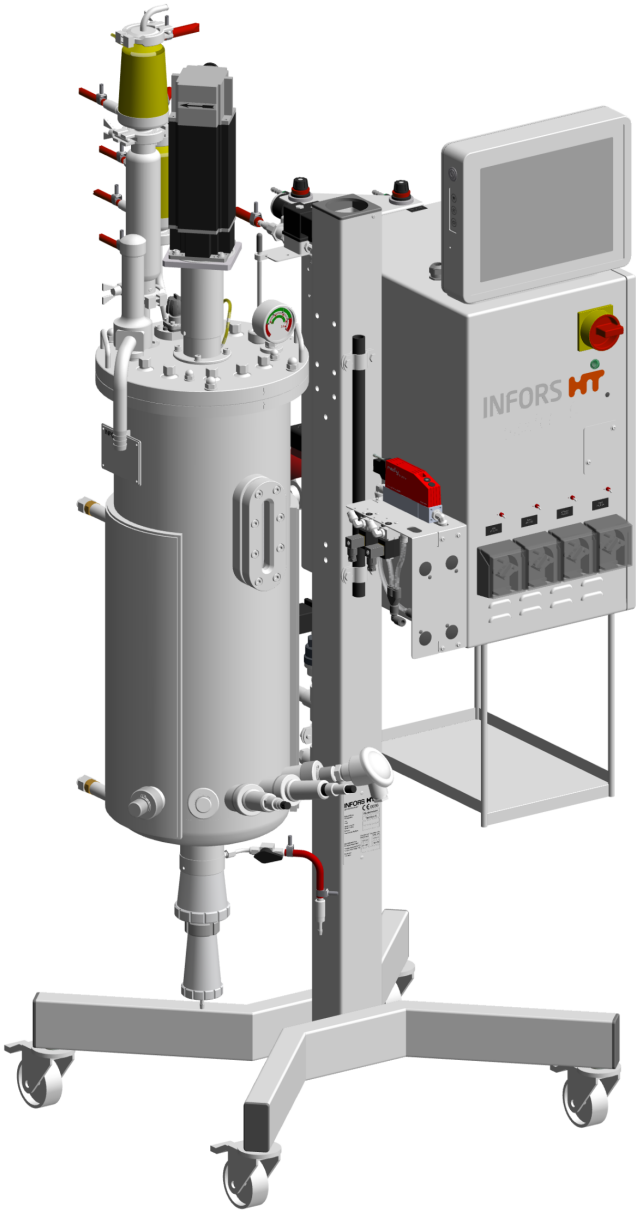
Techfors-S

Operating manual



We bring life to your laboratory.

INFORS HT

Techfors-S – Rel. 2.0
Pilot scale bioreactor
SW: 3.5

Doc-ID: D011, 1, en_GB – Original
Art. 79258

More information about the product is available online at:
http://www.infors-ht.com/en/techfors-s

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Supplemental directives

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 and the latest technological developments.

This operating manual is a component part of the device. It must be kept near the device unit and be accessible to staff at all times. All persons working on or with the device must read the operating manual thoroughly and fully understand its contents before beginning any work. Adhering to all the safety notes 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.

Customer Service and Services

The customer service of the manufacturer or the local licensed dealer is at your disposal for technical advice and specialist enquiries (contact details see ➦ https://www.infors-ht.com/en/contact/). Due to their familiarity with the potential applications of the device, the Customer Service team is able to provide information on whether the unit can be used for a specific application or modified to handle the planned process.

Declaration of Conformity

The device meets the general requirements of the following standards:

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

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

Table of contents

Table of contents

Table of contents

Table of contents

Table of contents

Table of contents

Table of contents

Table of contents

Table of contents

Table of contents

Table of contents

1 Safety and Responsibility

This chapter contains general information on safety when using the device. In the remaining chapters, warning messages are used only to highlight particular hazards directly arising from the actions being described.

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

This chapter 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.

1.1 Explanation of Special Displays

1.1.1 Warning Messages

Warning messages in this manual are indicated by a colored 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 fatal injuries if not avoided.

CAUTION

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

NOTICE

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

1.1.2 Other Messages

Texts that are marked in this way provide useful tips and recommendations for ensuring efficient, fault-free operation of the device.

1.2 Intended Use, Incorrect Use and Misuse

Intended Use

The pilot scale bioreactor Techfors-S that can be sterilized in situ has been specially developed for the cultivation of microorganisms for research and development in a biotechnology laboratory and exclusively for the use of fluids of group 2 according to Article 13 of the Pressure Equipment Directive 2014/68/EU.

⚠ WARNING

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

Each instance of non-conventional use of the device is considered incorrect use and may lead to dangerous situations.

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

- The installation site
- Personnel qualifications
- Correct operation and maintenance
- The use of undamaged reagent bottles and hoses

Incorrect Use/Misuse

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

Any use of the device outside the scope of the intended use as described above will 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.

To use the device for special applications not covered by conventional, intended use, the manufacturer must configure and certify the device accordingly.

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

1.3 Qualified Personnel

1.3.1 Operator

The operator operates the device in the context of the intended use. Only persons who have been trained for working in a biotechnology laboratory can be considered for the role of operator. These include, for example:

- Process technicians in the fields of biotechnology and chemistry
- Biotechnologists (biotechnicians)
- Chemists with a specialization 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

To be allowed to operate the device, the operator 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.

Persons 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.

1.3.2 Technician

The technician is an individual who, by virtue of their relevant professional education, training and/or experience, is competent to identify risks and prevent hazards arising from the use of the device. The technician is familiar with the environment in which they are operating and knows the relevant standards and regulations.

Technicians include, for example, the following groups of people:

- Qualified electricians
- Decontamination specialists
- Disassembly, disposal and recycling specialists

1.3.3 INFORS HT Service Technician or Licensed Dealer

Certain work may only be performed by the manufacturer's skilled personnel or by skilled personnel authorized by a licensed dealer. Other persons are not authorized to perform this work.

1.4 Unauthorized Persons

The term “unauthorized 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.

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

1.5 Responsibility of the Provider

Provider

The term “provider” applies to all persons who are responsible for making the device and the necessary infrastructure available. The provider bears a special level of responsibility with regard to the processes and the qualification and safety of the operators.

Provider Obligations

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 devices are fully functional and not disabled.
- The provider must ensure that the device is only operated by qualified personnel, and that said personnel receive sufficient training.
- The provider must ensure that the protective equipment required for working with the device is available and worn.
- The provider must ensure that this operating manual remains in the immediate vicinity of the device throughout its entire term of use.

1.6 Residual Risks

This chapter residual risks that are always present when using the device in accordance with normal, intended use.

Electric Current

The device is operated electronically. 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:

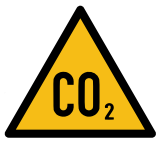
- In case of damage to insulation, disconnect the device from the power supply immediately and arrange for it to be repaired.
- Disconnect the device from the power supply before commencing any work on the electrical components.
- Always use qualified electricians for any work on the electrical components.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

Hot Surfaces

Vessels, piping and motor can get hot during operation. There is a risk of burns if you come into contact with hot surfaces.

- Avoid contact with hot surfaces.
- Always use appropriate protection for applications with high temperatures.

Dangerous Gases



The use or production of dangerous – i.e. toxic or asphyxiant – gases entails a significant health risk, especially in small rooms. 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 using dangerous gases are initiated.
- Check the seals on the device at regular intervals and replace them if necessary.
- Check gas-carrying hoses for leaks at regular intervals.
- Safely discharge exit gases.

Flammable or Explosive Substances

The use or production of flammable or explosive substances does not fall under the intended use, as the device is not explosion-proof. If the provider intends to use the device for such applications, it is essential to check the suitability of the device with the relevant local authorities.

There is a risk of explosions when using impure process gases: you must therefore only use process gases without impurities.

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 personnel.

- Safely discharge contaminated condensate.
- Check liquid-carrying hoses for leaks at regular intervals.
- When using or producing corrosive or toxic substances, use appropriate protection.
- Comply with internal safety regulations when handling corrosive and toxic substances.

Bioactive or Pathogenic Organisms

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

- Safely discharge condensate.
- Follow internal safety regulations when handling bioactive substances, pathogenic organisms or genetically modified cultures.

Excess Pressure or Vacuum

The vessel may be pressurized. Incorrect manipulation or exceeding the permissible working pressure can cause built-in-parts to be flung away. This can result in liquids and gases being expelled at high pressure.

- Observe the working pressure specified on the vessel identification plate.
- Observe the specified inlet pressures. The factory-set pressures of the pressure reducing valves preset must not be changed.
- Never operate the devices without having a safety valve installed.
- Prior to each manipulation of built-in-parts and the vessel top plate, make sure that the vessel depressurized.
- Prior to working on pressurized components ensure that the system is depressurized.
- Before use, ensure that the built-in-parts und pressurized components are mounted correctly.
- Check pressurized lines and connections for leaks at regular intervals.

Steam or Hot Liquid

Escaping steam or hot liquids can lead to severed scalding and burns.

- Check all steam-carrying components for damage and correct seating before each use.
- Safely discharge tap water and condensate.

Environmental Hazards

Inappropriate handling of environmentally hazardous substances, especially where disposal is involved, may lead to severe environmental damage.

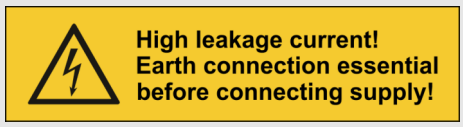
- Contaminated liquids must be disposed of in an environmentally suitable way.

Accessories and Spare Parts

Incorrect spare parts, imitations or spare parts that have not been authorized by the manufacturer and unauthorized accessories represent a significant safety risk. As such, we recommend procuring all spare parts and accessories from a licensed dealer or directly from the manufacturer.

1.7 Warning Symbols on the Device

The following warning symbols (stickers) are placed on the device:

Warning symbol	Position	Meaning
	On the instrumentation cabinet	Danger due to high leakage current. Before connecting to the supply circuit, a ground connection must be established.
	On the instrumentation cabinet	Danger due to electrical voltage. Turn off the device and pull out the power plug before opening the housing of the device.
	▪ Vessel ▪ Heating element (temperature control system)	Caution, there is a risk of severe burns due to hot surfaces.

WARNING

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

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

1.8 Declaration of Decontamination

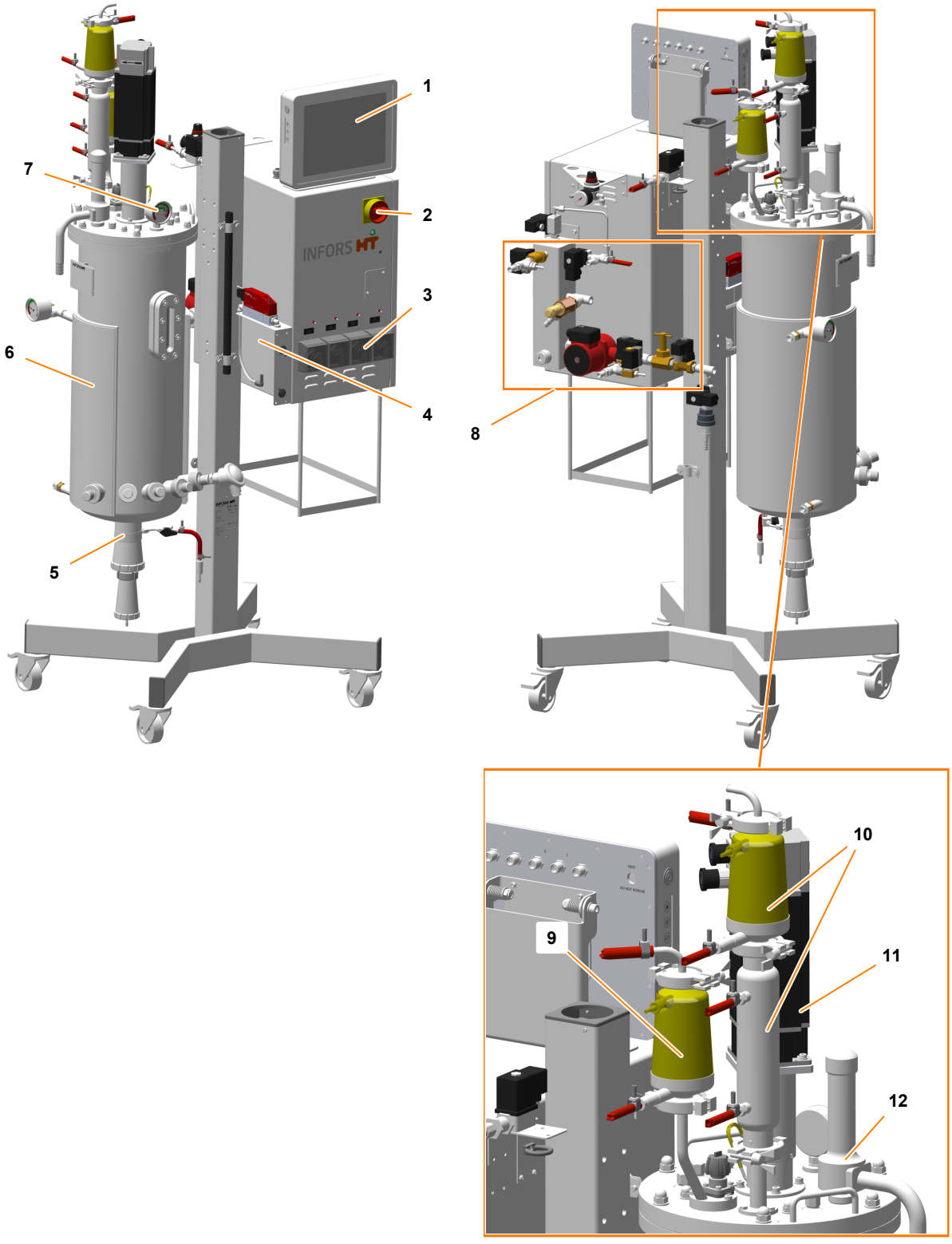
When returning the device for repair, disassembly or disposal, a legally compliant declaration of decontamination is required for the safety of all involved and due to legal requirements. The following must be observed if this is the case:

- The device, component or accessory which is to be repaired must be entirely decontaminated before being sent 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.

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).

2 Basic Unit

2.1 Overview Basic Unit

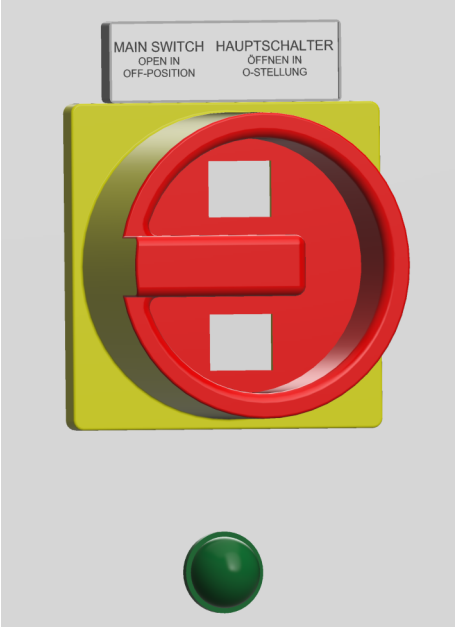


Basic Unit

Pos.	Designation	Additional Information
1	Operating panel	➦ Chapter 2.2.2, page 25
2	Main switch	➦ Chapter 2.2.1, page 25
3	Pumps	➦ Chapter 2.3.1, page 28
4	Gassing system	➦ Chapter 2.9.1, page 59
5	Harvest/sample valve (bottom valve)	➦ Chapter 2.5.1, page 42
6	Vessel	➦ Chapter 2.4.1, page 31
7	Vessel pressure display (manometer)	➦ Chapter 2.6.1, page 48
8	Temperature control system	➦ Chapter 2.8.1, page 55
9	Inlet air filter (gassing system)	➦ Chapter 2.9.1, page 59
10	Exit gas filter and exit gas cooler (exit gas system)	➦ Chapter 2.10.1, page 64
11	Motor (stirrer)	➦ Chapter 2.7.1, page 49
12	Safety valve	➦ Chapter 2.14.1, page 81
n/a	pH sensor (not shown) for pH control	➦ Chapter 2.11.1, page 70
n/a	pO_2 sensor (not shown) for pO_2 control	➦ Chapter 2.12.1, page 73
n/a	Antifoam sensor (not shown) for antifoam control	➦ Chapter 2.13.1, page 77

2.2 Operating and Display Elements

2.2.1 Main Switch



The main switch is located on the top right-hand corner on the front of the instrumentation cabinet.

- To switch on the device, turn the main switch clockwise (90 degrees) into position *I/ON*.

  The green power indicator light underneath the main switch lights up. The device is switched on and in idle state.
- To switch on the device, turn the main switch counter-clockwise (90 degrees) into position *0/OFF*.

  The green power indicator light switches off. The device is cut off from the power supply. Only the main power supply terminal is powered.

If necessary, for maintenance purposes, secure the main switch against being switched on again by attaching a lock (not included in the scope of delivery) and also disconnect the power plug.

NOTICE

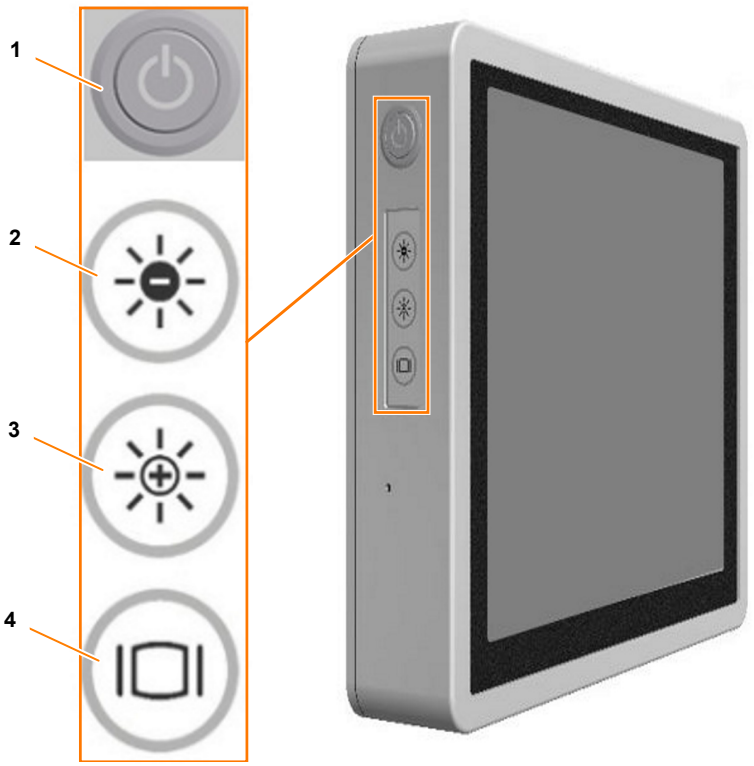
Switching off via the main switch without first stopping the running process and/or shutting down the system at the operating panel can result in damage to the operating panel!

2.2.2 Operating Panel

The operating panel is attached to a holder mounted on the top of the instrumentation cabinet. It has a 12" color touch screen with protection type IP66. The operating panel is switched on using the main switch.

Basic Unit

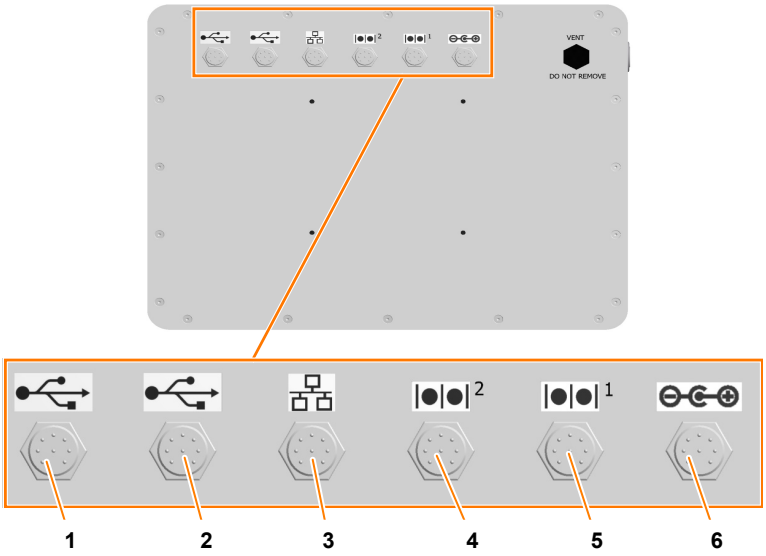
Monitor Buttons on the Operating Panel



1 **ON/OFF** key
2 **DARK** key: setting the screen illumination to darker
3 **LIGHT** key: setting the screen illumination to brighter
4 **DISPLAY** key: switching the screen on or off

The **ON/OFF** key lights up when the operating panel is switched on. Since switching on/off takes place via the main switch, there is no need for separate switching on/off via the **ON/OFF** key. Switching off via the **ON/OFF** key while a process is running has the same effect as a power failure.

Operating Panel Connections

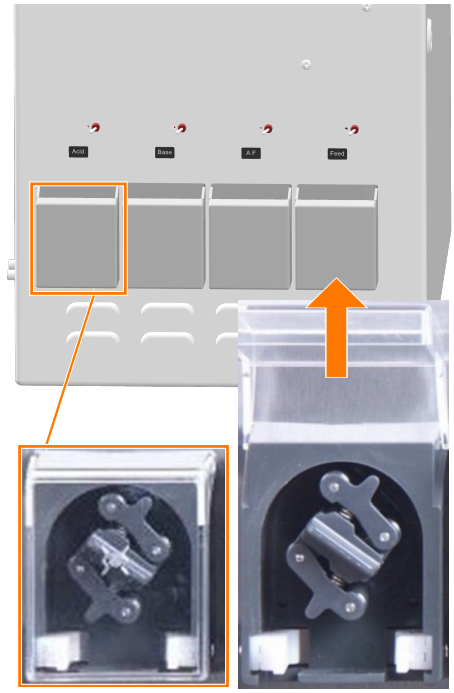


1 USB2.0 x 2: for backups and service purposes
2 USB2.0 x 2: reserve
3 Ethernet
4 COM2: reserve
5 COM1: port for display cable
6 DC: port for power supply cable

2.3 Pumps

2.3.1 Setup and Function

Function

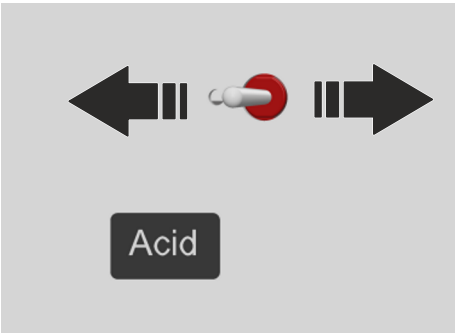


By default, the lower part of the instrumentation cabinet features four peristaltic pumps with hinged cover. The pumps are driven by stepper motors and run clockwise in automatic operation. The pumps are labelled from left to right according to their function:

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

Two additional feed pumps can be integrated optionally.

Operation



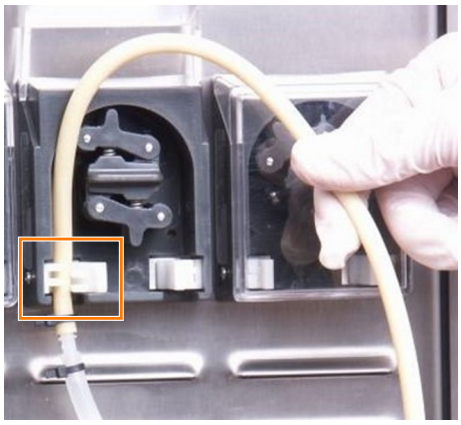
The pumps can also be operated manually via the rocker switches located above the pump heads when the device is switched on:

- Flick the rocker switch to the right: the pump runs clockwise.
- Flick the rocker switch to the left: the pump runs counter-clockwise.

2.3.2 Inserting the Pump Hoses

To insert the pump hoses, proceed as follows:

1. Lift up the pump cover on the instrumentation cabinet.
2. Press the left white clamp inwards and at the same time insert the pump hose according to the direction of pump rotation (clockwise).



