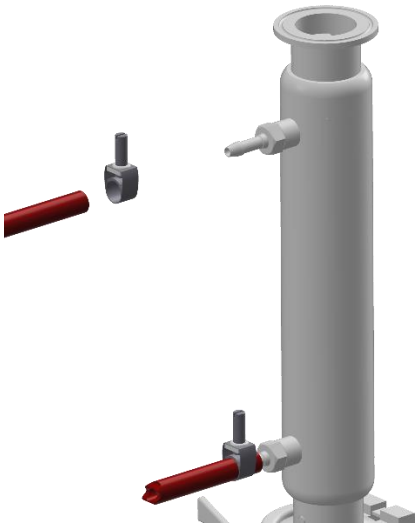
To thoroughly clean the exit gas cooler, its baffle body can be removed. Proceed as follows for removing, dismantling and cleaning the exit gas cooler:

Cleaning and Maintenance

Procedure

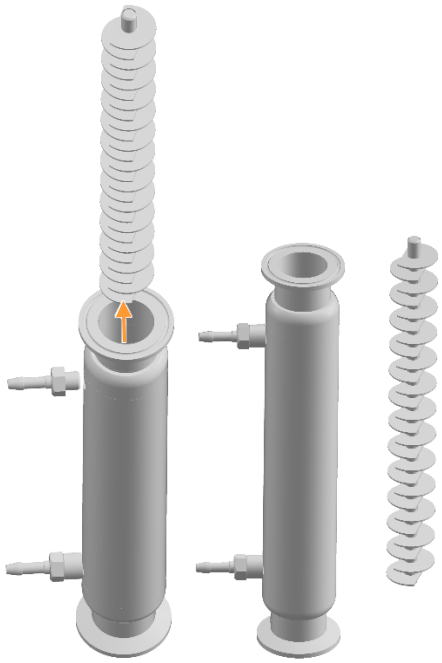


1. Open the clamp between the exit gas filter and the exit gas cooler.
2. Remove the clamp and flat gasket and put aside for subsequent installation.



3. Remove the hose clamps and disconnect the red pressure hoses for water intake and outlet from the exit gas cooler.

4. Remove the clamp and flat gasket between the exit gas cooler and connection flange on the vessel top plate in the same way as for the exit gas filter.



5. Carefully pull the baffle body from the exit gas cooler.

6. Place the exit gas cooler and baffle body into 0.1 N NaOH for 4 hours.
7. Then thoroughly rinse both parts with water.
8. Place both parts into an ultrasonic bath for 2 to 5 minutes.
9. Then thoroughly rinse both parts with distilled water.
10. Let both parts dry on a clean base and then re-assemble them.

11.5 Cleaning Reagent Bottles, Hoses and Built-in-Parts

Reagent bottles and hoses are separately autoclaved before cleaning. After autoclaving and cooling down, proceed as follows:

Procedure

1. If appropriate, carefully empty the reagent bottles, and dispose of the liquid respecting the internal safety regulations.
2. Thoroughly rinse reagent bottles, hoses, built-in-parts and accessories such as e.g. inoculation needles, push valves etc. with water.
3. Check silicone and pump hoses on damage and replace as necessary.

INFORMATION

Depending on user specifications, the hoses are replaced after every use.

4. Check reagent bottles and its components on damage and replace as necessary.
5. Check O-rings on built-in-parts and accessories as well as lid seals of the reagent bottles for damage, replace if necessary.
6. Leave to dry the reagent bottles, hoses, built-in-parts and accessories on a clean surface.

11.6 Cleaning the Sensors

Cleaning and maintenance of the individual sensors are described in the separate documentation of the respective sensor manufacturer. Read and follow these instructions.

Sensors of the device manufacturer (antifoam and level) are cleaned and maintained like other built-in-parts, e.g. inoculation needles and push valves. When not in use, these sensors must be stored clean and dry.

11.7 Cleaning Surfaces of the Instrumentation Cabinet and Operating Panel

If required, the surfaces of the instrumentation cabinet and the operating panel can be cleaned.

ATTENTION

Take the protection classes IP43 (instrumentation cabinet) and IP66 (operating panel) into account when cleaning!

Proceed as follows:

Procedure

1. Ensure the device is switched off at the main switch, switch off, where applicable.
2. Disconnect from the power supply.
3. Wipe the surface of the instrumentation cabinet and of the operating panel with a soft, damp cloth.

   Use an appropriate (non-aggressive!) disinfectant as necessary.
4. Clean the screen of the operating panel with a wipe suitable for computer or laptop screens.

11.8 Maintenance Plan

WARNING

Non-compliance of this maintenance plan contains a high risk!

It is the responsibility of the user, that this maintenance plan is complied with. Non-compliance will lead to exclusion of liability (see General Terms and Conditions).

The required maintenance for reliable operation is described in the following chapters.

Reduce the maintenance intervals in case increased abrasion is detected during regular checks.

Contact the manufacturer for questions concerning maintenance.

To be carried out by operator	
Interval	**Maintenance work**
Before every operation	Check hose lines and connections.
	Check all O-rings and seals and replace if necessary.
	Check the reagent bottles and any other work tool made of glass on intactness; replace if necessary.
	Lubricate the mechanical seal.
	Check the filters with a filter test device, if available.
After every cultivation	Sterilise and clean the vessel, the vessel top plate, built-in-parts of the vessel top plate, reagent hoses and bottles. Proactively replace silicone hoses (frequency depends on application).
After 20 – 50 sterilisations (rough recommendation)	Replace air filters. Reduce or enhance maintenance interval as necessary.
Every 6 months	Replace all pump and silicone hoses on the reagent bottles.
As required	Clean the surfaces of the instrumentation cabinet and the operating panel.

To be carried out by qualified personnel	
Interval	**Maintenance work**
Every 6 months	Replace O-rings and seals, reduce maintenance interval as necessary.
	Check functionality of measurement sections (temperature, pH, etc.), use simulator, where possible.
	Check the functionality of the safety valves according to the safety valve manufacturer's instructions.
Annually	Replace flat gasket(s), valve diaphragm(s), gaskets of the vessel sight glass.
As required	Replace hoses and hose connections.
According national regulations concerning safety valves	Have safety valves inspected by a competent external body in accordance with nationally applicable regulations.

To be carried out by INFORS HT service technician	
Interval	**Maintenance work**
Annually (recommendation)	Full maintenance of the device.
When signs of wear or damage are apparent or at maintenance intervals defined by the operator of the device.	Replace mechanical seal.

INFORMATION

Detailed information on the care and maintenance of components and accessories from other manufacturers, please refer to the documentation of the respective manufacturer and follow the instructions contained therein. This applies in particular to the safety valves.

11.9 Mechanical Seal

11.9.1 Important Information about the Mechanical Seal

Refilling glycerine

During operation, a small amount of glycerine is always used to lubricate the mechanical seal. Therefore, the chamber should be refilled regularly, e.g. after a few cultivations or each time the vessel top plate is cleaned. If the mechanical seal is in good condition, the glycerine will already escape from the overflow when refilling a small amount.

Discoloration glycerine

Due to normal wear of the mechanical seal, even after a short period of operation of the stirrer shaft, a dark discoloration of the glycerine occurs, which is visible in the silicone hose. This discoloration is completely normal and does not indicate progressive wear of the mechanical seal.

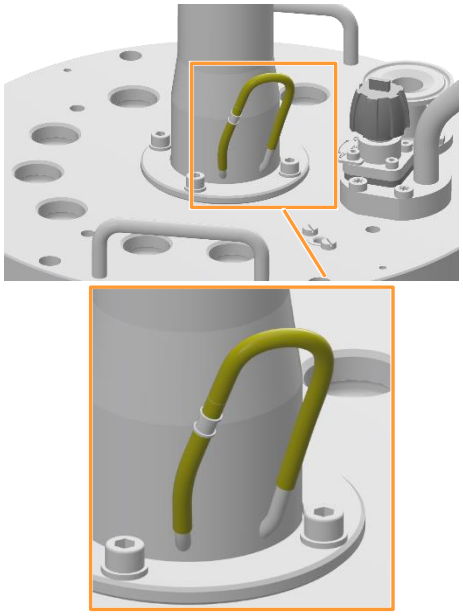
Loss of glycerine

If significant glycerine loss occurs during or between two cultivations, this may indicate a misaligned or defective mechanical seal. A significant loss of glycerine is indicated by either significantly more glycerine being consumed during refilling of the chamber and/or sudden dark discoloration of the culture liquid, due to glycerine running down the stirrer shaft.

Replacement mechanical seal

If a significant loss of glycerine occurs, an INFORS HT service technician must check, if the mechanical seal needs to be replaced.

11.9.2 Lubricating the Mechanical Seal



The two-part silicone hose at the bottom of the drive hub of the top plate must always be filled with liquid (glycerine), to ensure the mechanical seal is lubricated.

! ATTENTION

A mechanical seal, which has not been adequately lubricated is destroyed when running dry!

To lubricate the mechanical seal, proceed as follows:

Procedure

1. Pull off the longer piece of hose from the coupling on the shorter piece.
2. Fill a syringe with glycerine

3. Plug the syringe onto the open hose end.
4. Fill glycerine into the hose.
5. Plug the longer piece of hose onto the coupling of the shorter piece.

   If glycerine has come off the hose, wipe off as necessary.

12 Interferences

The following section describes possible reasons for interferences and how to resolve them. Reduce the service intervals in correspondence with the actual loads if interferences become increasingly common. Contact the manufacturer or licensed dealer for interferences that cannot be resolved by following the above instructions.

12.1 Interferences Basic Operation and Operating Panel

Interference		
Device does not work, green power indicator light is not illuminated, screen of the operating panel remains dark.		
Possible Causes	**Remedy**	**By**
Device is not switched on.	Switch on the device at the main switch	Operator
Power supply of the device is interrupted.	■ Check, if the plugs are connected. ■ Check the mains connection.	Operator
Circuit breaker(s) has/have tripped.	Open the instrumentation cabinet. Switch on both circuit breakers. Call INFORS HT service technician, if they are triggered again.	Qualified electrician

Interference		
Green power indicator light is illuminated, screen of the operating panel remains dark.		
Possible Causes	**Trouble shooting**	**By**
Monitor of the operating panel is switched off.	Switch the monitor of the operating panel on at the ON/OFF key.	Operator
Power supply cable is not connected to the operating panel.	Connect the power supply cable to the DC connection of the operating panel.	Operator

Interference		
No communication between device and operating panel. (Alarm *no communication).*		
Possible Causes	**Remedy**	**By**
iDDC-bus cable (display cable) is not connected to the operating panel.	Plug the round connector of the iDDC-bus cable in at the COM1 socket (labelled with RS-485) on the rear side of the operating panel.	Operator
iDDC-bus cable (display cable) is not connected to the controller inside the instrumentation cabinet.	Open the instrumentation cabinet. Connect the iDDC-bus cable (display cable) to the controller.	Qualified electrician

12.2 Interferences Drive System

Interference		
Motor does not start.		
Possible Causes	**Remedy**	**By**
Parameter *Stirrer* is not switched on.	Switch parameter *Stirrer* on.	Operator
Stirrer setpoint = 0.	Set *Stirrer* setpoint > 0 Check value in *Deadband* of parameter option *PID*: Value must be = 0 (zero)	Operator
Parameter pO_2 is switched on and set to work with stirrer. (Option *Cascade* in parameter pO_2)	Switch *Cascade* off and test operation via parameter *Stirrer*.	Operator