3. Release the clamp.

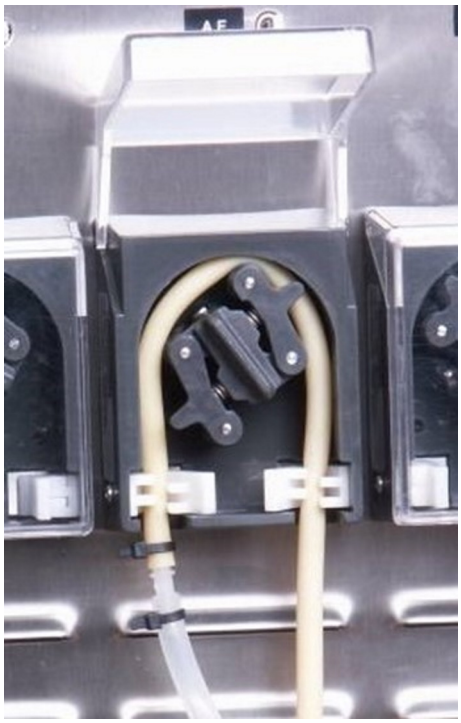
➡ The pump hose is now secured by the left clamp.

4. Thread the pump hose around the pump head and push in gently.

5. Slowly turn the pump head clockwise with one hand and support the pump hose guide with the other hand.

> **CAUTION**
>
> Danger of pinching fingers!
>
> If the pump is operated electrically (rocker switch) when the pump hose is inserted, this can lead to pinched fingers and damage to the pump hose.
>
> Always turn the pump head by hand when inserting the pump hose.

6. Press the white right-hand clamp inwards and insert the pump hose at the same time.



7. Release the clamp.

   ➡ The pump hose is inserted and is secured by the two clamps.

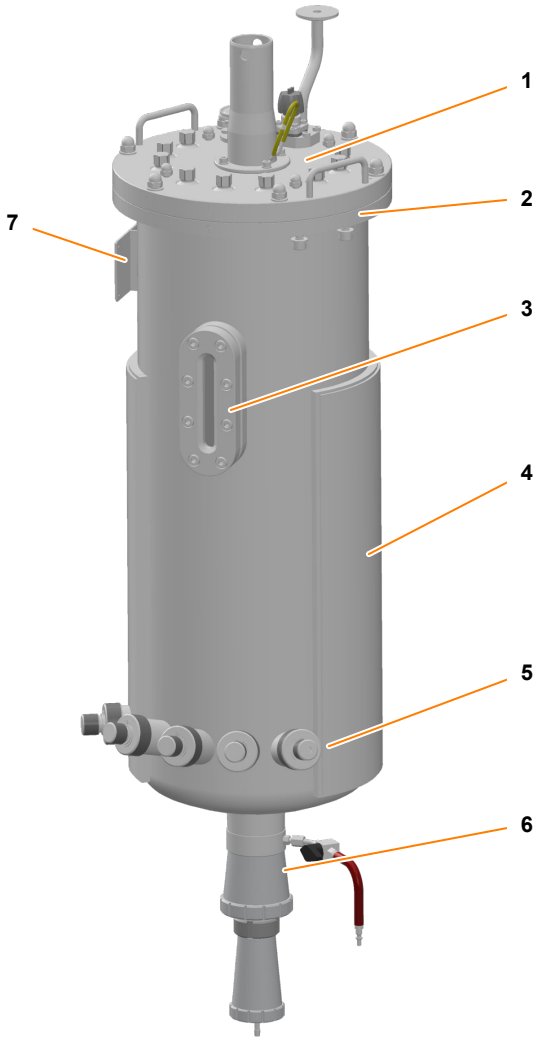
8. Fold down the pump cover.

9. Fill the hoses manually or via the touch screen software.

2.4 Vessel

2.4.1 Setup and Function

Overview

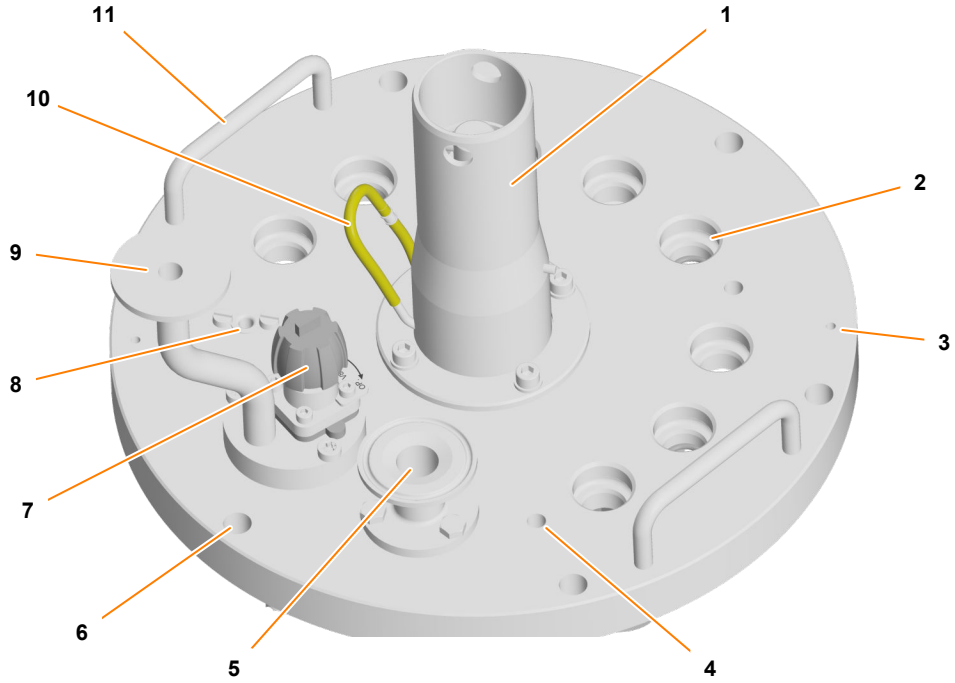


1 Vessel top plate
2 Vessel flange with six stud bolts
3 Sight glass (center of the sight glass = working volume)
4 Vessel jacket
5 Ingold nozzles
6 Harvest/sample valve (bottom valve) (➥ Chapter 2.5.1, page 42)
7 Vessel identification plate (➥ Chapter 2.15.3, page 86)

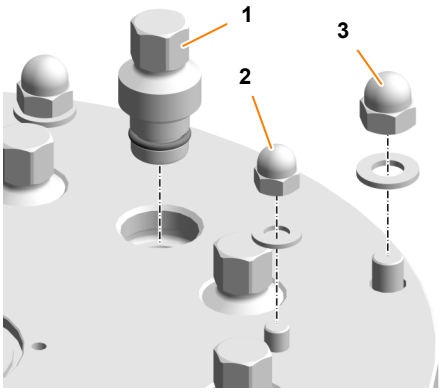
The pilot scale bioreactor Techfors-S is available in three vessel sizes: 15, 30 and 42 liter total volume. The only difference between the vessels is the number ports and the type of harvest/sample valve (bottom valve). The standard features of the three vessel sizes are described in the following sections.

Basic Unit

Vessel Top Plate

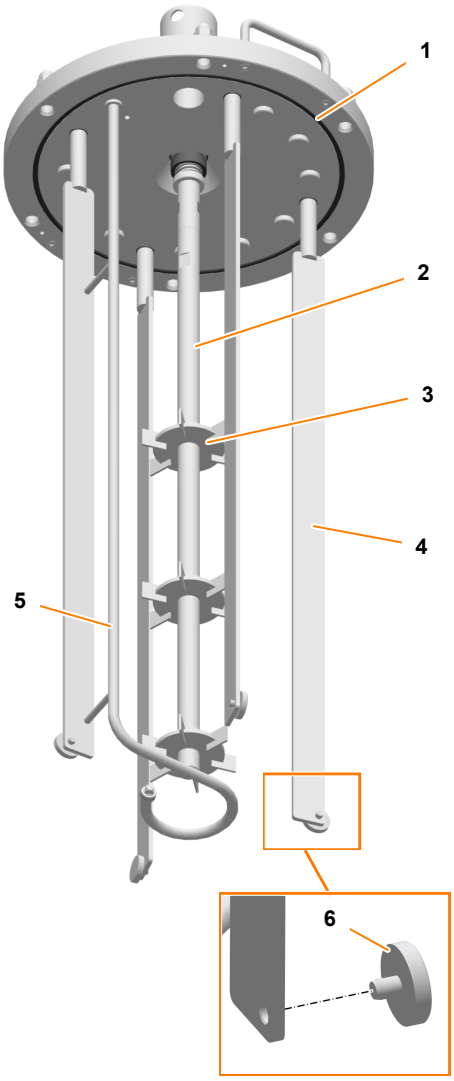


1 Drive hub for motor
2 19 mm port (8 or 9 x) for built-in-parts/accessories
3 4 mm bore hole (2 x) for ground connection of antifoam sensor
4 Bore hole (4 x) for baffles
5 Connection flange (Tri-Clamp) exit gas
6 Bore hole (6 x) for affixing the vessel top plate
7 Valve *02.16.01*
8 10 mm port with immersion pocket for the temperature sensor (Pt100) (only 15 L TV and 30 L TV)
9 Connection flange (Tri-Clamp) inlet air
10 Connection nozzle and silicone hose for lubricating the mechanical seal
11 Handle (2 x)



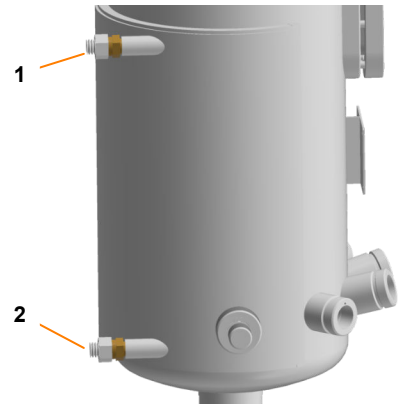
The vessel top plate is also equipped with the following components:

1 Blanking plug with O-rings for 19 mm ports (8 or 9 x)
2 M8 cap nuts (4 x) with washers for affixing the baffles
3 M10 cap nuts (6 x) with washers for affixing the top plate



1 O-ring (top plate seal)
2 Stirrer shaft
3 Rushton impeller (2 or 3 x)
4 Baffles (4 x)
5 Ring sparger
6 Spacer, demountable (4 x)

Vessel Jacket



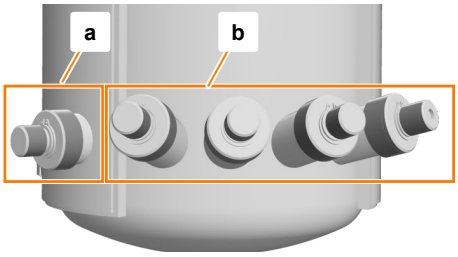
1 Water outlet
2 Water inlet

The temperature of the medium in the vessel is controlled by the water circulating in the vessel jacket. Depending on the chosen temperature control system, the water is heated electrically or with steam. (For details, see ➦ Chapter 2.8.1 'Temperature Control System and Sterilization' on page 55)

The pressure hoses for the water inlet and water outlet of the vessel jacket are connected ex-factory.

Basic Unit

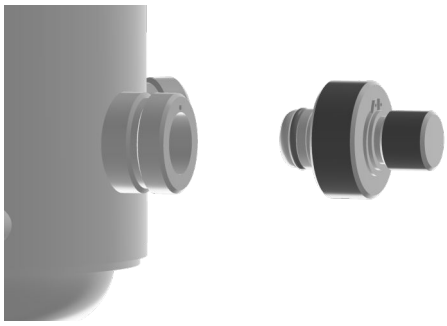
Ingold Nozzles



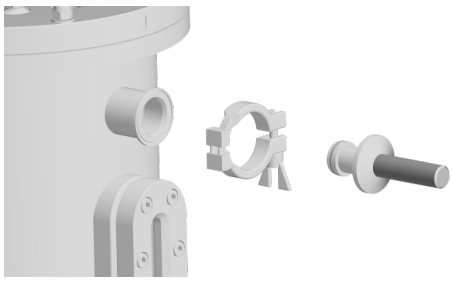
The Ingold nozzles are easily accessible on the bottom of the front of the vessel. The number of Ingold nozzles varies depending on the size of the vessel, see table.

Vessel TV (Total volume)	Number of Ingold nozzles iD = 25 mm, G G1-1/4"	
	straight (a)	angled, 15° (b)
15 L	1	2
30 L	1	3
42 L (figure)	1	4

The angled Ingold nozzles are, by default, intended for the pH and pO_2 sensors and, for the 42 liter vessel, also for the temperature sensor. The straight Ingold nozzle is used as backup or for the (optional) sample valve *17.13.01*.



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



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

2.4.2 Removing and Mounting the Vessel Top Plate

General Information

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

An optional lifting device for lifting and lowering the vessel top plate is available from the device manufacturer (for details, see ➦ Chapter 3.7 'Lifting Device for Vessel Top Plate' on page 96). We recommend using the lifting device due to the weight of the vessel top plate. The following section describes the procedure without lifting device. Mounting, 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!

Removing the Vessel Top Plate

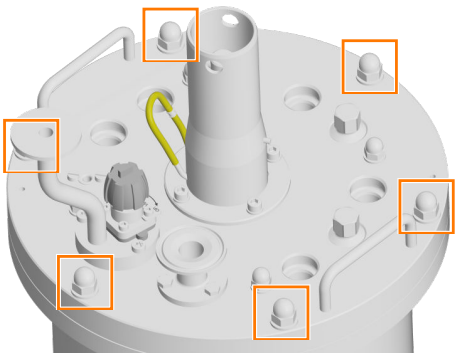
Before removing the vessel top plate, ensure the following:

- The device is switched off at the main switch.
- The vessel is de-pressurized.
- All cables and hose connections between the vessel top plate and the basic unit or instrumentation cabinet have been disconnected.
- The motor is disconnected.
- The inlet air filter and the exit gas cooler with exit gas filter have been removed.

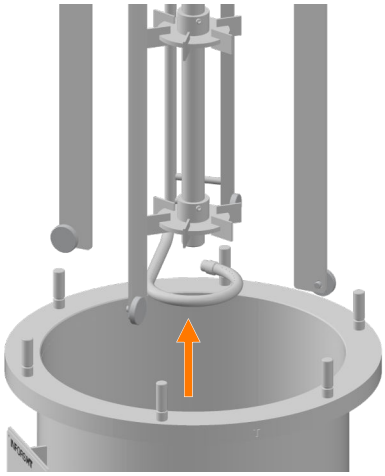
! NOTICE

Cables or hoses connecting the vessel or built-in parts to the instrumentation cabinet or the basic unit may break or otherwise be damaged if the connection has not been disconnected before removing the vessel top plate.

To remove the vessel top plate, proceed as follows:



1. Use a wrench (size 17 mm) to loosen the cap nuts (M10).
2. Remove the cap nuts and washers.
3. Disconnect all cables and hose connections between the vessel top plate and the basic unit or instrumentation cabinet.



4. Carefully and vertically lift the vessel top plate from the vessel using the two handles. In doing so, ensure that baffle, sparger and stirrer shaft do not touch the inside of the vessel.

NOTICE

If built-in-parts hit the inside of the vessel, this can result in micro scratches. In this case, the specified surface roughness on the inside of the vessel can no longer be guaranteed.

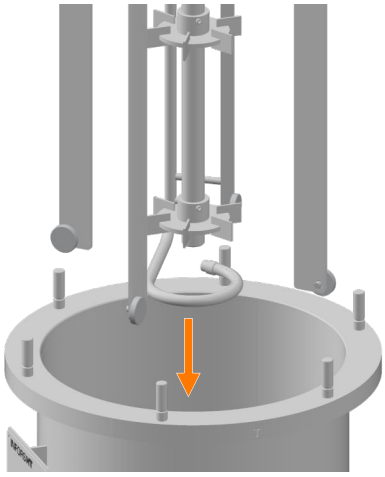
5. Carefully place the vessel top plate with the inside of the top plate facing upwards on a suitable support surface and ensure that it cannot tip away or fall down.

NOTICE

The stirrer shaft is sensitive and can be bent by impact. This causes an imbalance during operation, which can damage the mechanical seal and the bearings in the stirrer shaft hub.

Mounting the Vessel Top Plate

To mount the vessel top plate, proceed as follows:

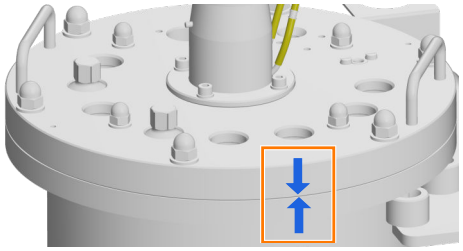


1. Lift the vessel top plate using the two handles.
2. Align the vessel top plate above the center of the vessel and lower it slowly.

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

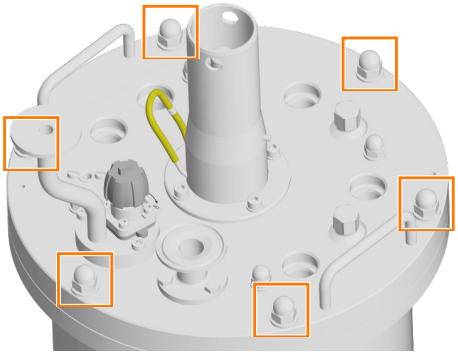
NOTICE

If built-in-parts hit the inside of the vessel, this can result in micro scratches. In this case, the specified surface roughness on the inside of the vessel can no longer be guaranteed.



3. Fit the stud bolts on the vessel flange into the bore 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. Attach the washers.
5. Attach the cap nuts (M10) and tighten them crossways using the wrench (size 17 mm).

2.4.3 Checking Impellers, Baffles and the Top Plate Seal

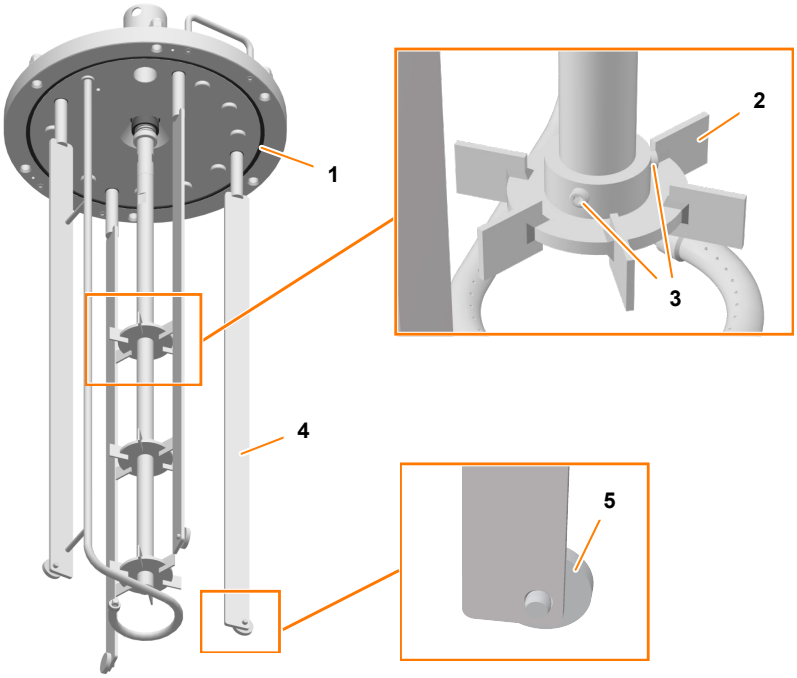
NOTICE

Manipulations on the mechanical seal can damage it.

Requirement:

- The vessel top plate has been removed.

Before cultivation, the correct fit of the impellers, baffles and the top plate seal must be checked. To do so, proceed as follows:



Stirrer Shaft and Impeller

1. Ensure that the impellers (2) on the stirrer shaft are set to the desired height and sit tightly.

   If necessary, loosen the two grub screws (M5x6) per impeller (3) on the impellers, correctly position the impellers and re-tighten the grub screws.

Baffles

2. Ensure that all four spacers (5) are placed on the baffles and fit tightly.

3. Ensure that the four baffles (4) 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) (1) is intact and firmly seated in the groove on the inside.

2.4.4 Equipping the Ports with the Septum and Septum Collar

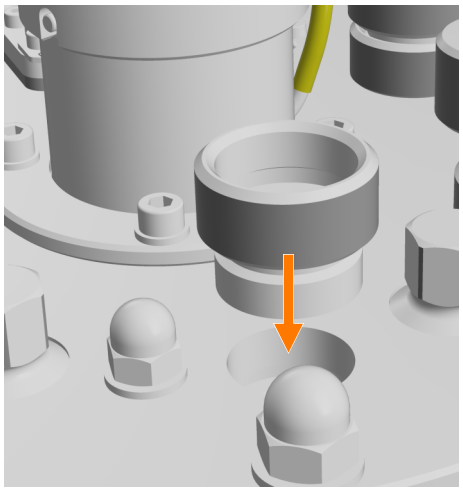
If the piercing method is used for inoculation, addition of reagents, antifoam agents and nutrient solution, the ports in the vessel top plate must be equipped with septa and septum collars. This also applies to the port for the antifoam sensor.

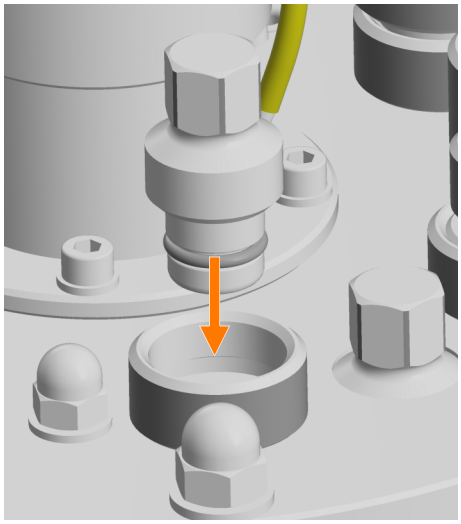
To do so, proceed as follows:

1. Release and remove the blanking plug using a hexagon socket spanner.

2. Insert the septum into the port.

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



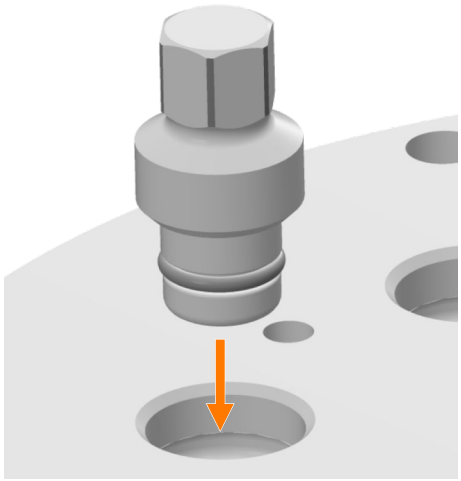


4. Screw the blanking plug with the O-ring into the septum collar by hand.
5. Use the hexagon socket spanner to tighten the blanking plug.

2.4.5 Closing Unused Ports

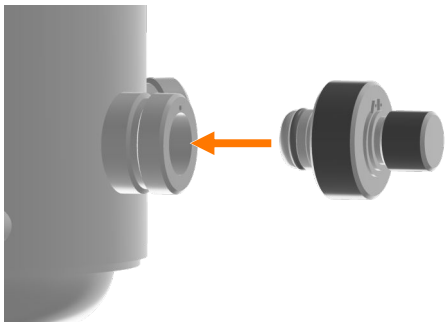
All unused ports and nozzles in the vessel top plate and on the vessel must be sealed with blanking plugs before sterilization. To do so, proceed as follows:

Vessel Top Plate Blanking Plug



1. Screw the blanking plug with the O-ring into the 19 mm port by hand.
2. Use the hexagon socket spanner to tighten the blanking plug.

Ingold Nozzle Blanking Plug



1. Insert the blanking plug with O-ring into the Ingold nozzle.
2. Tighten the blanking plug by hand.

2.4.6 Cleaning the Vessel

After completion of cultivation and, depending on the user's requirements, subsequent in situ sterilization for decontamination, the vessel must be cleaned.