Interference		
Motor does not start, parameter *Stirrer* is turned on, Cascade in pO_2 is not activated.		
Possible Causes	**Remedy**	**By**
Motor cable is not properly connected.	Connect the motor cable properly.	Qualified personnel
Motor is/was overheated or mains voltage of the motor is too low.	Turn the device off at the main switch. Wait for approx. 20 seconds. Turn the device on at the main switch. If this does not resolve the problem, see next section.	Operator
	Switch parameter *Stirrer* off. Open the instrumentation cabinet and check the LED display of the motor controller: ■ Error Code M: motor overheated ■ Error Code Z: low mains voltage. Press the **Reset** button of the frequency converter. Close the instrumentation cabinet. Switch on parameter *Stirrer*.	Qualified electrician

Interference		
Motor control is erratic		
Possible Causes	**Remedy**	**By**
Wrong settings in *PID* option of parameter *Stirrer.*	Reset default settings in *PID* menu.	Operator

12.3 Interferences Temperature Control System

Interference		
No temperature control.		
Possible Causes	**Remedy**	**By**
Temperature control is not activated.	Switch parameter *Temperature* on.	Operator
Stirrer is not activated and/or set-point = 0.	Switch parameter *Stirrer* on and enter setpoint > 0, as required.	Operator

Interference		
No cooling or inadequate cooling.		
Possible Causes	**Remedy**	**By**
No water supply or inadequate flow.	Ensure water supply is turned on and flow is sufficient.	Operator
Incorrect Neg. factor (negative factor) in option *PID* of parameter *Temperature*.	Check *Neg. factor* (negative factor) in option *PID* of parameter *Temperature*: Value must be positive.	Operator

Interference		
Temperature drifts up or down over time.		
Possible Causes	**Remedy**	**By**
Incorrect settings in option *PID* of parameter *Temperature*	Check settings in option *PID* of parameter *Temperature* and adjust as necessary (especially *P-term*).	Operator

Interference		
Alarm *no water detected in temperature control system, refill failed* appears. Temperature control is switched off, circulation pump and heating are deactivated, and active process continues running.		
Possible Causes	**Remedy**	**By**
Temperature control circuit is not filled.	Fill the temperature control circuit (according to description in “Process Sequences” in the technical documentation of the device).	Qualified personnel

Interference		
Negative temperature value.		
Possible Causes	**Remedy**	**By**
Broken cable or faulty sensor.	Replace the temperature sensor.	INFORS HT service technician

12.4 Interferences pH System

Interference		
No display or incorrect display of pH, digital measurement systems: the message ERROR is displayed instead of the current value.		
Possible cause	**Remedy**	**By**
Sensor cable is not connected or not properly connected.	Connect the sensor cable properly.	Operator
Analogue measurement system: *Temp. Compens*. (temperature compensation) is switched off.	Switch the function *Temp. Compens* on in Setpoint option of parameter *pH*.	Operator
pH drift during long cultivation.	Recalibrate pH with external measured values, respectively perform a product calibration.	Operator
Faulty pH sensor.	Test calibration with pH 4 and pH 7 buffer. Digital measurement systems: Note the error message(s) (*Show Sensor Status*) when calling up the calibration menu. Regenerate or replace the sensor. Consult the documentation of the sensor manufacturer!	Operator

Interference		
No pH control.		
Possible cause	**Remedy**	**By**
Parameter *pH* is not switched on.	Switch parameter *pH* on.	Operator
Incorrect dead band setting in PID	Check the dead band settings (*Dead Band* in parameter option *PID*): Switch off or enter a small value.	Operator
No addition of reagents (acids and base).	Check the reagent bottles: Refill if necessary. Check the hose connections between the reagent bottles and the culture vessel: Connect properly if necessary. Open/remove hose clamps if necessary. Open push valve(s)	Operator
Pump (base/acid) does not operate properly.	Check operation of pump(s) using the rocker switch(es). Check hose type, replace as necessary.	Operator

Interference		
pH value drifts up and down over time or acid and base are added almost continuously in turn.		
Possible cause	**Remedy**	**By**
Incorrect PID settings in *pH* parameter.	Check the PID settings and adjust as necessary. Change the special proportional factor (*Prop. Term)* or *Dead band* setting.	Operator
Incorrect strength of reagents: Concentration is too weak or too strong.	Check the strength of reagents. Adjust if necessary: 0.1 mol to 2.0 mol.	Operator

12.5 Interferences pO_2 System

Interferences		
No display or incorrect display of pO_2. Digital measurement systems: the message *ERROR* is displayed instead of the current value		
Possible cause	**Remedy**	**By**
Sensor cable is not connected or not properly connected.	Connect the sensor cable properly.	Operator
Analogue measurement system: pO_2 sensor is not polarised.	Polarise the pO_2 sensor	Operator
Faulty pO_2 sensor.	Check the calibration of the pO_2 sensor. Digital measurement systems: Note the error message(s) (*Show Sensor Status*) when calling up the calibration menu. Replace the sensor if necessary. Consult the documentation of the sensor manufacturer!	Operator

Interference		
No pO_2 control.		
Possible cause	**Remedy**	**By**
The *pO_2* parameter and/or cascaded parameter is/are not activated.	Activate parameters.	Operator
The cascade settings are incorrect.	Check the cascade settings and change as necessary.	Operator
No gas flow into culture vessel.	Refer to interferences in the gassing system.	Operator

Interferences

Interference		
Unstable pO_2 control.		
Possible cause	**Remedy**	**By**
Incorrect PID settings in the *pO_2* parameter.	Check the PID settings (*PID* parameter option) and adjust as necessary. Special proportional factor (*Prop. Term*) and dead band. Dead band value must be 0 (zero).	Operator

12.6 Interferences Antifoam Control

Interference		
Foam is not sensed.		
Possible Causes	**Remedy**	**By**
Sensor cables are not properly connected.	Connect the sensor cable properly.	Operator

Interference		
Foam is always/frequently detected.		
Possible Causes	**Remedy**	**By**
Sensor cables are not properly connected.	Connect the sensor cables properly.	Operator
Transparent insulation of antifoam sensor is damaged	Replace the transparent insulation of antifoam sensor.	Operator

Interference		
Antifoam pump does not work.		
Possible Causes	**Remedy**	**By**
Parameter *Antifoam* is not switched on.	Switch parameter *Antifoam* on.	Operator
Dosing time of parameter *Antifoam* = 0 (zero).	Set dosing time of parameter > 0.	Operator

Interference		
No or inadequate reagent.		
Possible Causes	**Remedy**	**By**
Reagent bottle is empty.	Refill the reagent bottle.	Operator
Wrong antifoam agent or wrong concentration of antifoam agent is used.	Replace the antifoam agent.	Operator
Hose line is blocked or clamped off.	Check hose line connection between reagent bottle and vessel, connect properly as necessary. Open/remove hose clamp, if necessary.	Operator
Push valve is closed.	Open the push valve.	Operator
Antifoam pump does not operate properly.	Check operation using the rocker switch. Check the hose type and replace it, if necessary.	Operator

12.7 Interferences Feed and Pump

Interference		
No or insufficient addition of liquid via feed pump.		
Possible cause	**Remedy**	**By**
Parameter *Feed* is not switched on.	Switch *Feed* parameter on.	Operator
Setpoint of parameter *Feed* = 0 (zero).	Enter setpoint of parameter *Feed* > 0.	Operator
Reagent bottle is empty	Refill the reagent bottle.	Operator
Feed hose line blocked or clamped off.	Check hose line connection between reagent bottle and vessel, connect properly as necessary. Open/remove hose clamp, if necessary.	Operator
Push valve is closed.	Open the push valve.	Operator
Valve(s) of the resterilisable feed line is/are closed.	Open valve **13.16.01** (vessel feed line) and valve **13.16.04** (reagent bottle feed line).	Operator
Pump does not operate properly.	Check operation using the rocker switch. Check the hose type and replace it, if necessary	Operator

12.8 Interferences Gassing System

Interference		
No gassing.		
Possible cause	**Remedy**	**By**
The on-site gas supply has been interrupted.	Stop the bioreactor. Check the on-site gas supply and switch it on, if necessary.	Operator
Depending on the configuration of the gassing system: The rotameter valve is not open. And/or: The *Flow* parameter(s) is/are not activated. And/or: Setpoint in the *Flow* parameter(s) = 0. Or: Parameter *GMFlow* = 0 and/or *GasMix* is/are not activated.	 Slowly open the rotameter needle valve. And/or: Activate the *Flow* parameter(s). And/or: Set the setpoint(s) in the *Flow* parameter(s) > 0. Or: Set parameter *GMFlow* > 0 and activate parameter G*asMix*.	Operator
Inlet air escapes via unused twist valves on the filters.	Close unused twist valves on the inlet air and exit gas filter.	Operator
Inlet air filter blocked.	Replace the inlet air filter under sterile conditions.	Operator

Interference		
The desired gas flow rate is not reached.		
Possible cause	**Remedy**	**By**
Inlet air or exit gas filter blocked.	Replace the filter under sterile conditions.	Operator
Wrong connection pressure of gas(es).	Check connection pressure of gas, adjust as necessary.	Operator

Interference		
Sudden increase in evaporation losses in the culture vessel.		
Possible cause	**Remedy**	**By**
The exit gas cooler does not cool.	Check the water supply to the exit gas cooler, restore it if necessary. Check and ensure that valve **01.06.06** is in automatic mode and activated: **Cooler** in main menu *Main* set to *AUTO* in green letters = *Exit gas cooler* set to ON in submenu *Valves*.	Operator

12.9 Behaviour in Case of Power Interruption

If the power supply to the device is interrupted during a running cultivation process (e.g. by turning off at the main switch or in case of a power failure), all parameter setpoints are stored.

After the power supply is restored, an interrupted cultivation process is automatically continued with the last stored setpoints. All other processes remain stopped.

The fact that a power interruption has occurred is indicated by the system alarm *Restart after power failure*. However, the duration of the event cannot be determined from the alarm.

12.10 Returning for Repair

The provider must return the device or the faulty component part(s) to the manufacturer if, after consulting the service department of the local dealer or the manufacturer, on-site diagnosis and/or repair is not possible.

INFORMATION

When returning the device, the component part or accessory for repair, it is required for the safety of all parties involved and because of legal provisions that a lawful declaration of decontamination is present. Refer to main chapter “Safety and Responsibility”, chapter “Declaration of Contamination” for details.

13 Disassembly and Disposal

The device must be disassembled and disposed of in an environmentally friendly manner if it is no longer in use.

INFORMATION

When returning the device for disassembly or disposal, it is required for the safety of all parties involved and because of legal provisions that a lawful declaration of decontamination is present. Refer to main chapter “Safety and Responsibility”, chapter “Declaration of Contamination” for details.

13.1 Disassembly

Prior to disassembly:

- Switch off the device and lock any isolation switch in the ‘off’ position.
- Physically disconnect the main energy supply from the device and wait for components to fully discharge.
- Remove and dispose of all additional consumable items, auxiliary components and/or spent processing material in an environmentally acceptable manner.

Clean and disassemble component parts professionally with regard to any local regulations concerning employment and environmental protection. If possible, separate materials.

13.2 Disposal

Recycle disassembled components if no agreement is made concerning reclaim or disposal.