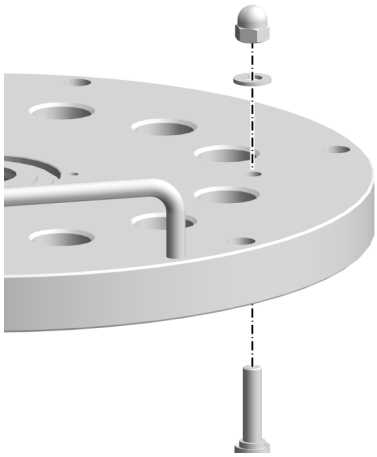
Depending on the degree and kind of contamination, rinsing with water can be sufficient. If remains of foam or protein are adhering to the inside of the vessel, then the following procedure will ensure sufficient cleaning:

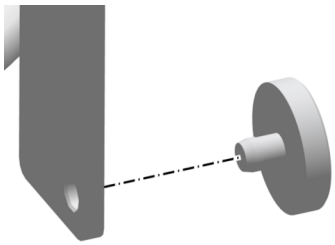
1. Carefully remove sensors from the ports and put aside in order to clean them separately according to the manufacturer's specifications.
2. Fill the vessel with 0.1 N NaOH.
3. Close all vessel ports and affix the vessel top plate.
4. Start the cultivation and stir strongly for 2 hours by using the stirrer function.

   Temperatures of e.g. 40 °C up to 60 °C improve the cleaning action, prolong stirring duration as necessary.
5. Stop the cultivation, shut down the system and switch off the device at the main switch.
6. Empty the vessel.
7. Thoroughly rinse the vessel with water.
8. 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.

2.4.7 Cleaning the Vessel Top Plate





Depending on the application, it might be necessary to separately clean vessel top plate. To thoroughly clean the vessel top plate, proceed as follows:

1. Lift off the vessel top plate, swing it off, lower it and place it on a suitable surface with the inside of the top plate facing upwards (for details, see ➦ Chapter 2.4.2 'Removing and Mounting the Vessel Top Plate' on page 35).
2. If necessary, dismantle the baffles:
   - Loosen the four cap nuts (M8) on the outside of the vessel top plate and remove them together with the washers.
   - Remove the baffles from the inside of the vessel top plate.

   The ring sparger is firmly welded to one of the four baffles and is therefore automatically disassembled as well.
3. If necessary, remove the spacers from the baffles and store them for subsequent use.
4. Carefully rinse the baffles und sparger with water.

   If necessary use 0.1 N caustic soda.
5. Carefully rinse the vessel top plate with water or wipe it down with a wet cloth or sponge.

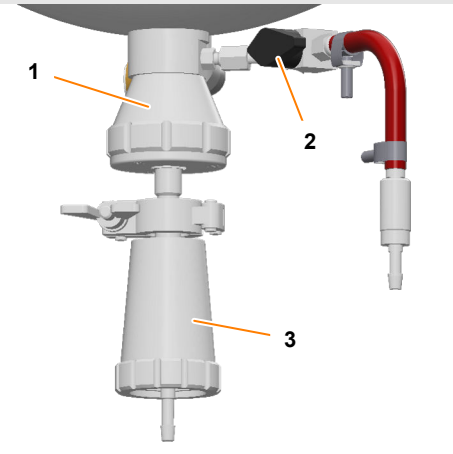
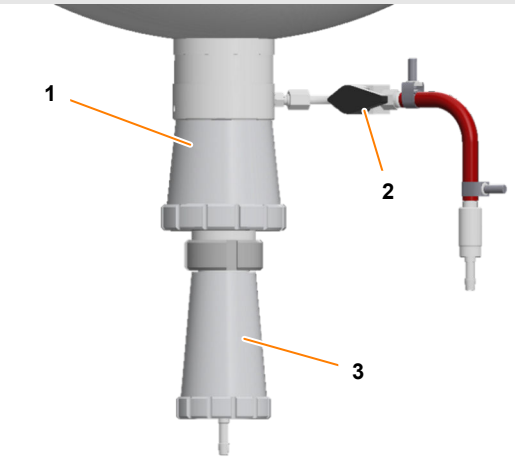
   If necessary use 0.1 N caustic soda.
6. Check the top plate seal (O-ring) and O-ring of all built-in-parts for damage and replace if necessary.
7. Let the vessel top plate and all built-in-parts dry or wipe them dry.
8. Mount the clean and dry baffles and sparger in the clean and dry vessel top plate.
9. Store the vessel top plate so that it is clean, dry and protected (e.g. from falls or other damage) if it is not used for the next cultivation.

2.5 Harvest/Sample Valve (Bottom Valve)

2.5.1 Setup and Function

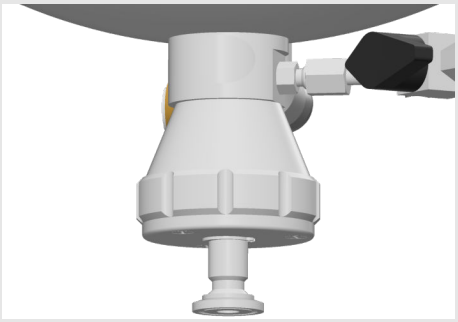
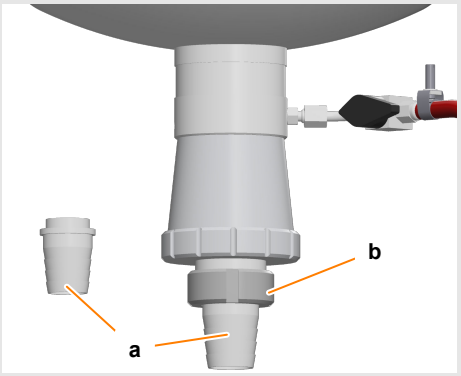
Overview

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

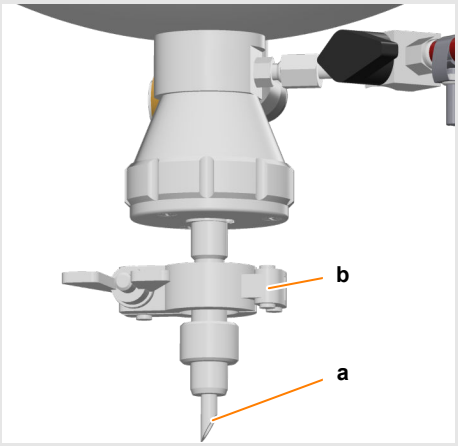
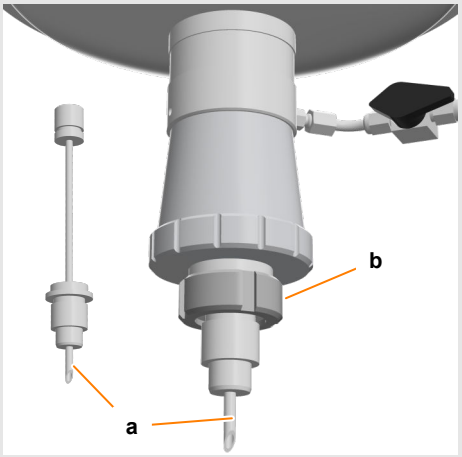
Valve Type for 15 L and 30 L TV	Valve Type for 42 L TV
	

1 Harvest/sample valve *05.12.01*
2 Clean steam valve (valve *05.10.01*) with steam line (pressure hose)
3 Steam trap

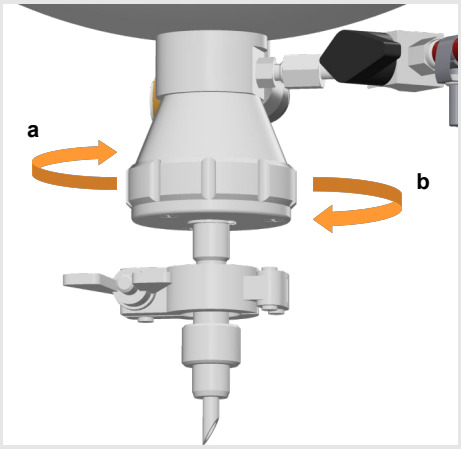
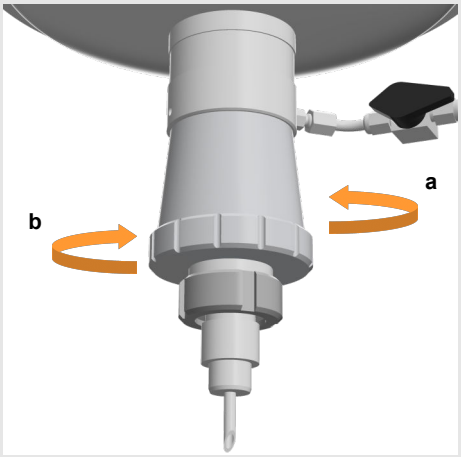
Harvest/Emptying

Valve Type for 15 L and 30 L TV	Valve Type for 42 L TV
	
For harvest/emptying, the provider's hose line can be affixed to the harvest/sample valve with a clamp and flat gasket.	To harvest/empty, a valve insert with a nozzle (a) is used to connect the hose line provided by the operator. This is affixed using a groove nut (b).

Sampling

Valve Type for 15 L and 30 L TV	Valve Type for 42 L TV
	
This valve type has a needle (a) for sampling. The inlet air filter is connected to the flange on the harvest/sample valve with a clamp (b) and a flat gasket. For sampling, the steam trap must be unscrewed from the needle.	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). For sampling, the steam trap must be unscrewed from the valve insert with needle.

Opening/Closing the Valve

Valve Type for 15 L and 30 L TV	Valve Type for 42 L TV
	
▪ Open the valve: turn clockwise (a). ▪ Close the valve: turn counter-clockwise (b).	▪ Open the valve: turn counter-clockwise (a). ▪ Close the valve: turn clockwise (b).

2.5.2 Using the Harvest/Sample Valve

Safety Notes

⚠ CAUTION

The harvest/sample valve becomes very hot during sterilization. Depending on the cultivation temperature, it can also become hot during operation. This causes a risk of burns when touching the harvest/sample valve.

– Let the harvest/sample valve cool down after sterilization.
– Wear heat-resistant protective gloves when operating the harvest/sample valve.

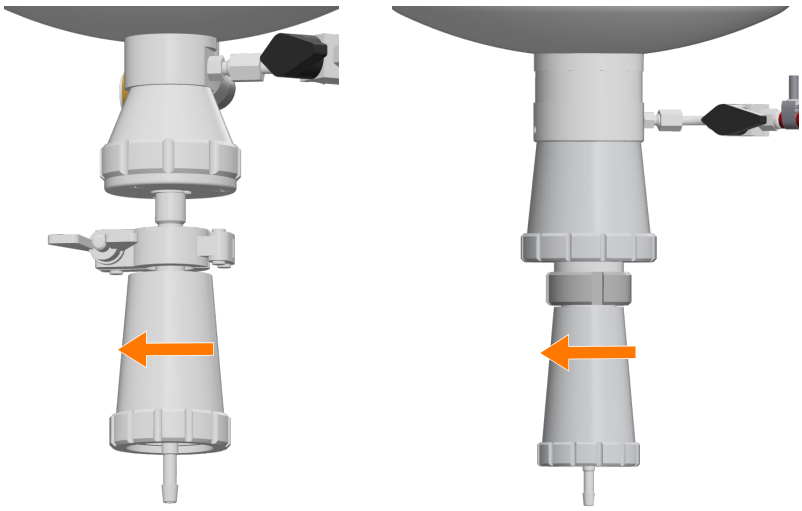
Sampling (both Valve Types)

If the optional sample valve *17.13.01* mounted in one of the Ingold nozzles is available, this can also be used for sampling (➦ Chapter 3.2.1 'Sample Valve' on page 88).

To take a sample, proceed as follows:

1. Have the sample bottle/container ready.

2. Unscrew the steam trap counter-clockwise from the needle in the valve.



➡ The needle is now visible.

3. Place 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 for 15 L and 30 L TV: turn the valve clockwise.
   - Valve type for 42 L TV: turn the valve counter-clockwise.

5. Fill the sample bottle with the required amount of liquid.

6. Close the valve:

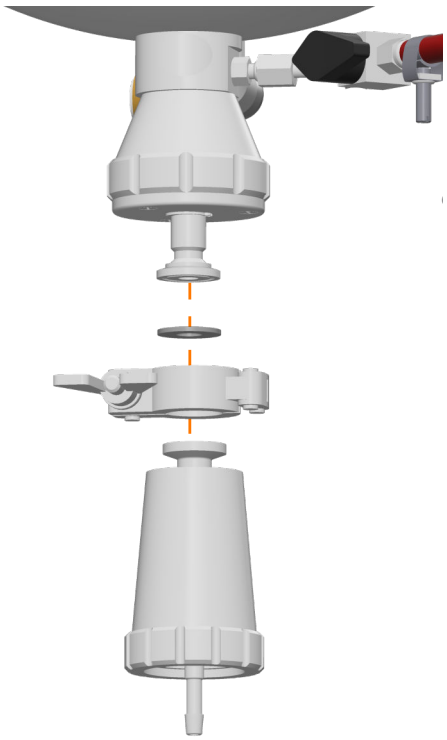
   - Valve type for 15 L and 30 L TV: turn the valve counter-clockwise.
   - Valve type for 42 L TV: turn the valve clockwise.

7. If necessary, 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 sterilized again to ensure it has cooled down sufficiently for the next round of sampling.

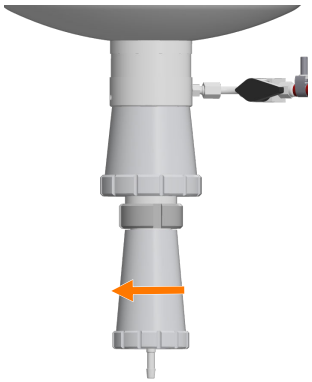
Harvest: Valve Type for 15 L and 30 L TV



To harvest the culture, proceed as follows:

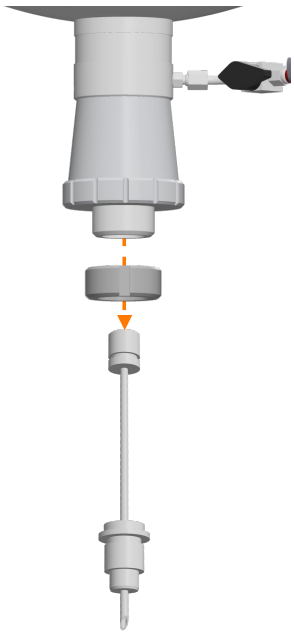
1. Open the clamp and remove the steam trap with the flat gasket from the connection flange of the harvest/sample valve.
2. Attach the harvest hose with flat gasket and clamp to the harvest/sample valve or place the vessel underneath the harvest/sample valve.
3. Open the harvest/sample valve clockwise.

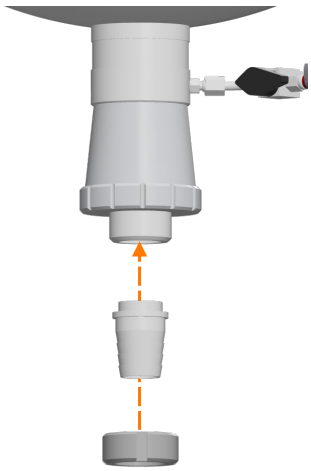
Harvest: Valve Type for 42 L TV

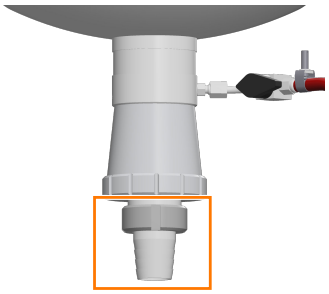


To harvest the culture, proceed as follows:

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.







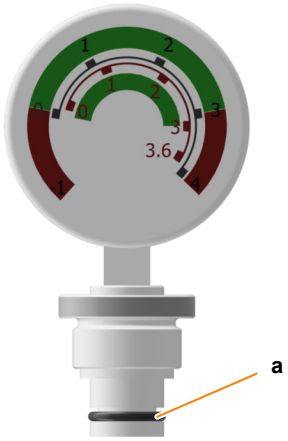
4. Attach the harvest hose to the nozzle of the harvest/sample valve or place the vessel underneath the harvest/sample valve.

> If no hose is connected, mounting of a valve insert with nozzle does not necessarily required.

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

2.6 Vessel Pressure Display (Manometer)

2.6.1 Setup and Function



The maximum permissible vessel pressure is 3.0 bar. Manometer *08.30.01* indicates the pressure in the vessel in a range from 0 bar to 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 is equipped with an O-ring (a) and is mounted in a 19 mm port in the top plate.

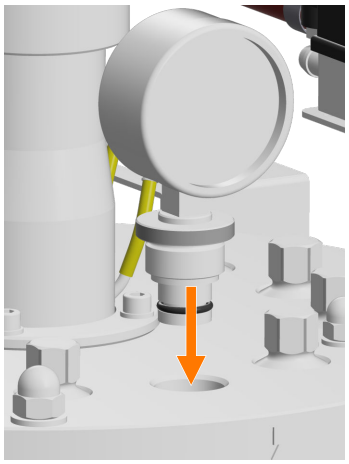
2.6.2 Mounting the Manometer

NOTICE

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!

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 sterilization. To do so, proceed as follows:



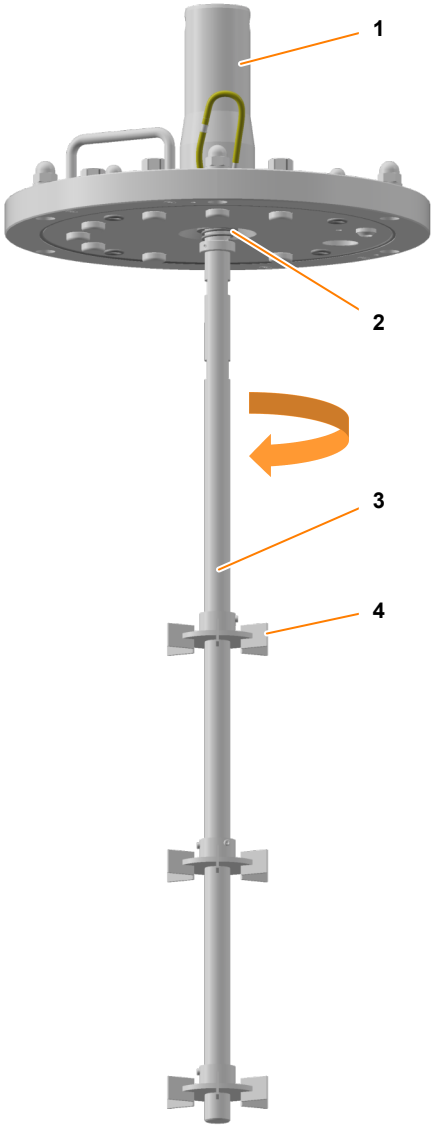
1. Carefully insert the manometer with O-ring into the port.
2. Manually tighten the manometer.

   Ensure that the manometer is screwed in straight.

2.7 Stirrer

2.7.1 Setup and Function

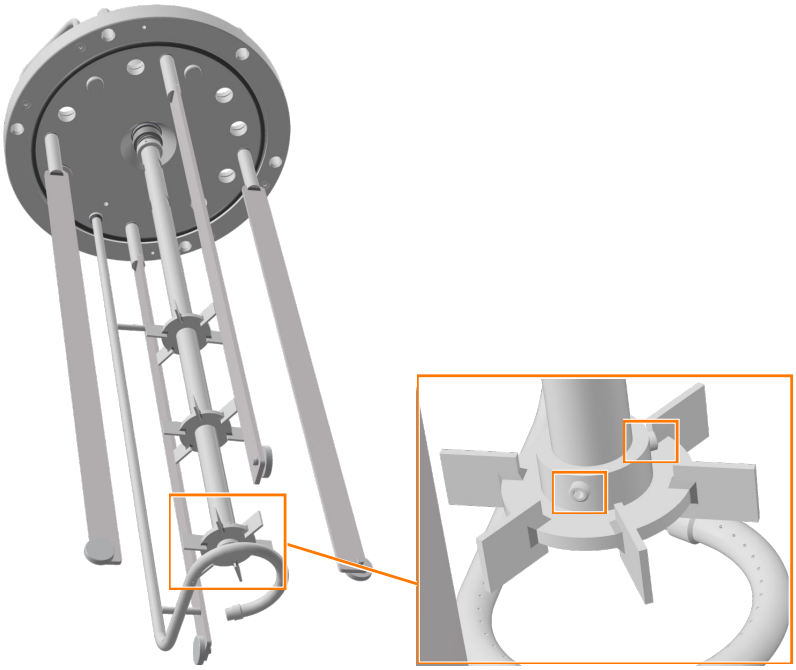
Overview



1 Drive hub
2 Mechanical seal
3 Stirrer shaft
4 Impeller

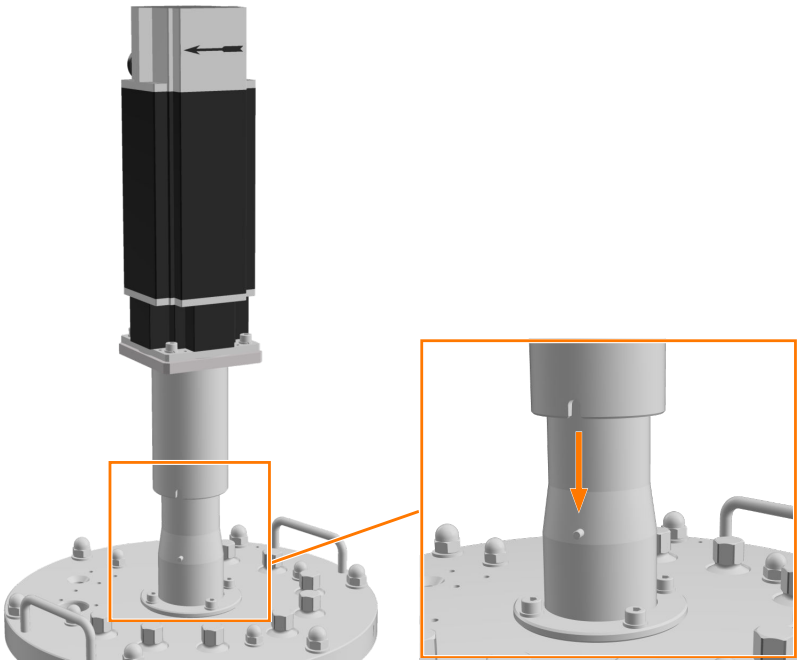
The stirrer shaft is driven from above and turns clockwise (right/top view). The stirrer shaft is screwed onto the drive hub in the top plate and sealed using a single mechanical seal.

Impeller



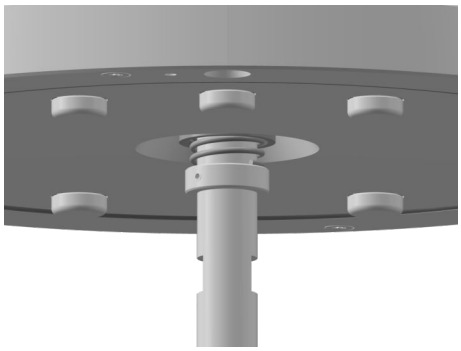
Depending on the vessel size, two (15 L TV) or three (30 L and 42 L TV) Rushton impellers are affixed to the stirrer shaft using grub screws.

Motor



An air-cooled servo motor is used as drive. The motor is coupled by placing it on the drive hub on the vessel top plate. Here, the groove on the motor must be aligned with the pin on the drive hub. This locks the motor into its position.

Mechanical Seal



The mechanical seal must always be lubricated. For this purpose, there are two connection nozzles with a silicone hose on the drive hub (➥ Chapter 2.7.3 'Lubricating the Mechanical Seal' on page 54).

NOTICE

Manipulations on the mechanical seal can damage it.

Important information on the mechanical seal	
Refilling glycerine	During operation, a small amount of glycerine is used for lubricating the mechanical seal. Hence, the chamber should be refilled at regular intervals, e.g. after a number of cultivations or every time the top plate is cleaned. If the mechanical seal is fine, glycerine will ooze out from the overflow even if only a small quantity is refilled.
Glycerine discoloration	Due to normal abrasion of the mechanical seal, dark discoloration of the glycerine, which is visible in the silicone hose, occurs even after a short period of operation of the stirrer shaft. This discoloration is completely normal and does not indicate advanced wear of the mechanical seal.
Loss of glycerine	If there is a significant loss of glycerine during or between two cultivations, this can indicate that the mechanical seal is not placed correctly or that it is defective. A significant loss of glycerine can be identified by the fact that either significantly more glycerine is consumed when refilling the chamber, and/or the culture solution turns dark due to escaping glycerine that has run along the stirrer shaft into the culture.
Replacing the mechanical seal	If there is a significant loss of glycerine, an INFORS HT service technician must check whether the mechanical seal needs to be replaced.