- Send metals for scrap.
- Send plastic components for recycling.
- Sort and dispose of the remaining components according their material composition.

WARNING

Electronic waste, electronic components, lubricants or other auxiliary materials/supplies are subject to hazardous waste regulations and may only be disposed of by registered specialist disposal firms.

For disposal, the system units are to be disassembled and dismantled into individual material groups. These materials are to be disposed of according to the applicable national and local legislation.

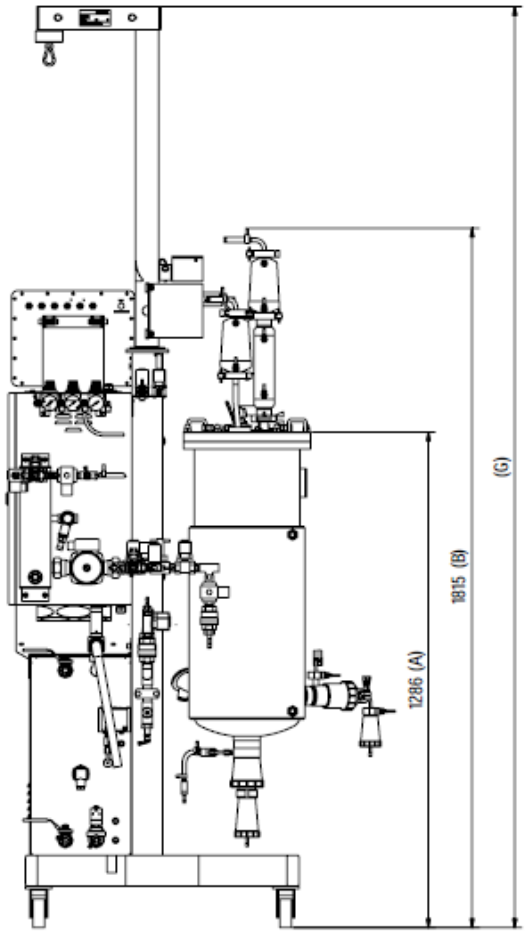
Local authorities or specialist disposal firms can provide information regarding environmentally acceptable disposal.

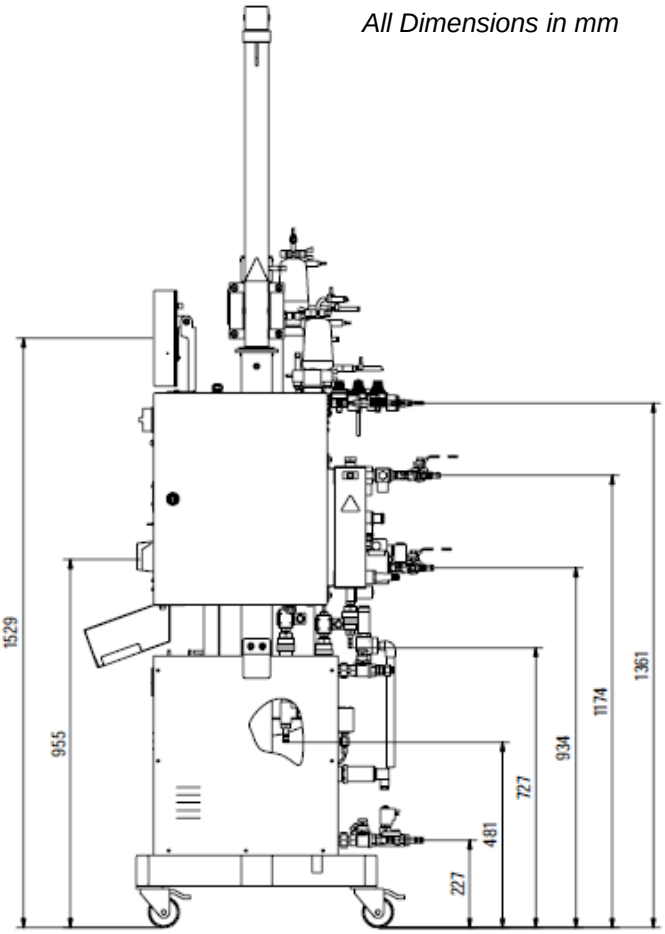
If no special arrangements have been made for return, INFORS HT units with the required declaration of decontamination can be sent back to the manufacturer for disposal.