2.7.2 Coupling and Uncoupling the Motor

Safety Notes

CAUTION

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

CAUTION

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

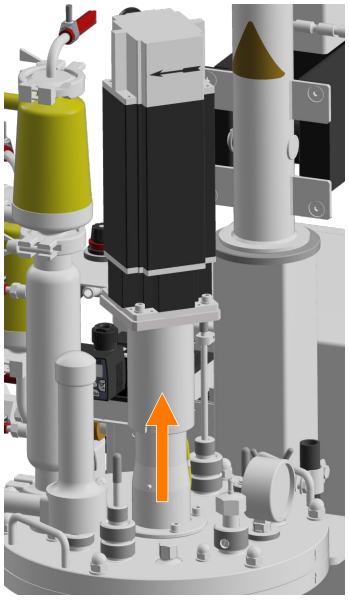
Uncoupling the Motor

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

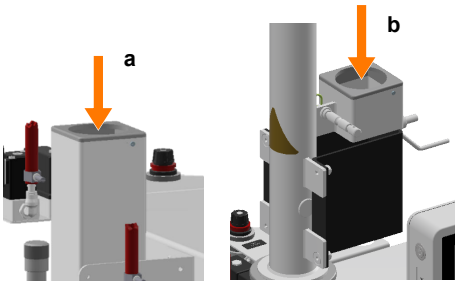
Prior to uncoupling the motor from the drive hub, ensure the following:

- The device is switched off on the main switch.
- The vessel is de-pressurized.
- The motor has cooled down.

Proceed as follows:

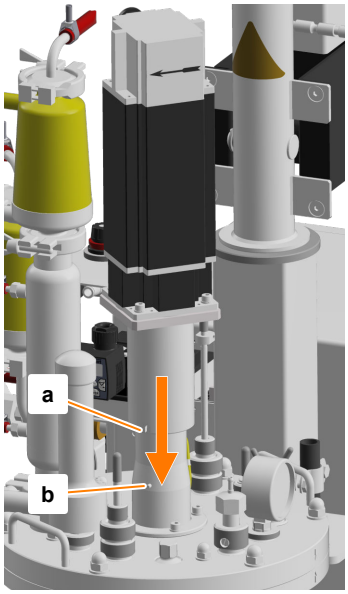


1. Get a second person to help lift the motor. If necessary, lightly shake the motor to loosen it from the drive hub.



2. Place the motor in the holder of the lifting device on the central column (a) or (if available) into the holder for the vessel top plate (b).

Coupling the Motor

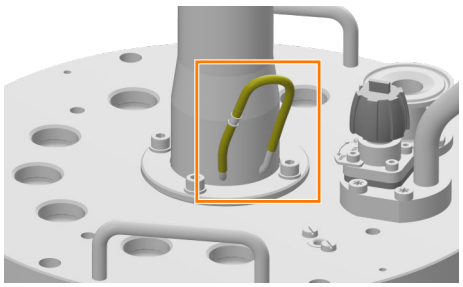


1. Remove the motor from the holder on the central column or from the holder on the lifting device for the vessel top plate (if available).

2. Place the motor on the drive hub of the vessel top plate. In doing so, align the groove on the motor (a) with the pin on the drive hub (b). A different position is not possible.

   ➡ The motor is thus held in its position.

2.7.3 Lubricating the Mechanical Seal



To ensure lubrication of the mechanical seal, the silicone hose at the bottom of the drive hub of the top plate must always be filled with liquid (glycerine).

NOTICE

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

- Before each cultivation, check the glycerine fill level in the hose.
- Refill glycerine if necessary.

To refill, proceed as follows:

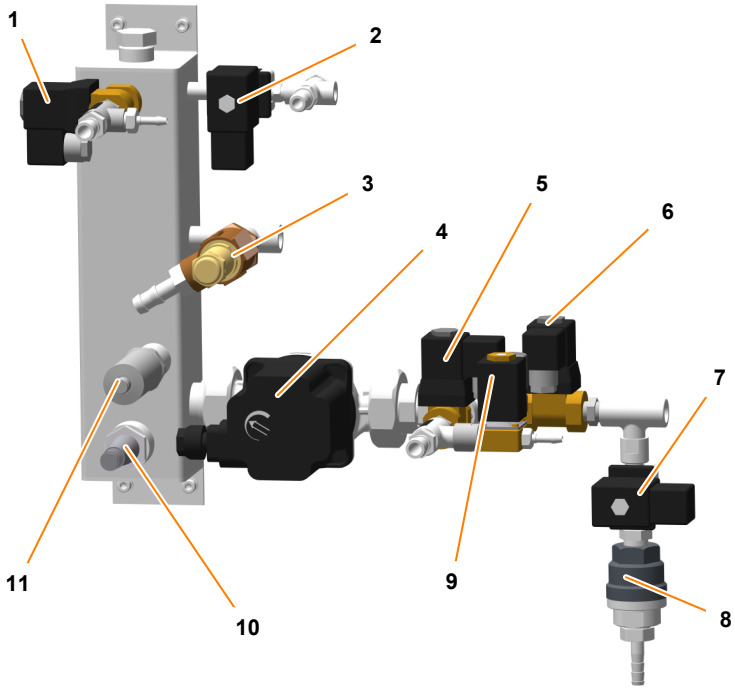
1. Carefully pull off the longer piece of hose from the coupling on the shorter piece.
2. Fill a syringe with glycerine.
3. Plug the syringe onto the open hose piece.
4. Fill glycerine into the hose.
5. Plug the longer piece of hose onto the coupling of the shorter piece.
6. If glycerine has come out of the hose wipe it off with a cloth.

2.8 Temperature Control System and Sterilization

2.8.1 Setup and Function

Overview

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 *01.06.02* (water outlet)
2 Solenoid valve *01.06.03* (clean steam in vessel jacket)
3 Safety valve *01.08.01* with hose nozzle (D = 13 mm)
4 Circulation pump *01.22.01*
5 Solenoid valve *01.06.01* (water inlet)
6 Solenoid valve *01.06.04* (temperature control system)
7 Solenoid valve *01.06.05* (condensate)
8 Steam trap *01.20.01*
9 Solenoid valve *01.06.06* (water inlet exit gas cooler)
10 Heating cartridge *01.25.01*
11 Level sensor *01.38.01*

Heating

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

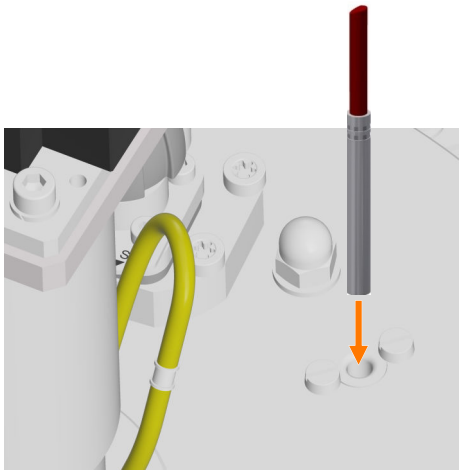
Cooling

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

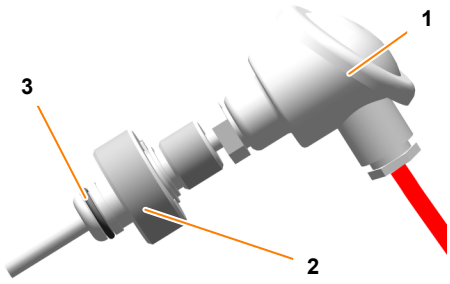
Optional 3-way ball valves on the water inlet and water outlet facilitate manual switching between tap water and chilled water (➦ Chapter 3.5 'Switching between Tap Water/Chilled Water' on page 95).

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 (1) and screw-in socket with coupling nut (2) for mounting in an angled Ingold nozzle on the vessel.

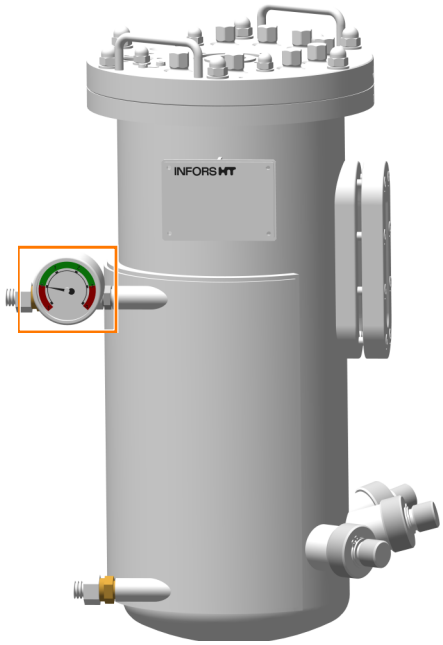
  An O-ring (3) on the screw-in socket is used as the seal. By tightening the coupling nut, the temperature sensor is affixed in the Ingold nozzle.

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).

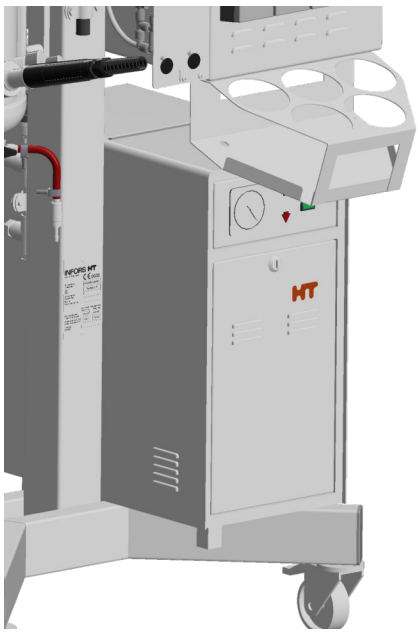
Circuit description: vessel jacket – heating element – circulation pump – vessel jacket

Pressure Indicator



The maximum permissible pressure in the temperature control system is 3.0 bar. The manometer *01.30.01* installed on the water outlet of the vessel jacket indicates the pressure in a range from -1.0 bar to +4.0 bar.

Sterilization



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

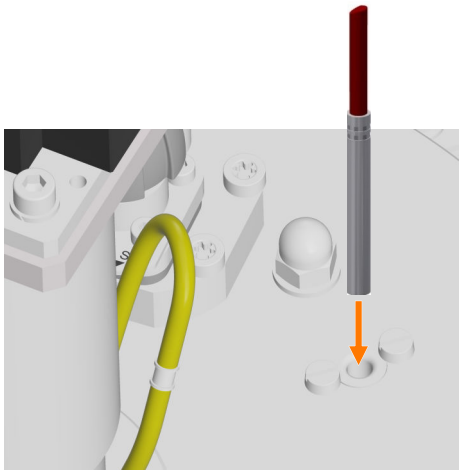
Steam is fed in either by steam supply provided by the provider or by an optional, integrated steam generator (example in figure on the left).

The harvest/sample valve (bottom valve *05.12.01*) is sterilized with clean steam from the same steam line. The same applies to the optional sample valve *17.13.01* (➦ Chapter 3.2.1 'Setup and Function' on page 88) and the optional resterilizable feed line (➦ Chapter 3.3.1 'Setup and Function' on page 90).

2.8.2 Mounting the Temperature Sensor

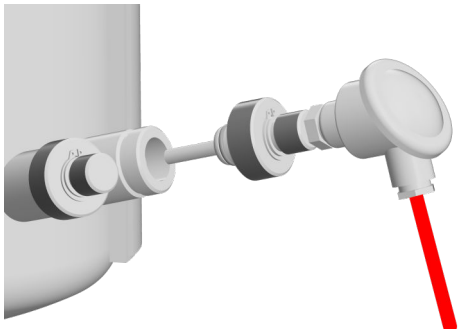
The mounting of the temperature sensor varies depending on the size of the vessel. For vessels with 15 L and 30 L TV, this happens in the vessel top plate. For vessels with 42 L , this happens in an Ingold nozzle.

15 L and 30 L TV

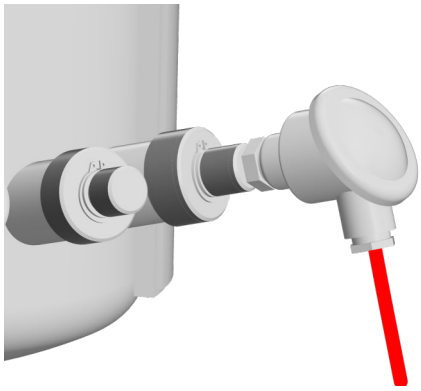


→ Insert the temperature sensor up to the mechanical stop (which can be felt) in the immersion pocket in the 10 mm port in the vessel top plate.

42 L TV



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



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

3. → Ensure that the temperature sensor is straight and attached securely.

2.9 Gassing System

2.9.1 Setup and Function

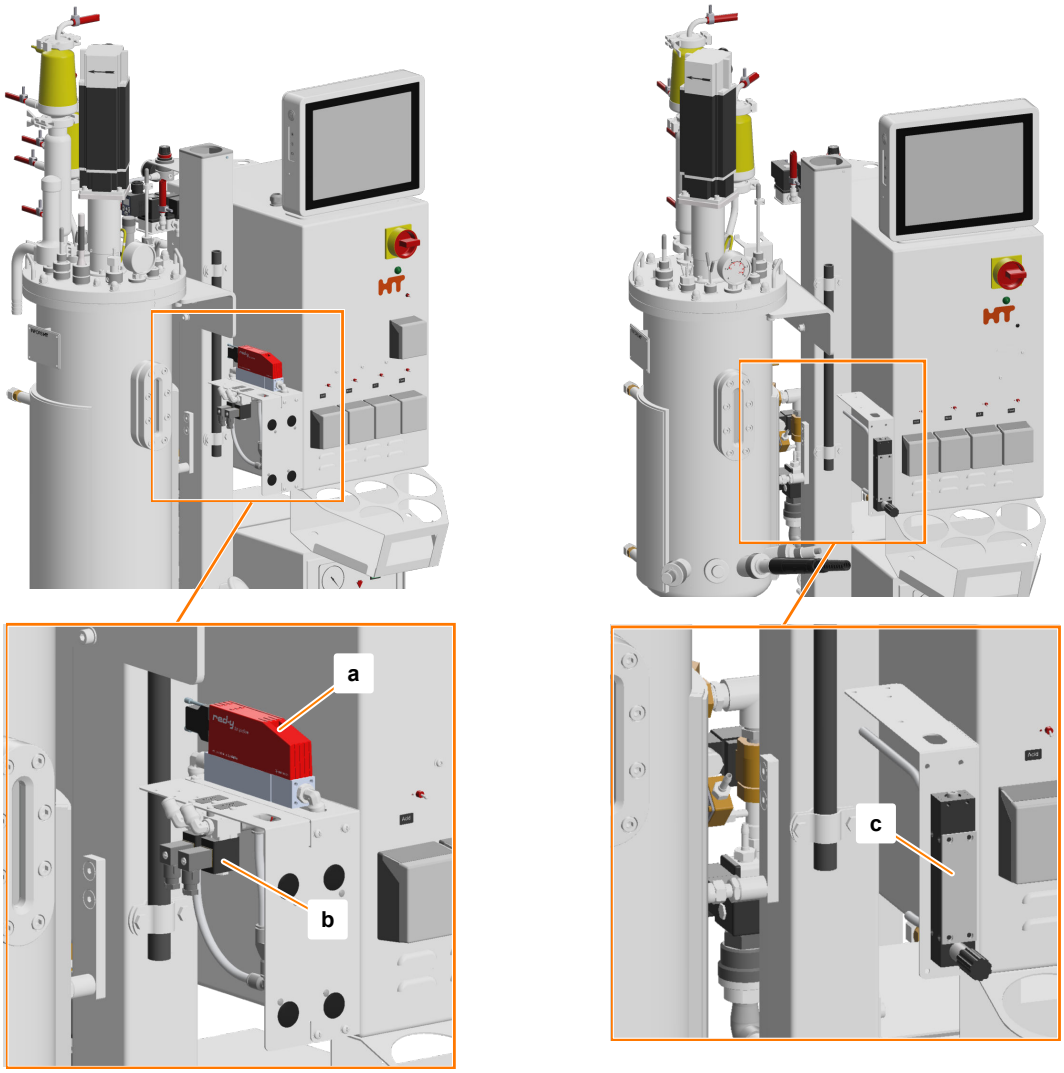
Gases

The following gases can be used:

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

Gassing Units

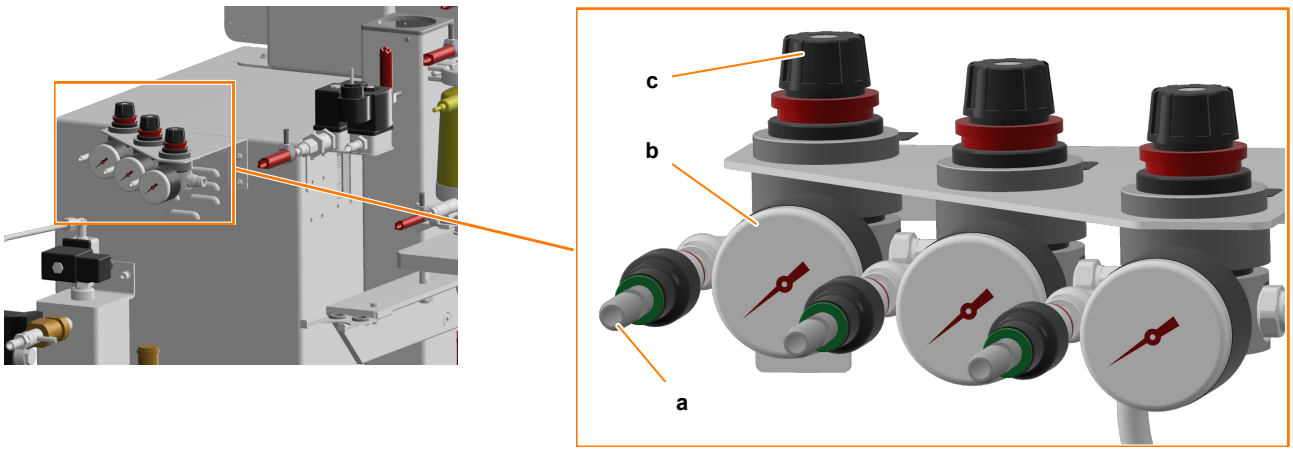
Depending on the chosen gassing strategy, the device is fitted and configured with the corresponding gassing units, that is, rotameter, solenoid valve and mass flow controller. In the example on the bottom, the left depicts a variant with mass flow controller (a) and two solenoid valves (b) and the right depicts a variant with rotameter (c).



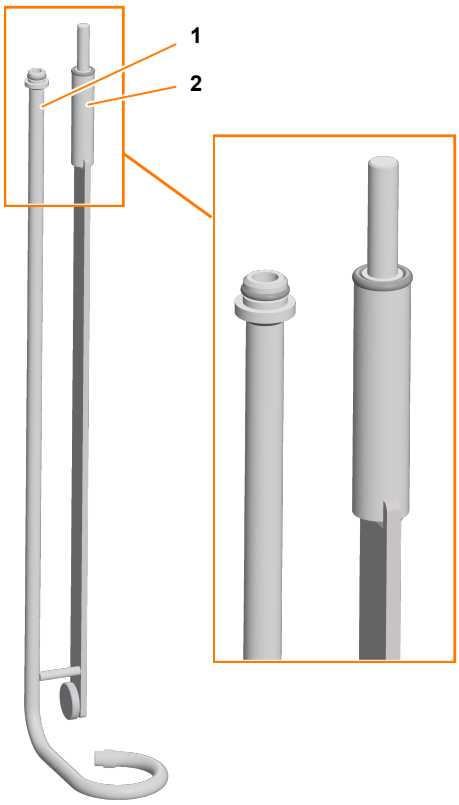
Basic Unit

Gas Connections

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.



Gas Entry

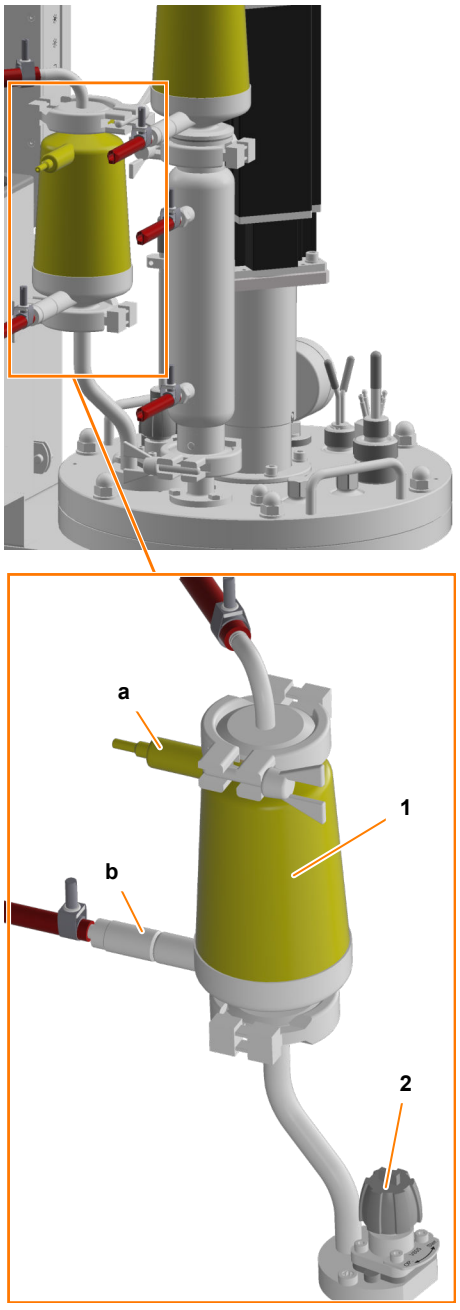


1 Ring sparger
2 Baffle (baffle plate)

Gas enters the vessel via a ring sparger. To stabilize the sparger in the vessel, this is welded to one of the four baffles.

The sparger is equipped with an O-ring at the top end and is mounted in the port, where the diaphragm valve *02.16.01* (see next section) is located. The baffle with O-ring has been inserted into the appropriate bore hole in the vessel top plate. It is affixed to the vessel top plate with metal washers and hexagon nuts (M8), like the other three baffles.

Inlet Air Filter and Valve *02.16.01*



1 Inlet air filter
2 Valve *02.16.01*

A steam sterilizable membrane filter is placed in the gassing line. 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.

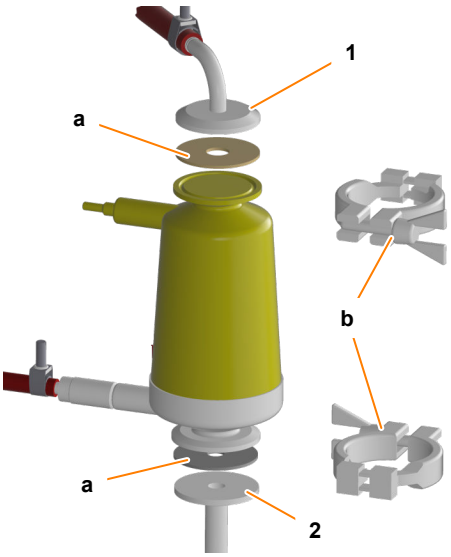
The valve *02.16.01* on the vessel top plate directs the process gas into the sparger during the cultivation, and air into the head space during the cool-down phase of full sterilization. The valve is operated manually:

- Position *STER*: valve position during sterilization.
- Position *OP*: after finishing the sterilization and reaching the pre-selected inoculation temperature for the cultivation, the valve must be returned to position *OP*.

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

Basic Unit

Mounting



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.

Gassing Strategy

The following variants can be selected as the gassing strategy:

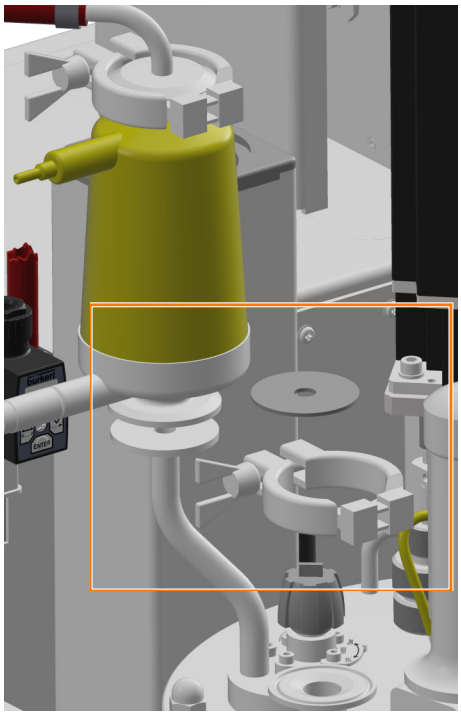
Strategy	Properties
Basic	▪ Manual flow control via rotameter ▪ Gasmix via solenoid valves
Standard	▪ Flow control via an electronic mass flow controller ▪ Gasmix via solenoid valves
High End	Flow control and gasmix via electronic mass flow controllers, 1 piece per gas

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.

2.9.2 Removing and Mounting the Inlet Air Filter

Removing the Inlet Air Filter

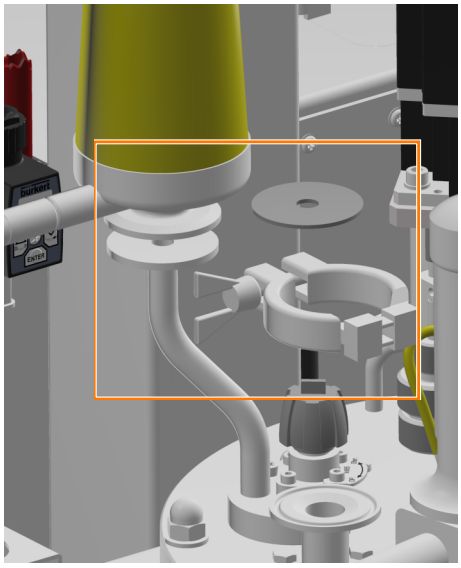


1. Remove the clamp between the inlet air filter and connection flange on the vessel top plate.
2. Remove the inlet air filter und flat gasket.
3. Securely store the clamp und flat gasket for mounting.

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

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

Mounting the Inlet Air Filter

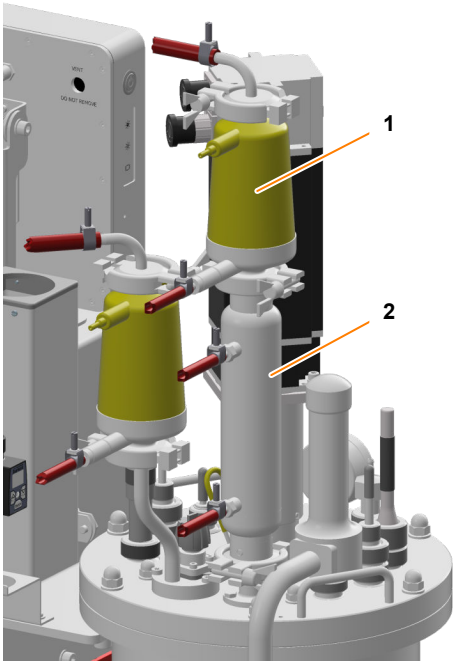


1. Place the flat gasket and flange of the inlet air filter flush on the flange of the vessel top plate.
2. Place the clamp around both flanges, close and tighten.
3. If the inlet air/gas hose line has been removed, mount it in the same way.

2.10 Exit Gas System

2.10.1 Setup and Function

Overview



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 every cultivation in a bioreactor.

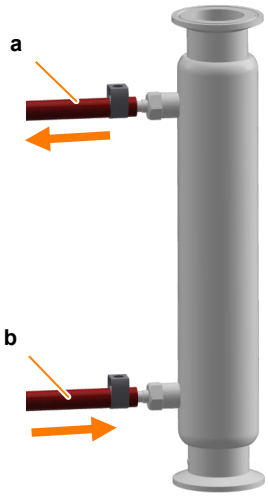
1 Exit gas filter
2 Exit gas cooler

Exit gas streams via 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 (➥ Chapter 3.9.1 'Pressure Control' on page 100).

It is also possible to analyze the exit gas while the cultivation is running (➥ Chapter 3.12 'Exit Gas Analysis' on page 105).

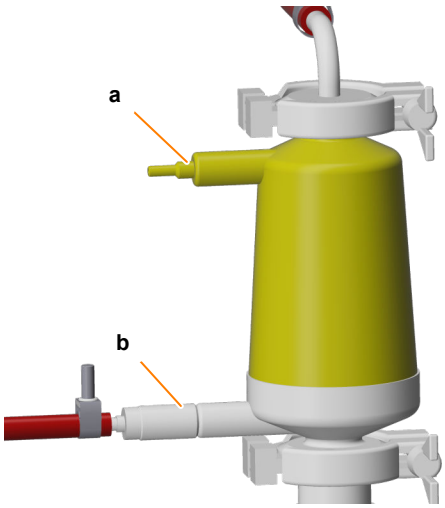
Exit Gas Cooler



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.

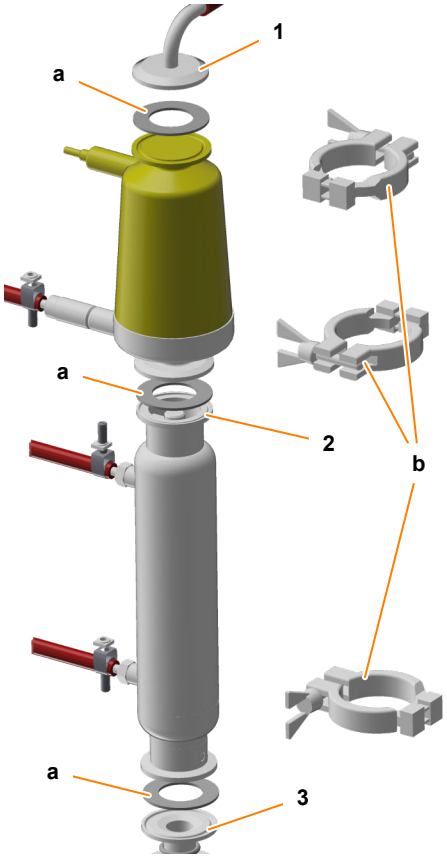
The exit gas cooler has pressure hoses for the water inlet (b) and outlet (a). Water is fed in from the supply for the temperature control system; this is done automatically during the cultivation and the full sterilization in accordance with the appropriately programmed process sequences.

Exit Gas Filter



A steam sterilizable membrane filter 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.

Mounting



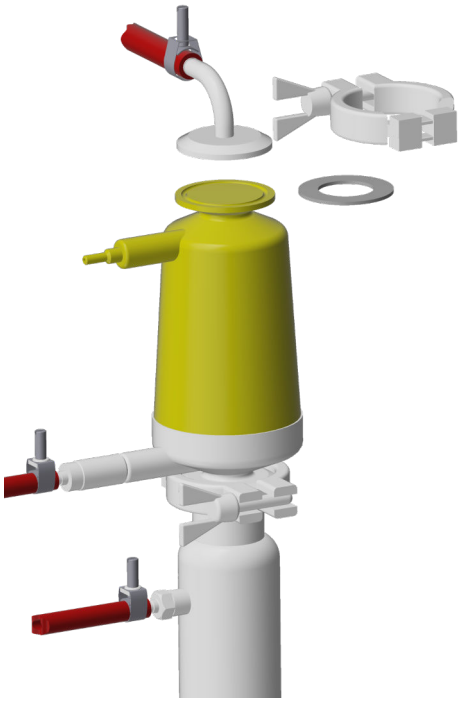
1 Exit gas flange
2 Upper exit gas cooler flange
3 Vessel top plate flange

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.

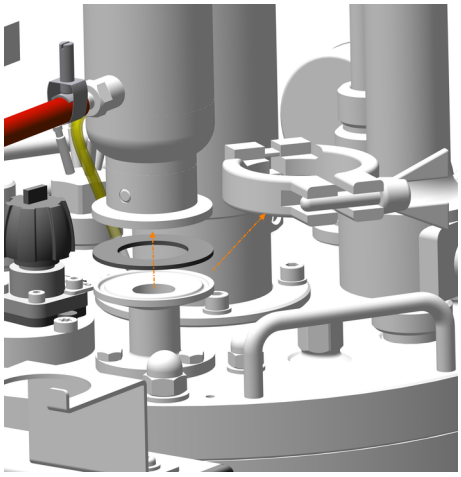
2.10.2 Removing and Mounting the Exit Gas Cooler with Exit Gas Filter

Removing the Exit Gas Cooler with Exit Gas Filter

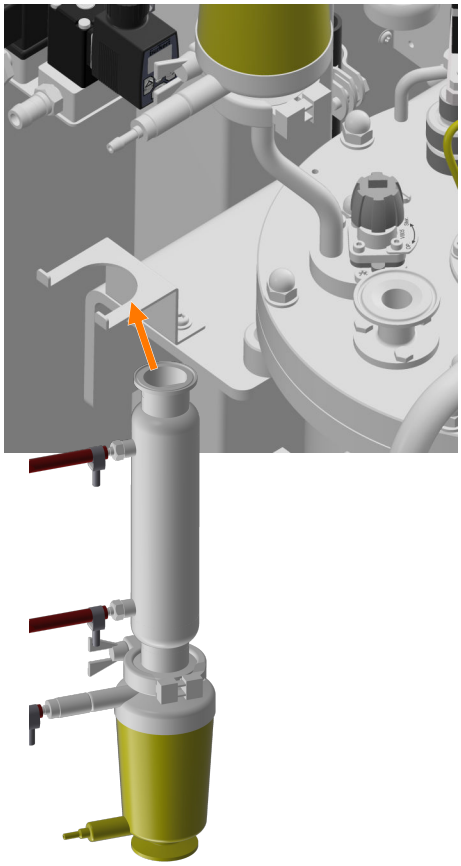
The exit gas cooler and exit gas filter can be removed as a unit. However, the exit gas hose line must be removed. Proceed as follows:



1. Remove the clamp between the exit gas filter and the exit gas hose.
2. Remove the inlet air filter und flat gasket.



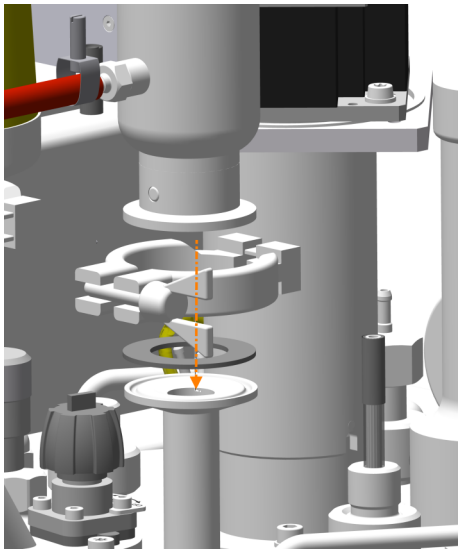
3. Remove the clamp, exit gas cooler and flat gasket between the exit gas cooler and connection flange on the vessel top plate in the same way.
4. Securely store the clamps und flat gaskets for mounting.



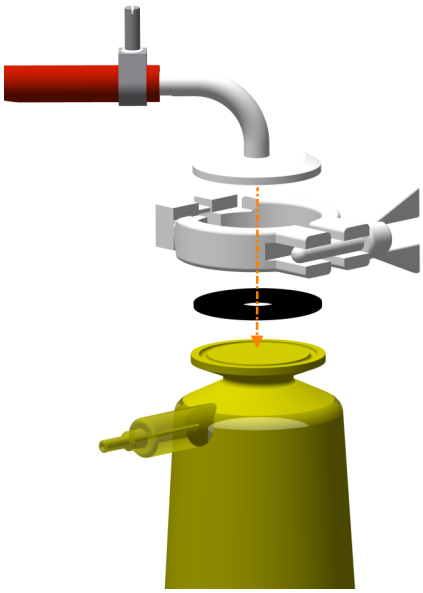
5. Turn over the exit gas cooler and place it in the holder on the vessel mounting.

Mounting the Exit Gas Cooler with Exit Gas Filter

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



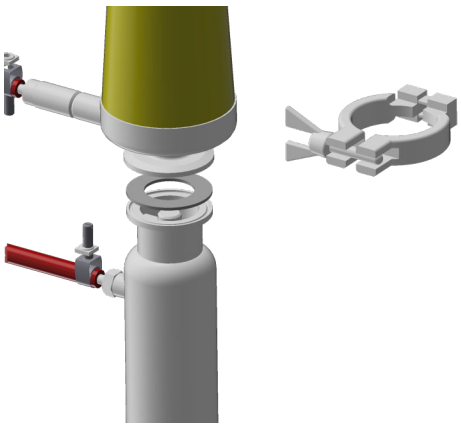
2. Place the flat gasket and exit gas cooler flush on the flange on the vessel top plate and secure them with a clamp.



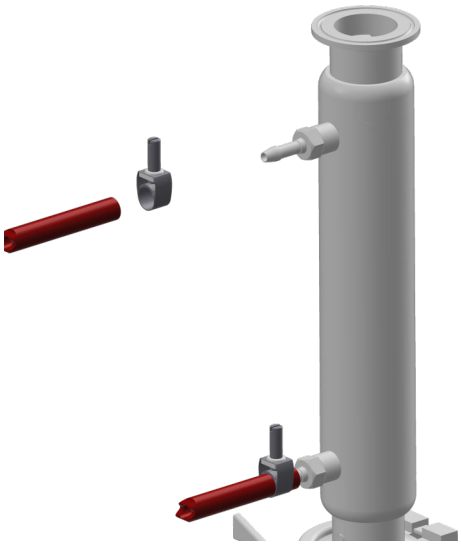
3. Place the flat gasket and flange of the exit gas hose flush on the flange of the exit gas filter and affix them with a clamp.

2.10.3 Cleaning the Exit Gas Cooler

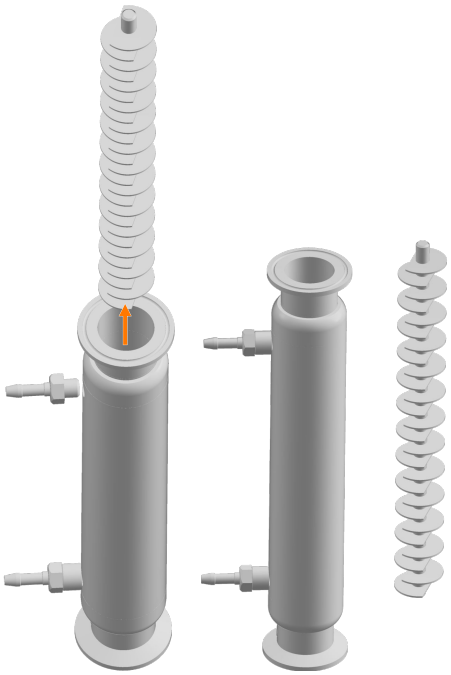
To thoroughly clean the exit gas cooler, its baffle body can be removed. Proceed as follows for removing, dismantling and cleaning the exit gas cooler:



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 mounting.



3. Remove the hose clamps and disconnect the red pressure hoses for water inlet 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 remove 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. Thoroughly rinse both parts with water.
8. Place both parts into an ultrasonic bath for 2 to 5 minutes.
9. Thoroughly rinse both parts with distilled water.
10. Let both parts dry on a clean base and then re-assemble them.

2.11 pH Control

2.11.1 Setup and Function

Function

The pH value in the culture medium is measured by the pH sensor and controlled by adding reagent (acid, base). Acid and base are added via the two digital peristaltic pumps *Acid* and *Base*.

The reagents are kept in reagent bottles that are connected via hoses, e.g. with a push valve or an inoculation needle in the vessel top plate and the two pumps.

Measurement System

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

The pH sensors of the Easyferm Plus ARC type have been preconfigured by the INFORS HT device manufacturer. Replacement sensors must be configured before use.

Measurement system	Properties
METTLER analog	▪ Conventional pH sensor (potential measurement against reference) ▪ Type: 405-DPAS-SC-K8S/120
METTLER digital	▪ Conventional pH sensor (potential measurement against reference) with built-in electronics ▪ Type: InPro 3253i, ISM
HAMILTON digital	▪ Conventional pH sensor (potential measurement against reference) with built-in electronics ▪ Type: Easyferm Plus ARC

Calibration

Generally speaking, the following applies: the calibration of a pH sensor is always performed BEFORE the sterilization.

The followings only applies to digital pH sensors:

If the pH sensor has already been calibrated externally, the bioreactor will use this data and there is no need for calibration process on the operating panel.

Mounting

The pH sensor is mounted into an Ingold nozzle in the vessel. The sensor's manufacturer includes suitable insertion housing with the sensors.

2.11.2 Mounting and Connecting the pH Sensor

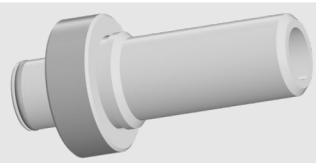
Insertion Housing

Insertion housing serves as a sensor adapter and also protects the sensor from physical damage.

The pH sensors, which vary depending on the pH measurement system used, are supplied with suitable insertion housing for mounting in the Ingold nozzles.

Mettler variant:

The pH sensor is supplied with suitable insertion housing of type InFit 761 with cable kink protection for installation in the Ingold nozzles.

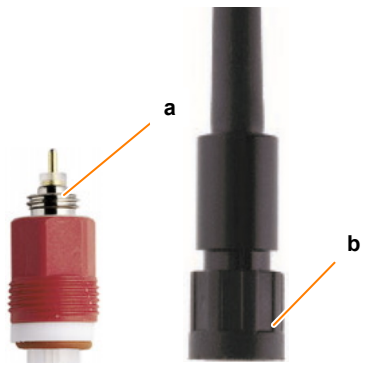


HAMILTON variant:

The pH sensor is supplied with suitable insertion housing of type Flexifit U Bio for installation in the Ingold nozzles.

Sensor and Cable Connections

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

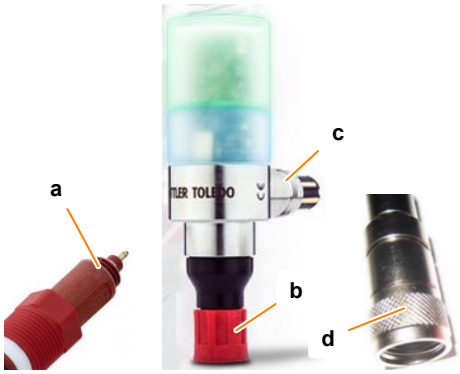


METTLER analog, type 405-DPAS-SCK8S/ 120	
Sensor head connection (a)	K8S
Cable socket (b)	AK9

NOTICE

The screening on the sensor cable may become damaged if it is kinked or twisted. This may lead to faulty measurements.

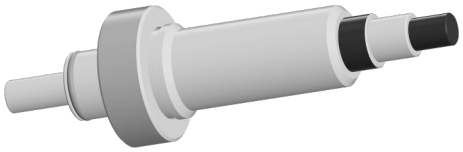
Basic Unit



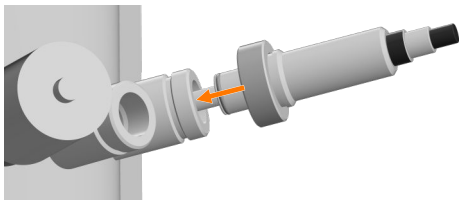
METTLER digital, type InPro 3253i with head transmitter M100	
Sensor head connection (a)	ISM
Cable socket (d)	VP8
Head transmitter M100: push-in fitting for sensor (b)	
Head transmitter M100: push-in fitting for cable (c)	

HAMILTON digital, type Easyferm Plus ARC	
Sensor head connection (a)	VP8
Cable socket (b)	VP8

Mounting and Connecting the pH Sensor



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



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

3. If necessary, mount the cable kink protection according to the manufacturer's specifications prior to connecting the cable.
4. Connect the sensor cable.

2.12 pO_2 Control

2.12.1 Setup and Function

Function

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

pO_2 increase	The concentration of oxygen dissolved in the medium (pO_2) can be increased using the following methods: ■ Increasing the rotation speed of the stirrer ■ 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.

Measurement System

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

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

Measurement system	Properties
METTLER analog	■ Traditional amperometric/polarographic pO_2 sensor ■ Type: InPro 6820 Polarographic pO_2 sensors must be polarized for commissioning or after they have been disconnected from the power source.
METTLER digital	■ pO_2 sensor with integrated opto electronics ■ Type: InPro6860i, ISM
HAMILTON digital	■ pO_2 sensor with integrated opto electronics ■ Type: Visiferm DO ARC / Visiferm RS485-ECS

Measurement und Calibration

Generally speaking, the following applies: unlike e.g. pH measurements, which are calibrated to absolute measurements, 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.

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.

Mounting

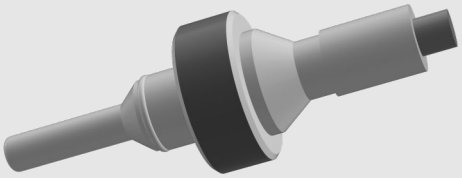
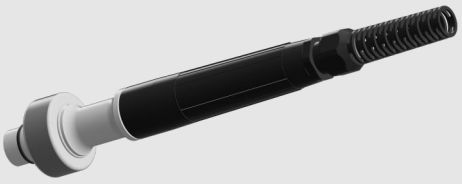
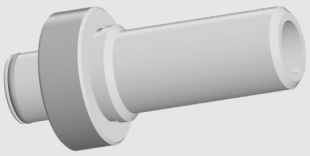
The pO_2 sensor is mounted into an Ingold nozzle in the vessel. Depending on the sensor type, it is mounted directly or with suitable insertion housing from the sensor manufacturer which is included in the delivery.

2.12.2 Mounting and Connecting the pO_2 Sensor

Insertion Housing

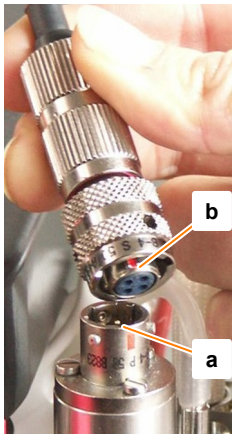
Insertion housing serves as a sensor adapter and also protects the sensor from physical damage.

The pO_2 sensors, which vary depending on the pO_2 measurement system used, are supplied with suitable insertion housing for mounting in the Ingold nozzles.

	METTLER analog variant: The pO_2 sensor is designed in such a way that it can be mounted directly in the Ingold nozzle, without insertion housing.
	METTLER digital variant: The pO_2 sensor is supplied with suitable insertion housing of type InFit 761 with cable kink protection for installation in the Ingold nozzles.
	HAMILTON variant: The pO_2 sensor is supplied with suitable insertion housing of type Flexifit U Bio for installation in the Ingold nozzles.

Sensor and Cable Connections

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



METTLER analog, type InPro 6820/25/080 (amperometric, polarographic)	
Sensor head connection (a)	T-82
Cable socket (b)	T-82

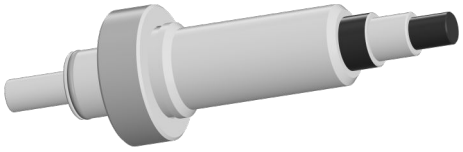
NOTICE

The screening on the sensor cable may become damaged if it is kinked or twisted. This may lead to faulty measurements.

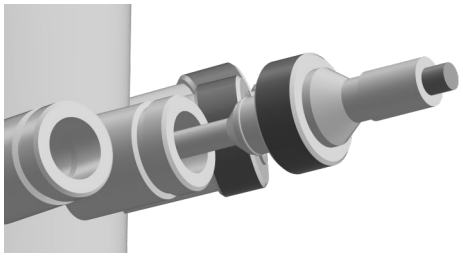
METTLER digital, type InPro6860i	
Sensor head connection (a)	VP8
Cable socket (b)	VP8

HAMILTON digital, type Visiferm DO ARC / RS485-ECS	
Sensor head connection (a)	VP8
Cable socket (b)	VP8

Mounting and Connecting the pO_2 Sensor



1. If necessary, insert the sensor into the insertion housing according to the sensor manufacturer's guidelines.



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

3. If necessary, mount the cable kink protection according to the manufacturer's specifications prior to connecting the cable.
4. Connect the sensor cable.