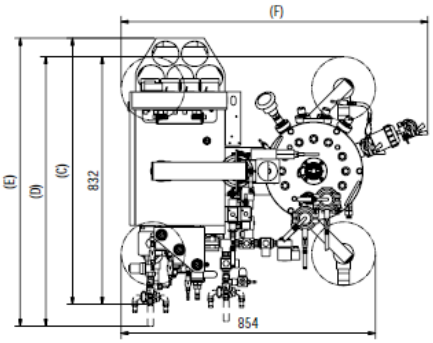
14 Technical Data

14.1 Dimensions

All Dimensions in mm





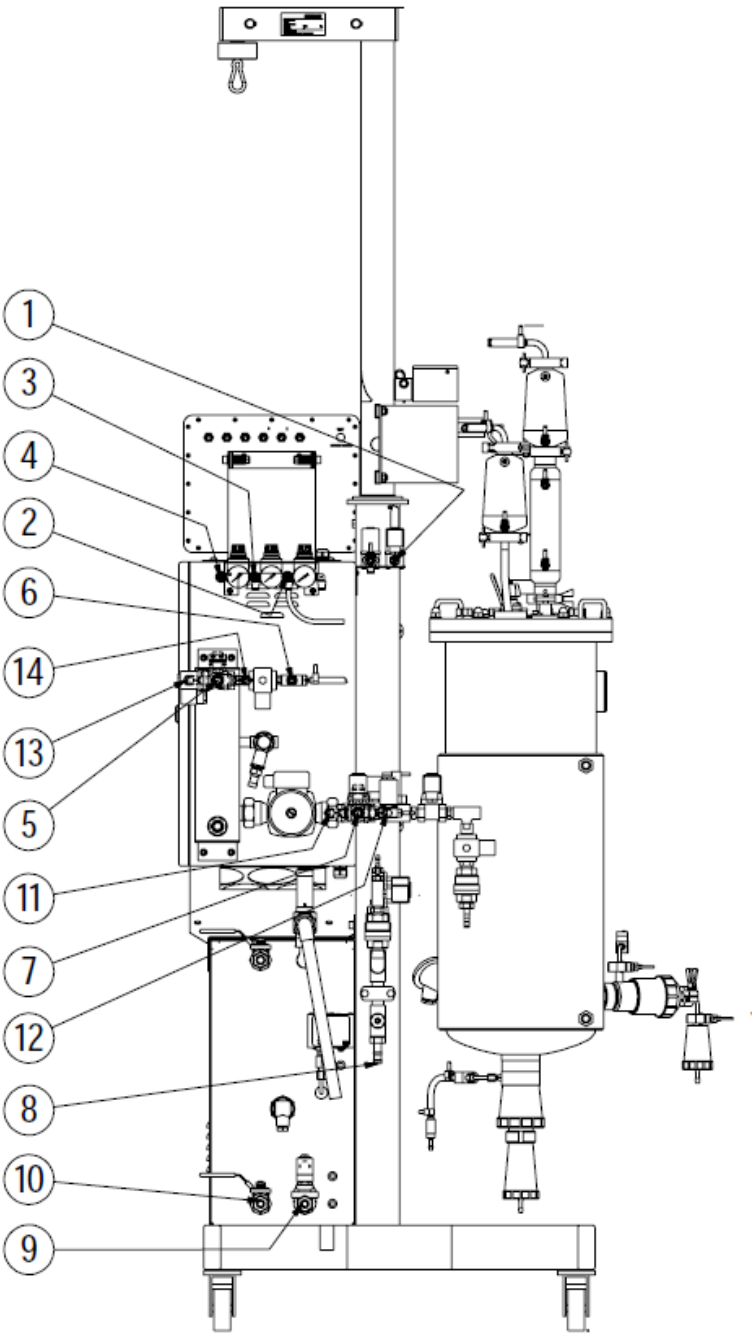


Dimensions with options	
Weight measurement	A = 1308 / B = 1838
Steam generator	C = 876
Switching tap water / chilled water	D = 872
Switching tap water / chilled water and steam generator	E = 934
Sample valve	F = 1017
Lifting device for vessel top plate	G = 2391

14.2 Connections

14.2.1 Overview

1 Exit gas
2 N_2 In
3 O_2 In
4 Air In
5 Tap water Out
6 Clean steam In
7 Tap water In
8 Condensate (contaminated) Out
9 Water In steam generator (option)
10 Water Out steam generator (option)
11 Tap water In (option)
12 Chilled water In (option)
13 Tap water Out (option)
14 Chilled water Out (option)



14.2.2 Connection Values

Pos.	Connection	Connection type	Connection value
1	Exit gas	Hose nozzle DN13	(no backpressure)
2	N_2 In	Hose nozzle DN8	3.0 to 6.0 bar
3	O_2 In	Hose nozzle DN8	3.0 to 6.0 bar
4	Air In	Hose nozzle DN8	3.0 to 6.0 bar
5	Tap water Out	Hose nozzle DN13	(no backpressure)
6	Clean steam In	Hose nozzle DN13	2.0 ± 0.2 bar
7	Tap water In	Hose nozzle DN13	2.0 ± 0.5 bar
8	Condensate (contaminated) Out	Hose nozzle DN13	(no backpressure)
9	Water In steam generator (option)	Hose nozzle DN6	2 ± 0.2 bar
10	Water Out steam generator (option)	Hose nozzle DN13	min. 3.0 bar
11	Tap water In (option)	Hose nozzle DN13	Not connected
12	Chilled water In (option)	Hose nozzle DN13	2 ± 0.5 bar
13	Tap water Out (option)	Hose nozzle DN13	2 ± 0.5 bar
14	Chilled water Out (option)	Hose nozzle DN13	(no backpressure)

Electrical connection values bioreactor				
Model	**Voltage**	**Frequency range**	**Max. current**	**Leakage current**
230 V / 50 Hz	230 V (± 5 %); 1 phase L1 + N (neutral) + PE (earth)	50 Hz	16 A	> 3.5 mA
200 to 230 V / 60 Hz	230 V (± 5 %); 1 phase L1 + N (neutral) + PE (earth)	60 Hz	16 A	> 3.5 mA

Electrical connection values steam generator (option)				
Type	**Voltage**	**Frequency range**	**Max. current**	**Connector**
6 kW	400 V (± 5 %); 3 phases L1 + L2 + L3 + N (neutral) + PE (earth)	50 / 60 Hz	14 A	CEE16/5
10 kW	400 V (± 5 %); 3 phases L1 + L2 + L3 + N (neutral) + PE (earth)	50 / 60 Hz	25 A	CEE32/5

14.3 Specifications

14.3.1 Instrumentation Cabinet

Description	Value	
Dimensions	W = 320 mm D = 450 mm H = 550 mm	
Protection class	IP43	
Material	1.4301	
Peristaltic pumps	Standard	*Acid*, *Base*, *Antifoam*, digital *Feed, analogue*
	Option	*Feed 2, Feed 3*

14.3.2 Operating Panel

Description	Value
HMI	Colour touch screen 12"
Protection	IP 66

14.3.3 Vessel

Vessel sizes

Total volume (TV)	Working volume (WV)		Total volume vessel jacket
	Max.	Min.	
15 L	10 L	3.0 L	1.3 L
30 L	20 L	5.3 L	2.0 L
42 L	30 L	6.0 L	3.1 L