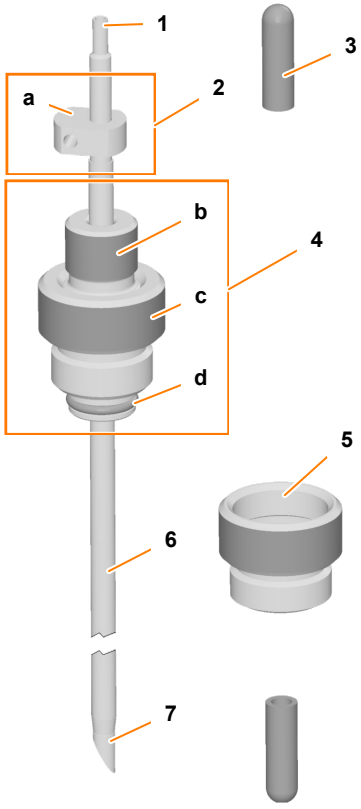
2.13 Antifoam Control

2.13.1 Setup and Function

Function

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



1 Hose connector
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!)

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

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

2.13.2 Preparing the Antifoam Sensor for Cultivation

The antifoam sensor is packed in aluminum foil, equipped with a silicone hose and reagent bottle and autoclaved separately.

Prior to autoclaving, the antifoam sensor should be set to the approximate mounting depth. It should be set too low rather than too high. Pulling out is possible even during cultivation and bears a significantly lower risk of contamination than pushing in.

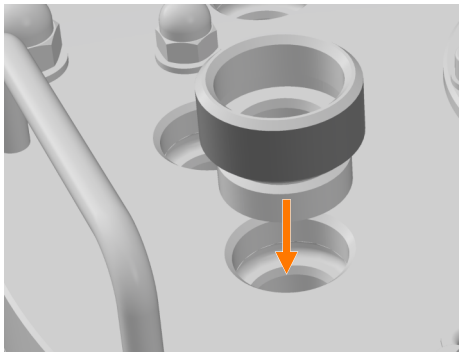
NOTICE

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

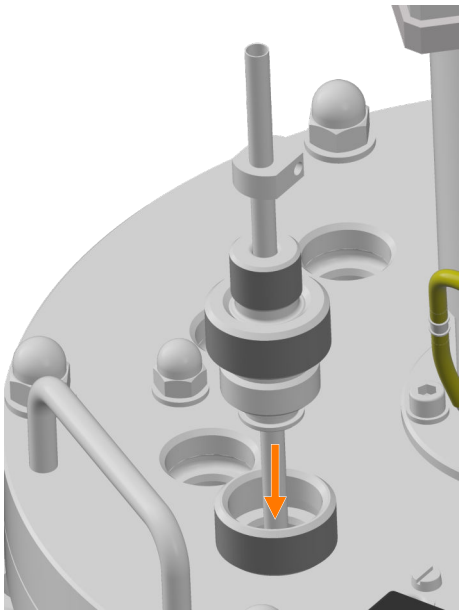
Requirements:

- The reagent bottle for antifoam agent is equipped (➥ Chapter 4.4.2 ‘Preparing Reagent Bottles for Cultivation’ on page 114).

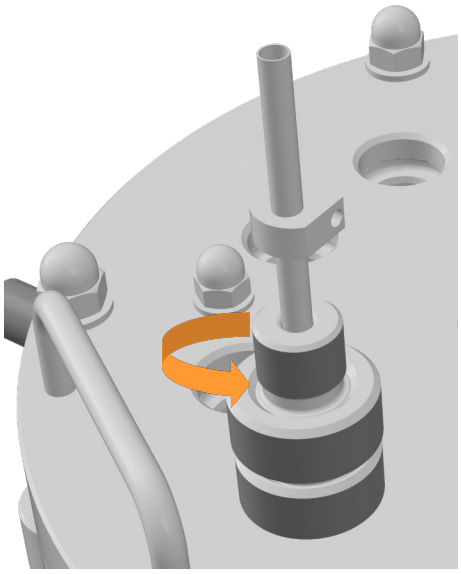
To prepare the antifoam sensor for use, proceed as follows:



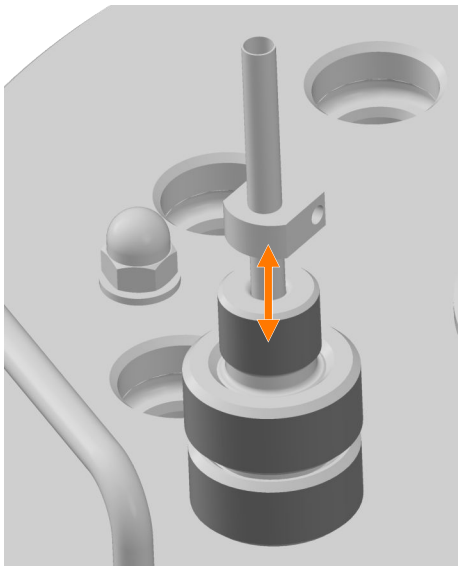
1. Manually screw the septum collar into the 19 mm port in the vessel top plate.
2. Remove the protective caps from the antifoam sensor.



3. Manually screw the antifoam sensor into the septum collar.



4. Carefully loosen the hollow screw by hand.



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

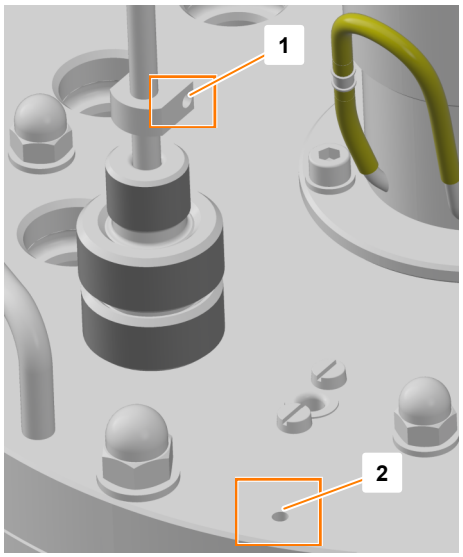
   Ensure that the sensor does not touch the hollow screw. Otherwise, a continuous signal is generated as soon as the sensor is connected.

6. Carefully tighten the hollow screw by hand.
7. Manually unscrew the antifoam sensor from the septum collar in the vessel top plate
8. Manually unscrew the septum collar from the port and put it aside for subsequent use.
9. Connect the hose of the reagent bottle for antifoam agent to the antifoam sensor.
10. Secure all hose connections with cable ties.
11. Lightly cover the filter of the reagent bottle and the antifoam sensor with aluminum foil, or pack the inoculation needle into the protective sheath.
12. Pinch off the hose with the hose clamp.
13. Autoclave everything together at 121 °C for e.g. 30 to 60 minutes.

2.13.3 Mounting and Connecting the Antifoam Sensor

After autoclaving and after in situ sterilization, proceed with mounting the antifoam sensor as with an inoculation needle. For details, see ➦ 'Using Inoculation Needles' on page 123.

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



1. Plug the red banana plug of the sensor cable into the side connection (1) of the antifoam sensor.
2. Insert the black banana plug into the ground connection (2) in the vessel top plate.

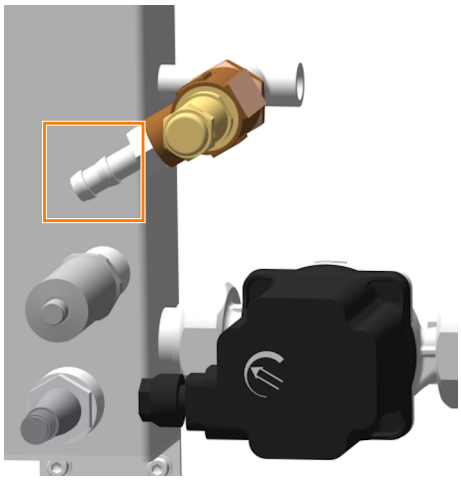
2.14 Safety Valves

2.14.1 General Information

All installed safety valves have been certified by the German Technical Inspection Association (TÜV). As with all safety-related components, they must be included in a maintenance plan; otherwise their operational safety cannot be guaranteed.

The provider must also subject the safety valves to regular checks in accordance with national regulations. For detailed information on the safety valves, refer to the corresponding manufacturer documentation.

2.14.2 Safety Valve Temperature Control Circuit

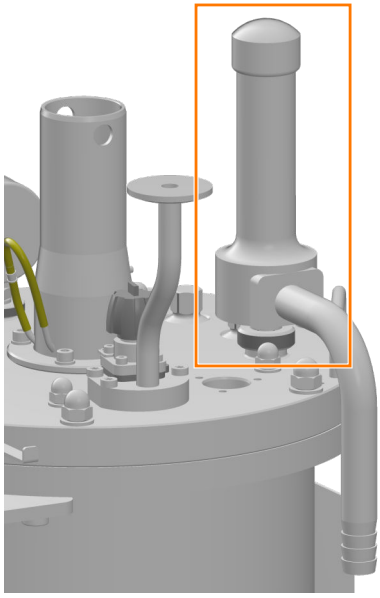


The safety valve in the temperature control circuit protects the vessel jacket against impermissible excess pressure. It is fitted and set by the device manufacturer. During normal operation of the device, the operator does not have to operate the valve.

The safety valve has a hose nozzle (Ø 13 mm) for the provider-side tube or hose line for the safe discharge of possibly escaping steam or hot water in case of possible triggering (opening) of the safety valve. For details, see also ↱ Chapter 2.14.1 'Safety Valves' on page 81.

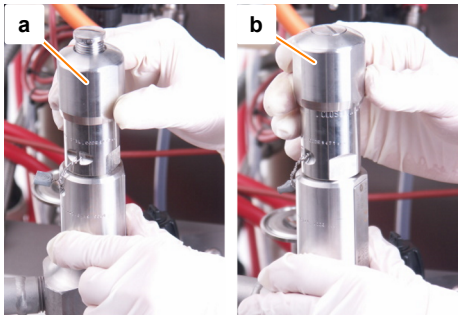
2.14.3 Safety Valve Vessel

Setup and Function



The safety valve mounted on the vessel top plate with lifting device protects the bioreactor vessel (not the vessel jacket) against an inadmissible overpressure. It must be mounted and intact at all times.

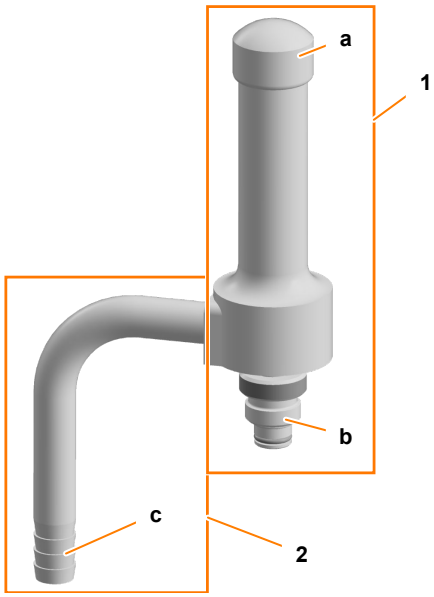
The safety valve normally remains closed. To ensure that the air is completely removed from all cavities of the safety valve and replaced by steam during sterilization, it is possible to vent the safety valve during the heating phase up to 103 °C.



- Venting: turn the lifting device downwards counter-clockwise (a), the engraving *CLOSED* disappears, the thread becomes visible at the top.
- Closing: turn the lifting device upwards clockwise (b) until the mechanical stop, the engraving *CLOSED* becomes visible, the thread disappears.

With this method, sterilization must take place in a supervised manner, and manual lifting of the hot valve involves a risk of injury. The risk of a safety valve that is not completely sterile, on the other hand, is hardly present with this valve type.

Overpressure Venting Pipe



The safety valve has a connection thread for mounting in the 19 mm port in the vessel top plate. It also has 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 connector Ø = 21 mm (c)

The open end of the overpressure venting pipe has a hose nozzle (Ø 21 mm) for the provider-side tube or hose line for the safe discharge of possibly escaping steam or hot and/or contaminated liquid in case of possible triggering of the safety valve. For details, see also ➥ Chapter 2.14.1 ‘Safety Valves’ on page 81.

2.14.4 Mounting the Vessel Safety Valve

The safety valve that protects the vessel against impermissible overpressure must always be mounted.

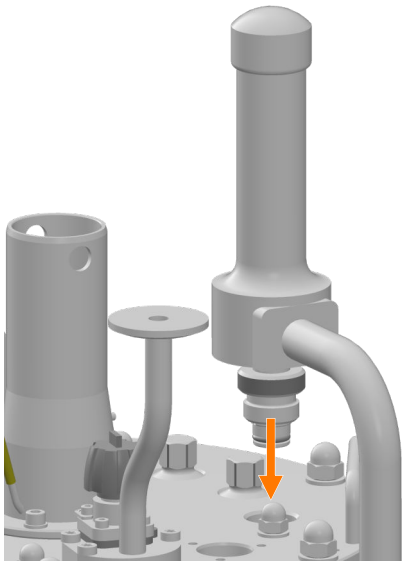
⚠ WARNING

If the safety valve is not mounted, the pressure cannot escape in a controlled manner if the permissible pressure in the vessel is exceeded.

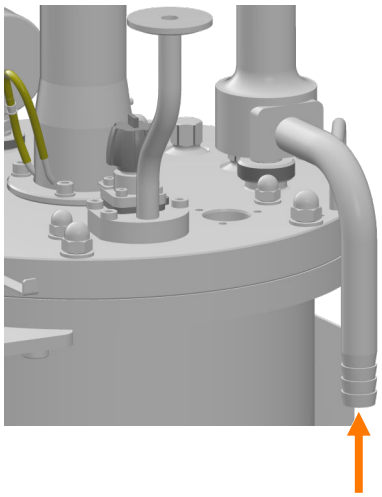
This can lead to pressurized components bursting or flying around.

For detailed information on the safety valve, see the separate documentation provided by the safety valve’s manufacturer.

Proceed as follows:



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



2. Ensure that the provider-side hose or piping is connected to the overpressure venting pipe; connect if necessary.

   For details, see also ➥ Chapter 2.14.1 'Safety Valves' on page 81.

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

   For details on the lifting device, see also ➥ 'Setup and Function' on page 82.

2.15 Identification of the Device

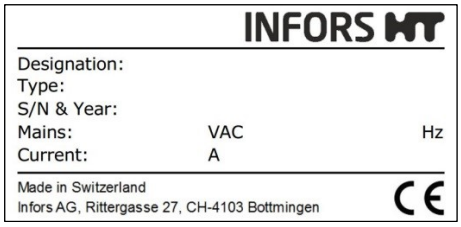
2.15.1 Identification Plate

Position

The identification plate for identifying the device is located on the instrumentation cabinet and on the support.

Content

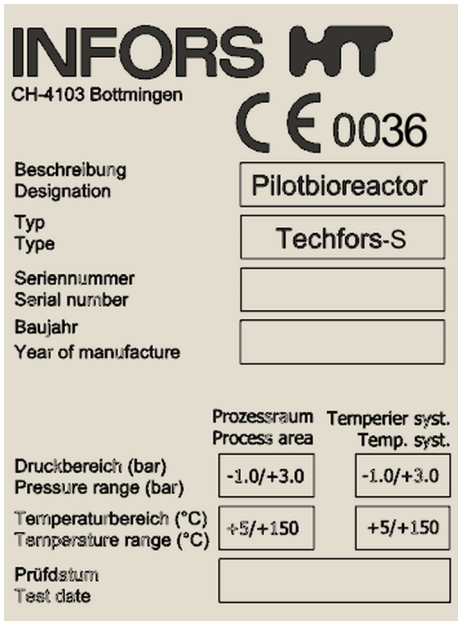
The identification plate is designed to allow clear identification of the device. It contains the following information:



- Manufacturer's name
- Designation = category of device
- Type = device type (name)
- S/N = serial number
- Year = year of manufacture
- Mains = nominal voltage and frequency
- Current = power consumption
- Manufacturer's address
- CE marking

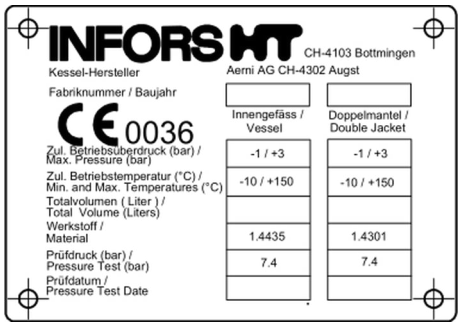
2.15.2 Plant Identification Plate

The plant identification plate is affixed to the central column and contains the following information:



- Device manufacturer and address
- Type of plant
- Device type (name)
- Serial number
- Year of manufacture
- CE marking
- Pressure ranges (bar) in process chamber and temperature control system
- Temperature ranges (bar) in process chamber and temperature control system
- Test date

2.15.3 Vessel Identification Plate



The vessel identification plate is welded on the outside of the vessel. It contains the following information:

- Device manufacturer and address
- Vessel manufacturer and address
- Factory number/year of manufacture
- Identification number of the testing agency

It also contains various values for the vessel and vessel jacket:

- Permitted overpressure during operation
- Permitted operating temperature
- Total volume (liters)
- Material
- Test pressure
- Test date

3 Options

3.1 Overview of the Options

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

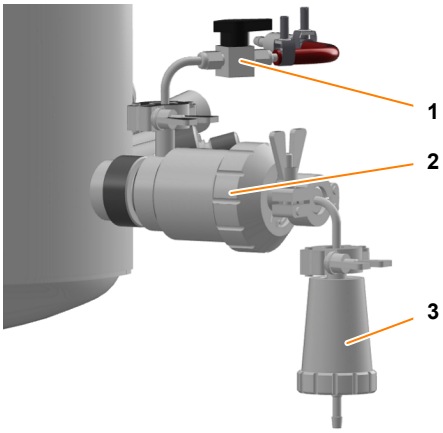
Designation	Additional Information
Lateral sample valve	➦ Chapter 3.2.1, page 88
Resterilizable feed line	➦ Chapter 3.3.1, page 90
Steam generator	➦ Chapter 3.4, page 94
Switch between tap water/chilled water	➦ Chapter 3.5, page 95
Recirculating chiller	➦ Chapter 3.6, page 95
Vessel top plate lifting device	➦ Chapter 3.7, page 96
Level detection	➦ Chapter 3.8.1, page 97
Pressure control	➦ Chapter 3.9.1, page 100
Weight measurement	➦ Chapter 3.10, page 102
Turbidity measurement	➦ Chapter 3.11.1, page 103
Exit gas analysis	➦ Chapter 3.12, page 105
pCO_2 measurement	➦ Chapter 3.13, page 107
Redox measurement	➦ Chapter 3.14, page 108
Permissive measurement	➦ Chapter 3.15, page 109
Pump(s)	➦ Chapter 3.16, page 109
Mobile CIP unit TechCIP	➦ Chapter 3.18, page 110

3.2 Sample Valve

3.2.1 Setup and Function

Overview

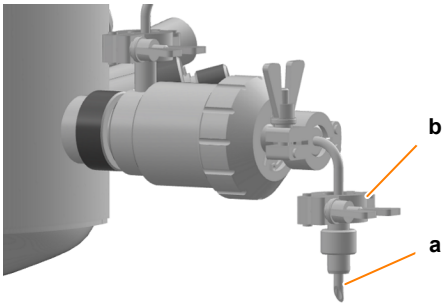
Sample valve *17.13.01* is installed in the Ingold nozzle on the side of the vessel. Also the steam trap is affixed to the valve using the condensate elbow and clamps, and the clean steam line (pressure hose) with manual valve *17.10.01* is mounted.



1 Clean steam valve (valve *17.10.01*) with steam line (pressure hose)
2 Harvest/sample valve *17.13.01*
3 Steam Trap

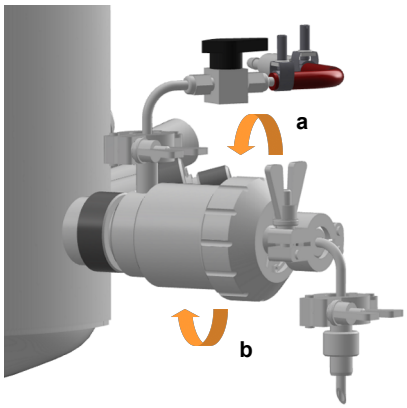
The sterilization of the harvest/sample valve is started via the touch screen software on the operating panel, see ➥ Chapter 8.9.5 'SIP Sample Valve – Sterilization Sample Valve' on page 234.

Sampling



The sample valve has a needle (a) for sampling. The needle is connected to the condensate elbow (b) with a clamp and a flat gasket. For sampling, the steam trap must be unscrewed from the needle.

Opening/Closing the Valve



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

3.2.2 Using the Sample Valve

Safety Notes

CAUTION

The sample valve gets very hot during sterilization. Depending on the cultivation temperature, it can also get hot during operation. This poses a risk of burns when touching the sample valve.

- After sterilization, let the sample valve cool down.
- Wear heat-resistant protective gloves when operating the sample valve.

Sampling

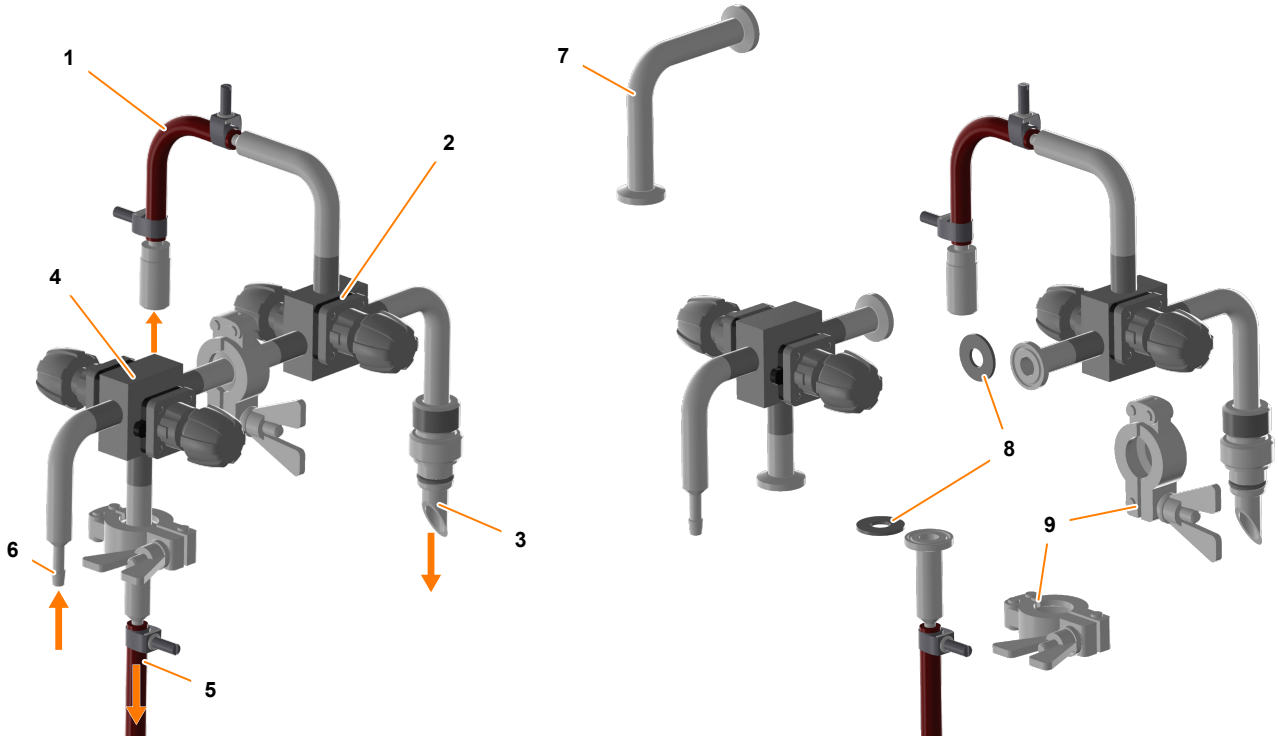
To take a sample, proceed as follows:

1. Have the sample bottle/container ready.
2. Unscrew the steam trap counter-clockwise from the needle in the valve.
   ➡ The needle is now visible.
3. Place the sample bottle under the needle. Or, if necessary, use the needle to pierce the septum on the sample bottle.
4. Open the valve. To do so, turn the valve counter-clockwise.
5. Fill the sample bottle with the required amount of liquid.
6. Close the valve. To do so, turn the valve clockwise.
7. If necessary, pull the needle out from the septum in the sample bottle.
8. Screw the steam trap to the needle clockwise.

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

3.3 Resterilizable Feed Line

3.3.1 Setup and Function



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 Reagent bottle connection, hose nozzle Ø 13.5 mm
7 Condensate elbow
8 Flat gasket
9 Clamp

The resterilizable feed line enables a sterile connection between the bioreactor and a container, e.g. a reagent bottle for adding sterile liquid, e.g. nutrient solution etc.

Before sterile liquid can be added to the vessel via the resterilizable 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. Sterilization in the autoclave: the block valve (sterile cross) *13.16.02* / *13.16.04* and the container/reagent bottle are sterilized separately in the autoclave.

2. Full sterilization: the block valve (sterile cross) *13.16.01* / *13.16.03* is mounted and sterilized in situ together with the vessel.

3. Sterilization of the feed line: the block valve (sterile cross) *13.16.02* / *13.16.04* is mounted, and the feed line is sterilized.

3.3.2 Preparing the Resterilizable Feed Line

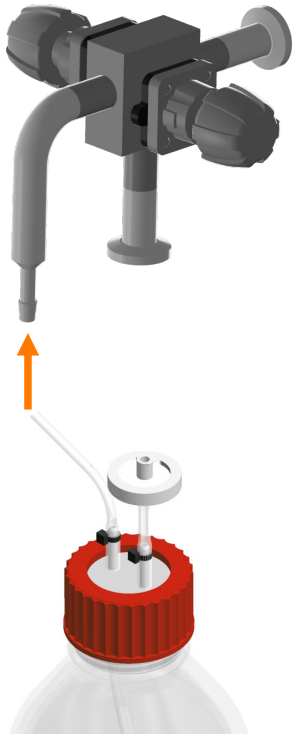
Safety Notes

CAUTION

The components of the feed line get very hot during sterilization.

- After sterilization, let the feed line cool down.
- Wear heat-resistant protective gloves when operating the valves of the feed line.

Autoclaving the Block Valve *13.16.02 / 13.16.04* and Reagent Bottle



For autoclaving the block valve *13.16.02 / 13.16.04*, proceed as follows:

1. Prepare/equip the reagent bottle for sterilization in the autoclave (➥ Chapter 4.4.2 'Preparing Reagent Bottles for Cultivation' on page 114).

   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 mounted.

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.

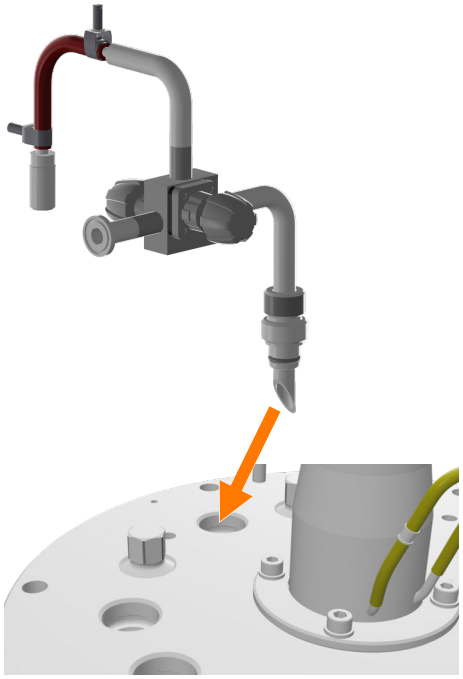
3. Connect the hose line of the reagent bottle to the block valve *13.16.02 / 13.16.04* and secure with cable ties.

4. Close both valves.

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

Options

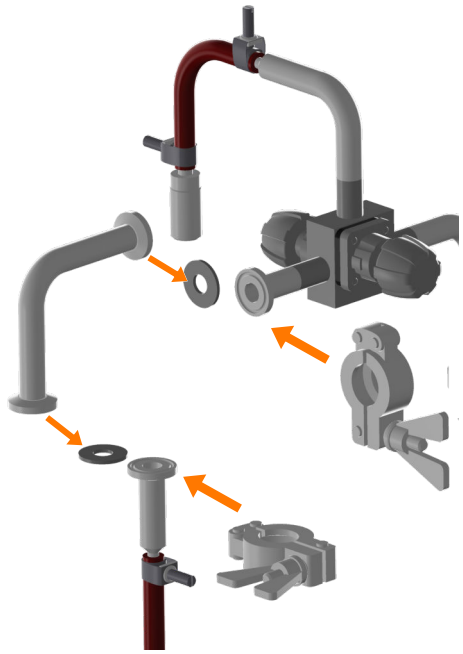
Sterilize Block Valve *13.16.01 / 13.16.03* in situ



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

1. Insert the connection nozzle of the block valve *13.16.01 / 13.16.03* into in a 19 mm port in the vessel top plate and tighten manually.

   Ensure that the connection nozzle is equipped with an intact O-ring.



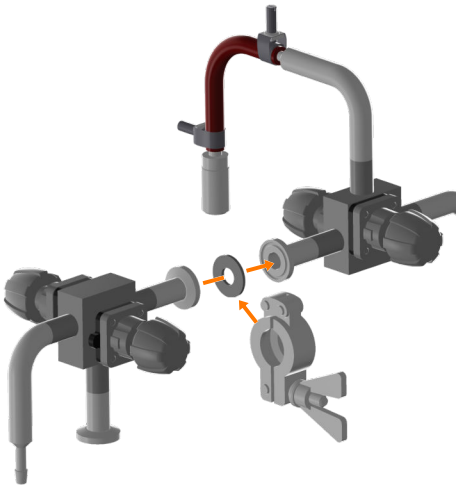
2. Use the clamps to connect the condensate elbow to block valve *13.16.01 / 13.16.03* and connect to the condensate line.

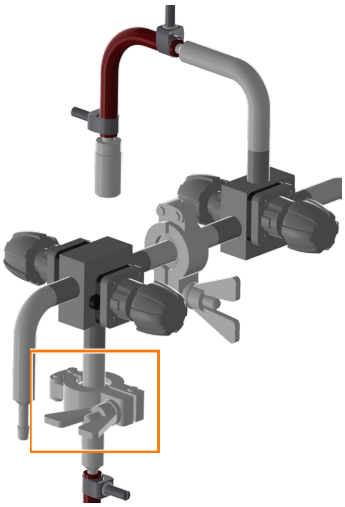
   Ensure that the flat gaskets are placed between the connection flanges.

3. Sterilize together with the vessel.

   For a detailed description of the sterilization, see ➦ Chapter 8.9.3 ‘Full Sterilization’ on page 228.

Sterilizing the Feed Line





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

1. Loosen the clamp and remove it together with the condensate elbow from the block valve *13.16.01* / *13.16.03*.
2. Use a clamp to connect 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.

> 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*.

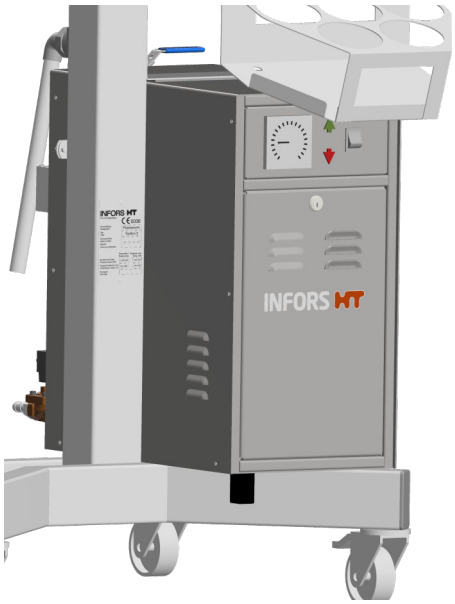
   Ensure that the flat gasket is placed between the connection flanges.
4. Connect the reagent bottle to the pump (➥ Chapter 2.3.2 ‘Inserting the Pump Hoses’ on page 28).
5. Sterilize the feed line.

   For a detailed description of the sterilization process, see ➥ Chapter 8.9.6 ‘SIP Feed Line – Sterilization Feed Line’ on page 236.

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

3.4 Steam Generator

Function



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

The steam generator is available in two variants with different output. The variant used depends on the vessel volume:

- 6 kW: total volume of vessel 15 L
- 10 kW: total volume of vessel 30 L and 42 L

Requirements for the Mains Connection

The steam generator has a separate mains connection.

To avoid dangers due to electrical current, the in-house mains connection must meet the following requirements:

- Tri-phase, constant power supply
- In the building, the power supply must be protected using a fault current protection switch (RCD – Residual Current Device).

Refer to the technical data for the electric connection values, see ➦ 'Electric Connection Values' on page 264.

For details on the steam generator, see the separate documentation provided by the manufacturer. Read the manual before commissioning the device and follow the instructions.

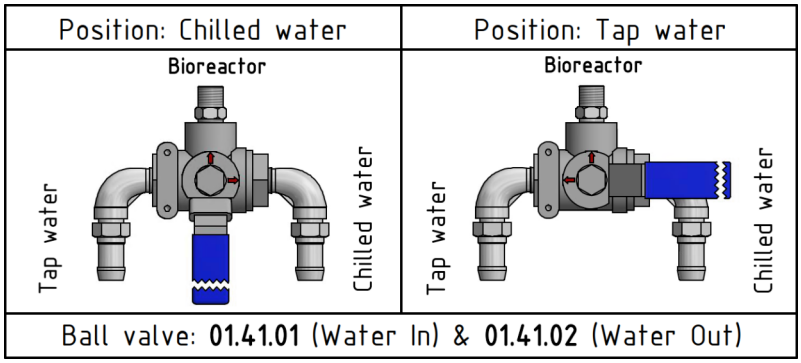
3.5 Switching between Tap Water/Chilled Water

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) can be used to switch between tap water and chilled water.

NOTICE

An incorrect position of the ball valves (tap water IN open/chilled water OUT open) for tap water/chilled water can lead to overfilling or overflowing of the cooling circuit!

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

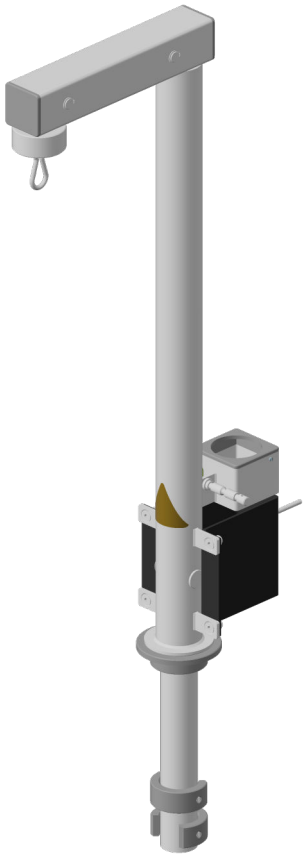


Suitable instructions for the process are also displayed in various dialog boxes in the touch screen software.

3.6 Recirculating Chiller

The device can also be supplied with chilled water via a separately available recirculating chiller. In this case, as when using a cooling water system on the house side, the optional 3-way ball valves *01.41.01* and *01.41.02* for switching between tap water and chilled water are required and automatically integrated into the device.

3.7 Lifting Device for Vessel Top Plate



A lifting device is available for lifting and lowering the vessel top plate. This device is mounted on the central column of the basic unit and operated using a rope winch. We recommend using a lifting device in particular for vessels with a total volume of 30 liters and 42 liters.

All information regarding function, operation, technical data and safety is available in the separate operating manual.

3.8 Level Detection

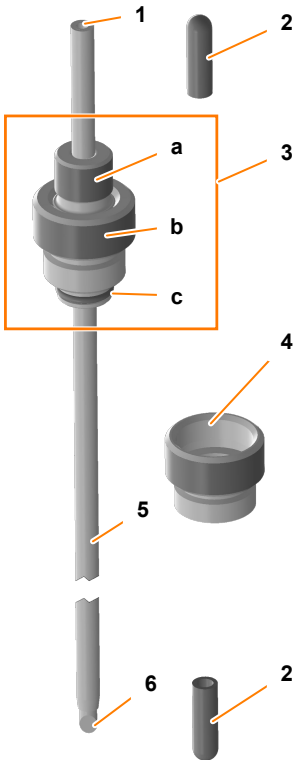
3.8.1 Setup and Function

Function

The level sensor detects liquid in the vessel. As soon as it detects liquid, a signal is generated. The *Output* of the parameter *Level* indicates "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. Configurations of this type are available on request.

Level Sensor



1 Cable connection sensor head
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!)

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

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

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.

3.8.2 Mounting and Connecting the Level Sensor

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 sterilization. Pulling out, however, is possible even during cultivation and bears a significantly lower risk of contamination.

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.

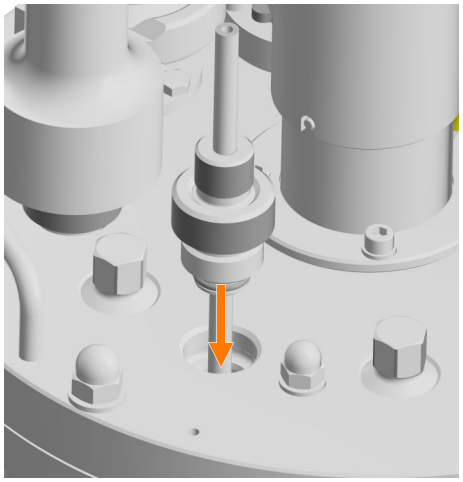
Options

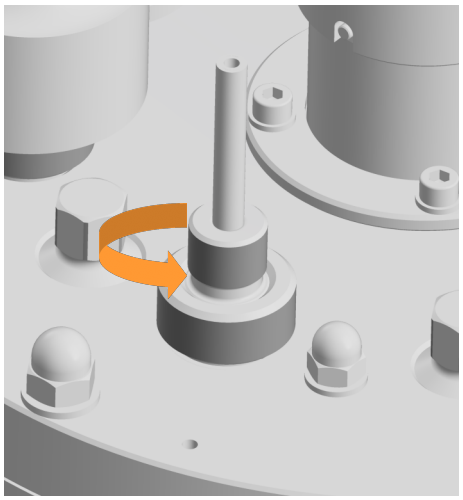
NOTICE

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 adaptor is tightened, the transparent insulation may be damaged.

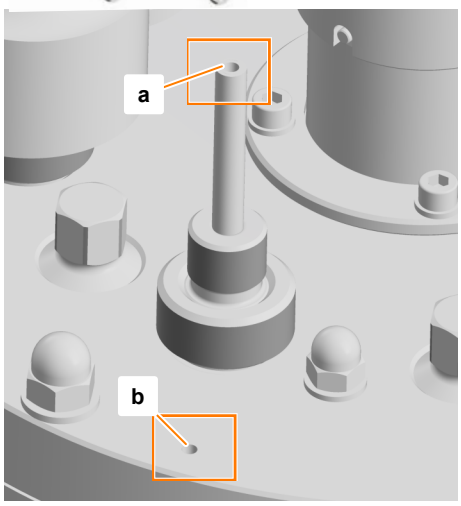
Proceed as follows:

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



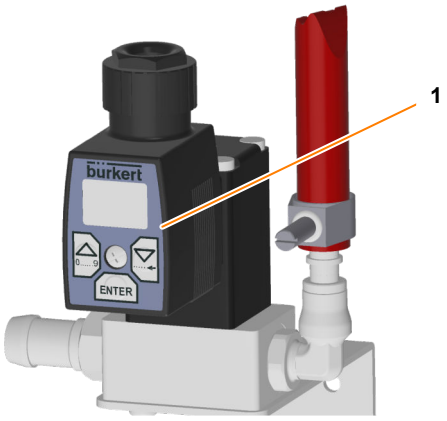
6. Connect the sensor cable with the two banana connectors:

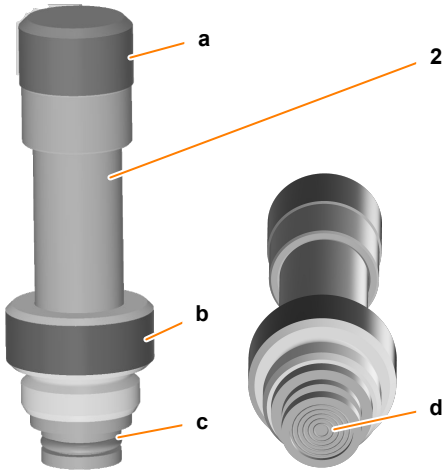
- Insert the red banana connector into the connector (a) on the top of the sensor.
- Insert the black banana connector into ground connection (b) in the vessel top plate.

3.9 Pressure Control

3.9.1 Setup and Function

Function





1 Pressure control valve *03.11.01* (*exit gas*)
2 Pressure sensor *08.31.01*

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

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

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

Maintenance

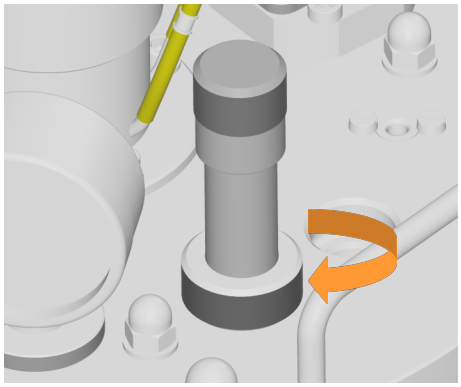
The pressure sensor is generally maintenance free. The re-calibration cycle depends on the conditions under which it is used. However, we do recommend annual re-calibration by the sensor's manufacturer.

3.9.2 Mounting and Connecting the Pressure Sensor

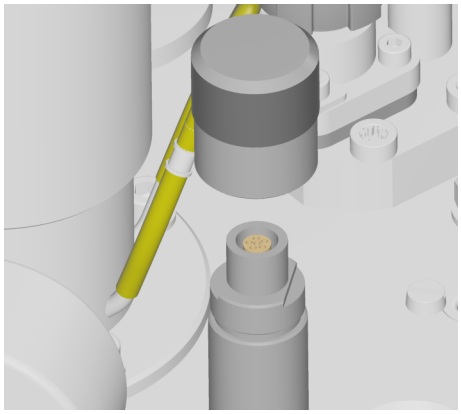
The pressure sensor must be mounted and connected prior to sterilization. To do so, proceed as follows:

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

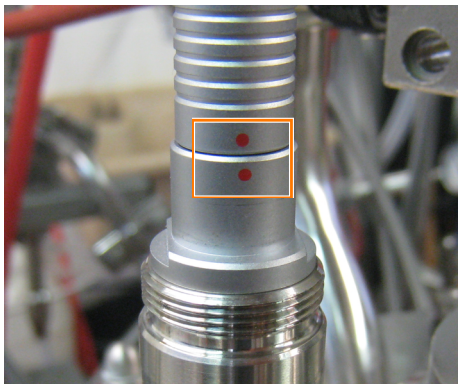
> **NOTICE**
>
> The steel membrane is very delicate and can be damaged by friction or knocks from hard objects.



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



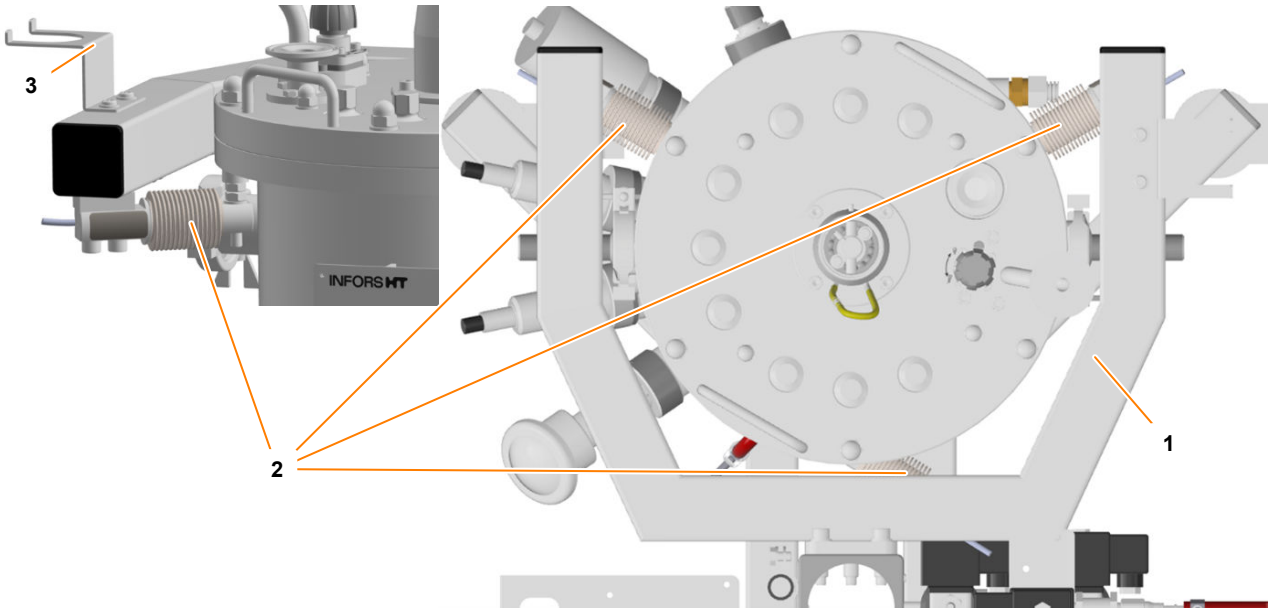
3. Manually remove the steel cap from the sensor head connection.



4. Connect the sensor cable. In doing so, align the red marking of the cable plug with the red marking on the sensor head connection.

3.10 Weight Measurement Vessel – Load Cell

Setup and Function



1 Frame of the weighing system
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 screwed to the central column of the device. The load cells are distributed evenly and placed on the underside of the system frame. Bolts on the underside of the vessel flange are used as load application points of the vessel.

Measurements are output in the *Weight* parameter in the touch screen software. The weight display can also be tared there.

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

3.11 Turbidity Measurement

3.11.1 Setup and Function

Function

The ASD25-N measurement system from the manufacturer Optek 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.

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

Depending on the cell density, sensors with different path lengths are available:

- OPL01: for very high cell densities
- OPL05: for higher cell densities
- OPL10: for lower cell densities

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.

Calibration

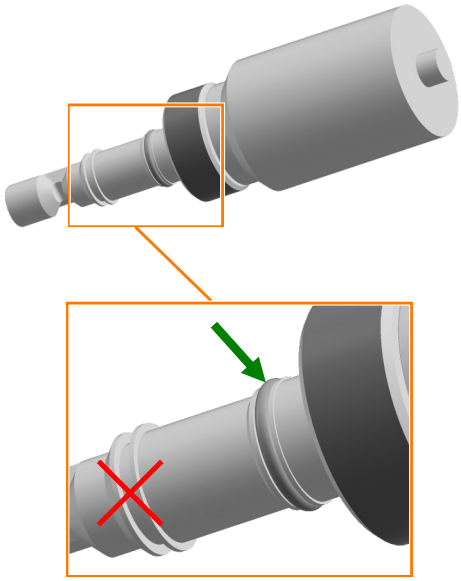
The turbidity sensors are pre-calibrated ex-factory. Inserts are available for reference measurement.

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 sterilization, depending on the application in question.

Mounting

The turbidity sensor is mounted into an Ingold nozzle in the vessel.

3.11.2 Mounting and Connecting the Turbidity Sensor



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:

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

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

2. Insert the turbidity sensor into the Ingold nozzle.
3. Manually tighten the coupling nut.
4. Connect the sensor cable.