Dimensions

Vessel TV	Height [1)]	Innner-Ø	Ratio H/D
15 L	508 mm	200 mm	2.5 : 1
30 L	646 mm	250 mm	2.5 : 1
42 L	761 mm	267 mm	2.9 : 1

1) *Without top plate and harvest/sample valve*

Technical Data

All vessel sizes	
Temperature range	Vessel inside: -10 up to +150 °C Vessel jacket: -10 up to +150 °C
Pressure range	Vessel inside: -1 up to +3 bar Vessel jacket: -1 up to +3 bar
Permitted load changes	Vessel: 12860 Vessel jacket: 85289
Material in contact with media	stainless steel 1.4404 or 1.4435 = AISI 316L with finish Ra ≤ 0.6 µm, electropolished
Material not in contact with media	stainless steel 1.4301 = AISI 304 with finish Ra ≤ 1.0 µm, electropolished
Accessories	Sight glass (115 x 15 mm) vessel identification plate 4 baffles, removable ring sparger

Ports and Ingold nozzle

Port vessel top plate	15 L TV	30 L TV	42 L TV
Tri-Clamp ISO DN25/1, connection-Ø = 50.5 mm (Exit gas)	1	1	1
Tri-Clamp ISO DN08, connection-Ø = 50.5 mm (Inlet air/gas)	1	1	1
Ø 19 mm (Rd28x1/8")	8	8	9
Ø 10 mm (for temperature sensor)	1	1	--
Ingold nozzle	**15 LTV**	**30 L TV**	**42 L TV**
Ø 25 mm, angled (15°)	2	3	4
Ø 25 mm, horizontal	1	1	1

Harvest/sample valve 05.12.01

Inner-Ø	15 L TV	30 L TV	42 L TV
Harvest	8 mm	8 mm	25 mm
Sampling	8 mm	8 mm	4 mm

14.3.4 Temperature

Description		Value	
Heating		Electrical or steam heating [1]	
Cooling	Standard	Tap water / cooling water system (on site)	
	Option	Switching from tap water to chilled water via 3-way ball valves	
		Separate chiller	
Sterilisation		Automatic with (clean) steam [1]	
Sensor, Pt-100		15 L TV vessel 30 L TV vessel	class B, 1/3 DIN
		42 L TV vessel	class A, 1/3 DIN
Temperature range		Sterilisation	110 °C to 125 °C
		Cultivation [2]	20 °C to 79 °C
Accuracy temperature measurement and control (cultivation)		± 0.3 °C at ≤ 60 °C ± 0.5 °C at > 60 °C	

[1] *Either via house steam supply or optional integrated steam generator.*

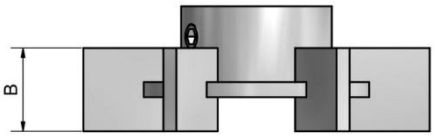
[2] *Min. temperature depends on ambient temperature, used cooling system, stirrer rotation speed and medium viscosity.*

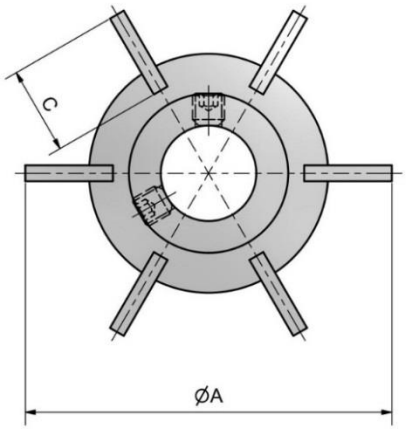
14.3.5 Stirrer

Description	Value	
Drive	Top drive, with single mechanical seal	
Direction of rotation of drive shaft	Clockwise (top view)	
Motor type	AC servomotor, brushless	
Range of rotation speed [1]	15 L TV vessel 30 + 42 L TV vessel	20 to 1500 min^{-1} 20 to 1200 min^{-1}
Accuracy control	± 5 min^{-1} at 20 to 1000 min^{-1} 1 % setpoint at > 1000 min^{-1}	

[1] *Valid for liquid with viscosity similar to water, without gassing, with 2, respectively 3 Rushton impellers*

Technical Data





Impellers

Type	Material		
Rushton with 6 blades	316L, electropolished, Ra 0.8 µm		
Number	**Dimensions**		
	A	**B**	**C**
15 L TV vessel / 2 pieces	66 mm	13 mm	16 mm
30 L TV vessel / 3 pieces	80 mm	16 mm	20 mm
42 L TV vessel / 3 pieces	89 mm	18 mm	23 mm

14.3.6 Gassing

All vessel sizes and gassing variants		
Gas entry	Ring sparger	
Specific gassing rate	Calculated for max. working volume	2 min^{-1}
Filter	Type	Novasip, steam sterilisable
	Model	C3PFRP1A
	Max. pressure	6.5 bar
	Max. temp.	142 °C
	Retention rate	0.2 µm
	Manufacturer	PALL
Mass flow controller (MFC)	thermic	Red-y-smart series, “High Performance”
	Manufacturer	Vögtlin Instruments
Steam trap	Themostatic capsule steam trap	

Variant Basic

Gas(es)	Manual gas flow control	Accuracy rotameter	Gas mix control
Air	1 rotameter	± 4 % FS	----
Air + O_2	1 rotameter		2 solenoid valves
Air + N_2	1 rotameter		2 solenoid valves
Air + O_2 + N_2	1 rotameter		3 solenoid valves

Variant Standard

Gas(es)	Gas flow control	Accuracy MFC	Gas mix control
Air	1 MFC	± 2.0 % FS	----
Air + O_2	1 MFC		2 solenoid valves
Air + N_2	1 MFC		2 solenoid valves
Air + O_2 + N_2	1 MFC		3 solenoid valves

Variant High End

Gas	Gas flow control	Accuracy MFC
Air	1 MFC	± 2.0 % FS
Gases	**Gas flow control and gas mix control**	
Air + O_2	2 MFC	
Air + N_2	2 MFC	
Air + O_2 + N_2	3 MFC	

Measurement ranges MFCs [1] and rotameters

Vessel Max. WV [2] (Litres)	Measurement range rotameter L min^{-1} (Variant Basic)	Measurement range MFC L min^{-1} (Variants Standard and High End)
10.0	0.20 to 20.0	0.20 to 20.0
20.0	0.40 to 40.0	0.40 to 40.0
30.0	0.60 to 60.0	0.60 to 60.0

1) *Mass flow controller*

2) *Working volume*

INFORMATION

The mass flow controllers are calibrated by their manufacturer ex works at standard conditions, i.e. at 1.013 bar and 20 °C. Therefore, for every gas flow rate the gas volume flow is given in L min^{-1} .

14.3.7 Exit Gas

Description	Value
Outlet	Via exit gas cooler and exit gas filter into atmosphere
Exit gas cooler	Material: Stainless steel
Filter	Manufacturer: Pall Type: Novasip, steam sterilisable Model: C3PFRP1A Max. pressure: 6.5 bar Max. temperature: +142 °C Retention rate: 0.2 µm
Steam trap	Type: balanced pressure thermostatic steam trap Material: stainless steel

Detailed information about the filter body & element can be found in the separate documentation from the manufacturer PALL.

14.3.8 pH

Description	Value
Control	Peristaltic pumps *Acid* and *Base*
Control range	pH 2 to 12
Measurement accuracy	pH ± 0.1

Variants of measurement systems

Measurement system analogue		
With traditional pH sensor (potential measurement against reference)		
Variant METTLER	Sensor type	405-DPAS-SC-K8S/120
	Manufacturer	METTLER TOLEDO
	Measurement range	pH 2 to 12

Measurement systems digital		
With traditional pH sensor (potential measurement against reference) with integrated electronics		
Variant HAMILTON	Sensor type	Easyferm Plus ARC
	Manufacturer	HAMILTON
	Measurement range	pH 0 to 14
Variant METTLER	Sensor type	InPro 3253i, ISM
	Manufacturer	METTLER TOLEDO
	Measurement range	pH 0 to 14

INFORMATION

pH sensors type Easyferm Plus ARC are preconfigured by the device manufacturer INFORS HT. Replacement sensors must be configured before use.

Details about technical data, use and maintenance of the pH sensors are in the separate documentation from the sensor manufacturers.

14.3.9 pO_2

Description	Value
Control	Cascaded stirrer Cascaded flow Cascaded gasmix Cascaded O_2 addition *The functionality of the parameters depends on the hardware configuration of the device.*
Control range	0 to 100 %
Measurement accuracy	1 % FS

Variants of measurement systems

Measurement system analogue		
With traditional amperometric/polarographic pO_2 sensor		
Variant METTLER	Sensor type	InPro 6820/25/080
	Manufacturer	METTLER TOLEDO
	Measurement range	0 to 150 %
Measurement systems digital		
With pO_2 sensor with integrated optical electronics		
Variant HAMILTON	Sensor type	Visiferm DO ARC
	Manufacturer	HAMILTON
	Measurement range	0.05 % to 300 % air saturation
Variant METTLER	Sensor type	InPro6860i, ISM
	Manufacturer	METTLER TOLEDO
	Measurement range	0.05 % to 300 % air saturation

INFORMATION

Digital pO_2 sensors are pre-configured from the device manufacturer INFORS HT. Replaced sensors must be configured again before use!

Details about technical data, use and maintenance of the pO_2 sensors are in the separate documentation from the sensor manufacturers.

14.3.10 Antifoam

Description	Value
Sensor	Conductive with dosing needle, adjustable mounting depth
Control	Peristaltic pump *Antifoam*
Range	0 / 100 % (OFF/ON)

14.3.11 Pumps

Description	Value	
Type	Peristaltic	
Digital	3 pieces	*Acid* *Base* *Antifoam*
Analogue	1 piece	*Feed*
Rotation speed	Digital	150 min^{-1} / fixed rotation speed
	Analogue	150 min^{-1} / max. rotation speed, adjustable in steps of 0.1 % within range of 0 % to 100 %
Accuracy	± 5 min^{-1}	

Pump hose	
Inner diameter	3.2 mm
Wall	1.6 mm
Material	Bioprene

14.3.12 Pressure Indication Vessel

Description	Value
Type	Manometer (**08.30.01**)
Connection	19 mm port in vessel top plate
Range	0 to 4.0 bar
O-ring	EPDM

14.3.13 Safety Valves

Description	Value
Safety valve vessel	Clean-Service spring safety valve Set pressure: 3 barg
Safety valve temperature control circuit	Standard safety valve, angle type, spring-loaded Set pressure: 3 barg

14.4 Operating Conditions

Description	Value
Ambient temperature	5 °C to 35 °C
Relative air humidity, non-condensing	20 % to 90 %
Altitude operating location	Max. 2000 m.a.s.l
Pollution degree, according to EN 61010-1	2
Min. distance from walls, ceilings [1)] and other appliances	150 mm

1) *The distance from the ceiling must be chosen in such a way that the vessel top plate including its built-in parts can easily be lifted from the vessel.*

14.5 Operating Materials

Application	Permitted products
Lubricant for the single mechanical seal	Medicinal Glycerine 85 % Quality: PhEur

14.6 Emissions

Description	Value	Units
Noise emission	<70	dB (A)