3.12 Exit Gas Analysis

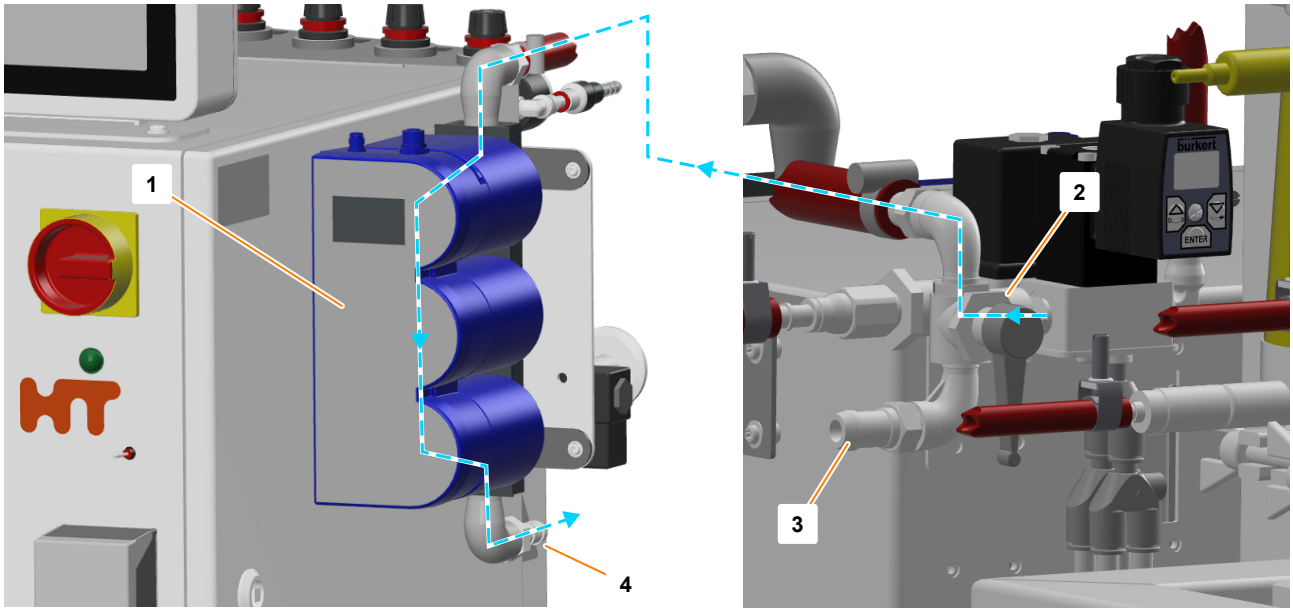
Setup and Function

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 analyzed in the exit gas flow of the bioreactor.

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 BlueSens are available.

Connection and Exit Gas Routing

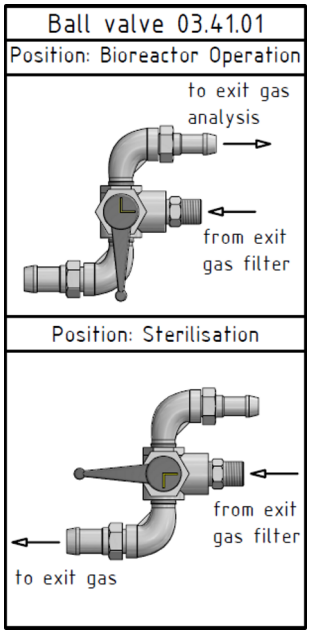
The gas sensors are installed ex-factory. The figure shows the BlueVary type as an example of a gas sensor.



1 BlueVary gas sensors
2 3-way ball valve *03.41.01* (here: position Bioreactor Operation = exit gas analysis)
3 Direct exit gas outlet (without exit gas analysis)
4 Outlet of exit gas from exit gas analysis

(both connections for a provider-side exit gas system/hose)

Options



During cultivation, exit gas is routed through the gas sensors. During sterilization, it must be discharged directly into the provider'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*.

NOTICE

Moisture ingress into gas sensors for exit gas analysis can damage them or falsify the measurement results.

The exit gas line leading through the exit gas analysis must be closed during sterilization.

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

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

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

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.

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.

3.13 pCO_2 Measurement

Setup and Function

The saturation of dissolved carbon dioxide (CO_2) in the culture is measured using a digital CO_2 sensor with integrated temperature sensor. Measurements in hPa are displayed on the corresponding transmitter and also in the touch screen software.

The measurement display of the pCO_2 parameter on the touch screen software is set similarly to the measurement display of the transmitter to a range of 0 hPa to 1000 hPa.

Measurement system	Properties
METTLER digital	▪ Measurement principle: potentiometric ▪ Type: InPro5000i, ISM (digital)

Mounting

The pCO_2 sensor is mounted into an Ingold nozzle in the vessel. To this end, the sensor is supplied with suitable insertion housing by the sensor's manufacturer.

Calibration

The sensor is calibrated directly at the transmitter and in accordance with the information provided by the manufacturer of the sensor and transmitter.

3.14 Redox Measurement

Overview

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 analog sensors by the manufacturer METTLER or digital sensors by the manufacturer HAMILTON.

Measurement system	Properties
METTLER analog	▪ Classic combined sensor (oxidation reduction potential measurement against a reference) ▪ Type: Pt4805-DPAS-SC-K8S To use the sensor, the device must feature a corresponding connection.
HAMILTON digital	▪ Classic combined sensor (oxidation reduction potential measurement against a reference) with integrated electronics ▪ Type: Easyferm Plus ORP ARC 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 connection cable is required.

Mounting

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

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.

3.15 Permissive Measurement

Setup and Function

Sensors of the ABER Futura system 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.

Calibration

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

3.16 Pumps

In addition to the four standard pumps integrated into the device, additional peristaltic pumps are available. Up to two additional analog pumps can be integrated. The number of possible external pumps depends on the options that already exist.

Specifications	Can be integrated	External, Watson Marlow	External, Masterflex
			
Type	analog (*Feed 2* and *Feed 3*)	120 U/DV	L/S Cytoflow, 3-roll pump head
Max. speed	150 min^{-1}	200 min^{-1}	600 min^{-1}
Setting range	0 % to 100 %	0 % to 100 %	0 % to 100 %
Increment	0.1 %	0.1 %	0.1 %

For more information on the external pumps, see the separate documentation from the pump manufacturers.

3.17 Balances

The touch screen software allows the connection of one balance to the bioreactor. If more than one balance is to be connected, the connection via the bioprocess software eve® is required.

Balances of the following type are available from the device manufacturer:

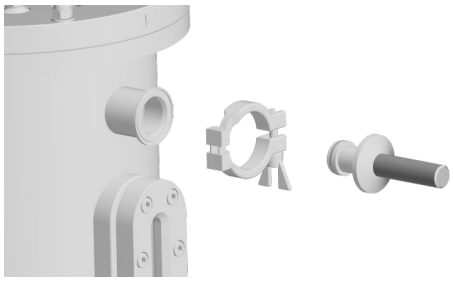
- Kern DS 30K0.1-A
- Kern FKB 6K0.02-B
- Mettler MA6002
- Mettler MA32001L

In addition to a specific device firmware, these balances also require a suitable configuration, which is carried out by the device manufacturer. This is the only way to ensure smooth functionality.

Non-configured and non-listed models are not supported. If, however, a non-listed balance is to be integrated or several balances of a compatible type are to be used, there is the option of integration into the bioprocess software eve®. Please contact the device manufacturer INFORS HT for further information.

3.18 Mobile CIP Unit TechCIP

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



To be able to clean the bioreactor with the CIP unit, an adjusted Techfors-S vessel design is required. In this case, the vessel has two additional tri-clamp ports with blanking plugs.

4 Accessories, Material and Hoses

4.1 Overview of the Accessories

By default (column S), the device is supplied with some accessories and material. Additional accessories are optionally available (column O).

Designation	S	O	Additional Information
Starter set	x		➦ Chapter 4.2, page 111
Connection set	x		➦ Chapter 4.3, page 112
Reagent bottles	x	x	➦ Chapter 4.2, page 111 ➦ Chapter 4.4.1, page 113
Push valves		x	➦ Chapter 4.5.1, page 117
Inoculation needles		x	➦ Chapter 4.6.1, page 121
Vessel light		x	➦ Chapter 4.7.1, page 124

4.2 Starter Set

The starter set contains the same material for all three available vessel sizes.

Designation	Use
Reagent bottle, 500 mL	Addition of reagent and nutrient solution
Hexagon socket spanner SW17	Blanking plugs in 19 mm ports
Septum, Ø = 19 mm, MVQ silicone, transparent	For inoculation in 19 mm ports
Cable tie, polyamide 2.4 x 85 mm, black	Attachment for silicone hoses and pump hoses
Hose connector, 1/8" x 1/8", PVDF	Connection of pump heads to the hose with inside Ø 2.5 mm

4.3 Connection Set

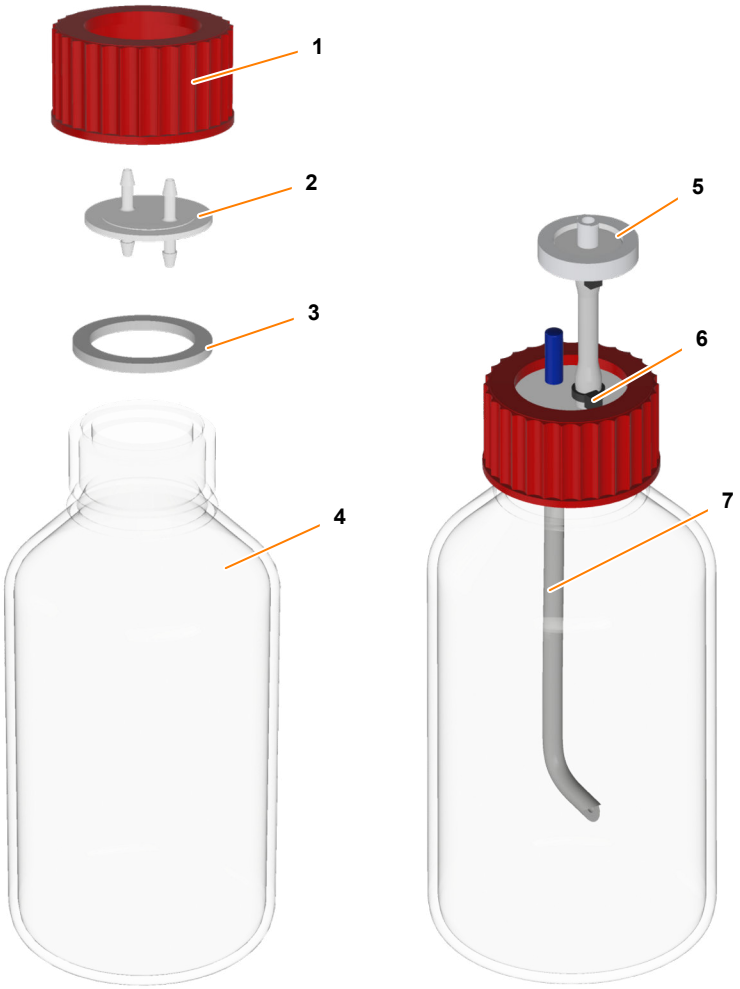
The connection set contains the same hose and attachment material for all vessel sizes.

Accessories	Ø mm	Use
Pump hose (Marprene/Bioprene)	3.2 x 6.4	Connection reagent bottle to peristaltic pump
Pressure hose	8.0 x 14.5	Gas connection
	10.0 x 17.0	Steam connection
	12.5 x 21.0	Condensate
Hose clamp	17.0	Gassing/inlet air hose attachment
	19.0	Attachment for water inlet and outlet hoses as well as steam inlet hoses
	12 – 22	Condensate hose attachment

4.4 Reagent Bottles

4.4.1 Setup and Function

Overview



1 Screw cap
2 Hose connector plate
3 Flat gasket
4 Laboratory bottle
5 Filter
6 Cable tie
7 Silicone hose

Function

Reagent bottles are used as containers for reagent and nutrient solution. Connected to the appropriate peristaltic pump and an addition utensil, e.g. an inoculation needle, the liquid is pumped into the vessel. Different sizes of reagent bottle are available. They are delivered equipped with hoses and filters.

Silicone hoses or, depending on on-site specifications, weldable hoses for sterile hose connections are not included in the scope of delivery. Pump hoses are included in the starter set (➥ Chapter 4.2 'Starter Set' on page 111).

4.4.2 Preparing Reagent Bottles for Cultivation

Reagent bottles are autoclaved together separately with the addition utensils (e.g. inoculation needles). The same goes for the bottle that is filled aseptically with the stock culture (inoculum) shortly before inoculation.

NOTICE

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

- Equip each reagent bottle with an open pressure equalization line and a clean and dry filter.
- Use only clean and intact hoses and affix these properly.

To equip a reagent bottle for use, proceed as follows:

1. Unscrew the screw cap together with the hose connector plate.
2. Fit a piece of silicone hose onto one of the two hose connectors on the inside of the plate.

   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.

   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 all hose connections with cable ties.

4. Place a long piece of silicone hose on the equilateral connection on the outside of the hose connector plate.

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

5. Place a short piece of silicone hose on the second connection on the outside of the hose connector plate.

6. Fit the filter on the short hose piece.

7. Secure the hose connections with cable ties.

8. Before autoclaving, thoroughly rinse the hose of the reagent bottle with distilled water.

9. Depending on the application, fill the reagent bottle and close the screw cap or fill the reagent bottle under sterile conditions after autoclaving, if necessary.

NOTICE

Use of highly corrosive reagents, such as hydrochloric acid HCl, can cause damage to components that come into contact with it.

Fill reagent bottles with heat-resistant reagents only. Sterilize non-heat-resistant nutrient solution separately and only transfer it in a sterile manner to the reagent bottle after autoclaving.

10. Ensure the flat gasket between bottle neck and screw cap sits and seals correctly.

11. Clearly label the reagent bottle according to its content.

12. Connect a suitable piece of pump hose (Marprene/Bioprene recommended) to the silicone hose of the reagent bottle using a hose connector.

13. Connect a fitting piece of silicone hose with a hose connector to the open end of the pump hose.

14. Connect the silicone hose to the addition utensil (e.g. inoculation needle).

15. Secure all hose connections with cable ties.

16. Autoclave the reagent bottle with the addition utensil. For details on autoclaving addition utensils, refer to the corresponding chapter of the addition utensil.

4.4.3 Specifications

Volumes/Hoses

Size/volume	Silicone hose diameter
500 mL	2 x 6 mm
1000 mL	3 x 5 mm
2000 mL	3 x 5 mm
5000 mL	3 x 5 mm
10000 mL	3 x 5 mm

Filter

Data	Value	Unit
Filter diameter (hydrophobe)	25	mm
Filter retention rate	0.45	µm

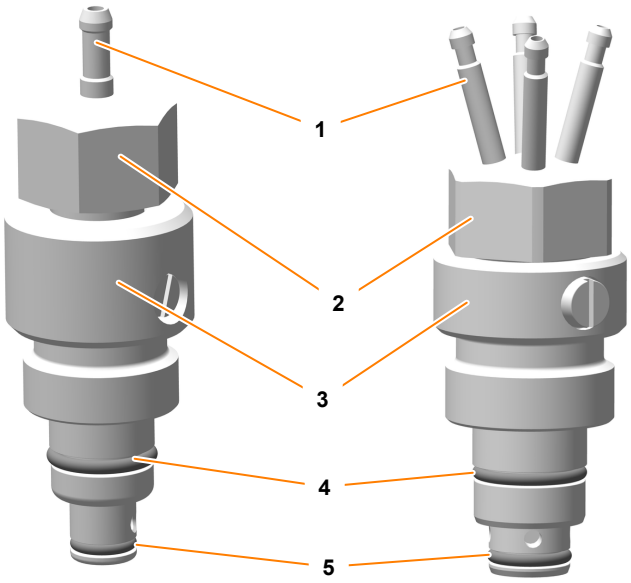
Materials

Data	Value
Laboratory bottle	Borosilicate
Flat gasket	Silicone
Filter membrane	PTFE
Hose connector plate	PDVE

4.5 Push Valves

4.5.1 Setup and Function

Overview



1 Hose connector, 1 x or 4 x
2 Rotary piston
3 Valve body
4 Valve body O-ring
5 Rotary piston O-ring

Function

Push valves are used for the sterile addition of liquids such as reagents or nutrient solution into the vessel.

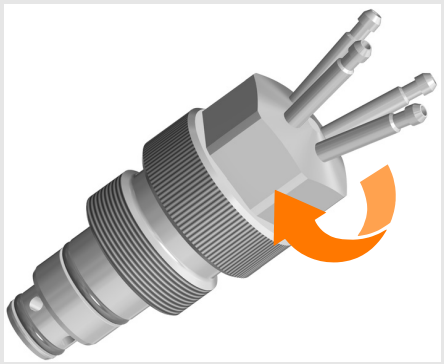
Two push valve designs are available: the figure shows a push valve with a hose connector on the left and a 4 inlet push valve with four hose connectors on the right. Both push valves are depicted in their open state.

Mounting

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

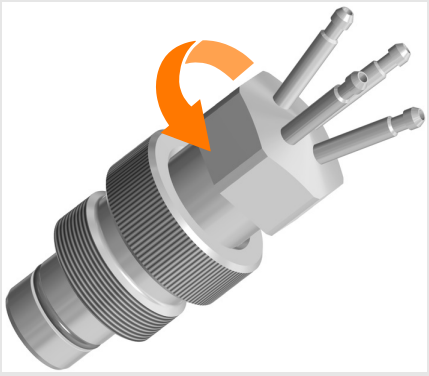
Hose connector push valve	Inside Ø	3.0 mm
	Outside Ø	6.0 mm
Hose connectors 4 inlet push valve	Inside Ø	2.0 mm
	Outside Ø	4.0 mm

Opening/Closing Push Valves



- Opening the push valve: 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.



- Closing the push valve: turn the rotary piston counter-clockwise.

The lower part of the rotary piston is retracted. The upper part protrudes from the valve body.

4.5.2 Preparing Push Valves for Cultivation

Preparation und Use

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

- Sterilization in an autoclave: sterilize the closed push valve together with a prepared reagent bottle/laboratory bottle separately in the autoclave.
- In situ sterilization: connect the reagent bottle to the (calibrated) pump and sterilize the closed push valve together with the vessel in situ.
- Cultivation: open the push valve.

For more information, see the following chapters:

- ➥Chapter 4.4.2 ‘Preparing Reagent Bottles for Cultivation’ on page 114
- ➥Chapter 8.8.2 ‘Calibrating the Pumps’ on page 221

Autoclaving a Push Valve

Proceed as follows:

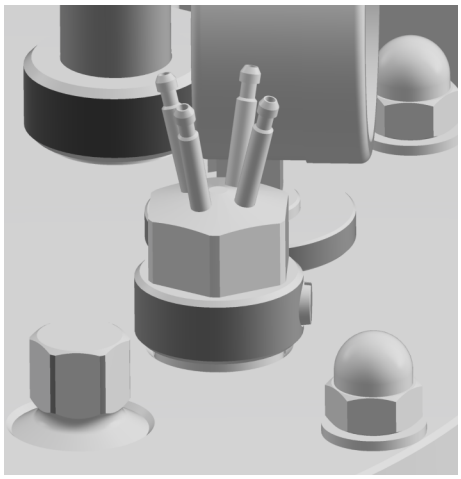
1. Connect the hose of the reagent bottle to the push valve.

   When using a 4 inlet push valve, up to four reagent bottles can be connected.

2. Close any unused connection on the 4 inlet push valve.

3. Ensure that the push valve is closed, and close it if necessary.
4. Secure all hose connections with cable ties.
5. Lightly cover the filter of the reagent bottle(s) with aluminum foil.
6. Wrap the push valve in aluminum foil.
7. Pinch off the hose/hoses with hose clamps.
8. Autoclave everything together e.g. at 121 °C for e.g. 30 to 60 minutes.

Sterilizing Push Valves in Situ



After autoclaving and sufficient cooling down time, proceed as follows:

1. Manually screw the closed push valve into a 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) (➥ Chapter 2.3.2, page 28).
3. Sterilize the push valve together with the vessel in situ.

   ➡ The part of the push valve that is exposed after autoclaving is now sterile again as well.

Using Push Valves

Proceed as follows:

1. Open the push valve on the rotary piston clockwise.
2. Open the clamp.
3. Fill the hose with the liquid to be pumped via the corresponding pump up to the visible inlet in the push valve (➥ Chapter 8.8.4, page 224).
4. Start the cultivation (➥ Chapter 8.9.7, page 239).

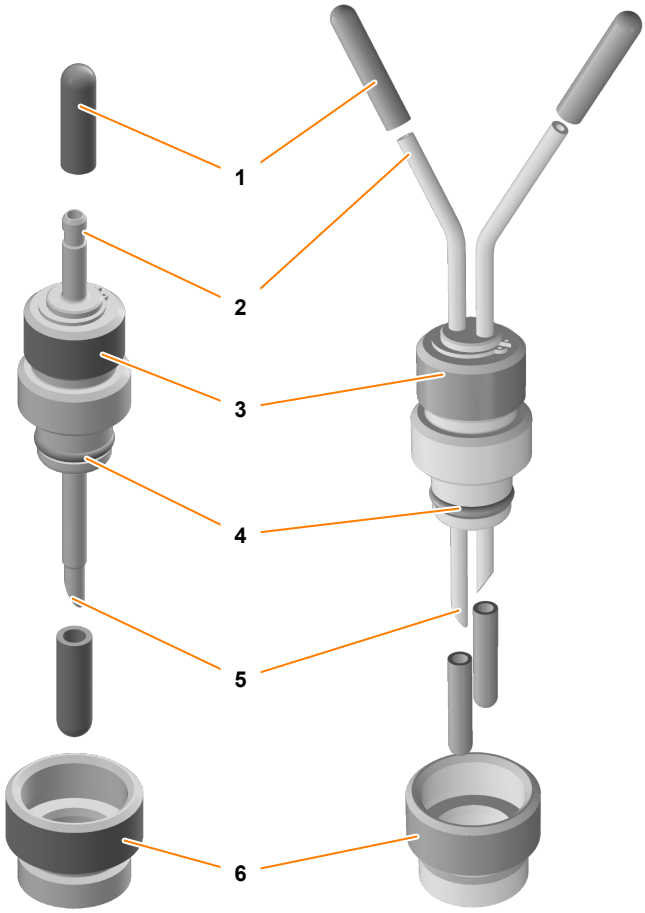
4.5.3 Specifications

Data	Value
Material in contact with medium	316L
Surface in contact with medium	Ra 0.8 µm, electropolished
Material O-rings	EPDM

4.6 Inoculation Needles

4.6.1 Setup and Function

Overview



1 Protective cap (cannot be sterilized!), 2 x or 4 x
2 Hose connector, 1 x or 2 x
3 Hollow screw
4 O-ring
5 Needle, 1 x or 2 x
6 Septum collar

Function

Inoculation needles are used to add liquids such as reagent, nutrient solution or the inoculation culture (inoculum) to the vessel. For this purpose, a septum, which is fixed with a septum collar in the port in the vessel top plate, is pierced with the inoculation needle.

The inoculation needles are supplied with a septum collar. Their tip is cut on a bias to enable easy piercing. The hose connector and the very sharp tip are provided with non-autoclavable protective caps.

Two inoculation needle designs are available. The figure on the left shows a single inoculation needle and the figure on the right shows a double inoculation needle.

Mounting

A thread is used for mounting it in the 19 mm port or the septum collar.

Hose connector (1 x or 2 x)	Inside Ø	4.0 mm
	Outside Ø	6.0 mm

4.6.2 Preparing Inoculation Needles for Cultivation

Preparation und Use

Preparation and use of an inoculation needle mainly comprise the following three steps:

- Sterilization in an autoclave: sterilize the inoculation needle together with a prepared reagent bottle/laboratory bottle separately in the autoclave.
- Prior to in situ sterilization: equip the port in the vessel top plate with the septum and septum collar.
- After in situ sterilization: connect the reagent bottle with the (calibrated) pump and use the inoculation needle to pierce the septum and screw the needle into the septum collar.

For more information, see the following chapters:

- ➦ Chapter 4.4.2 ‘Preparing Reagent Bottles for Cultivation’ on page 114
- ➦ Chapter 8.8.2 ‘Calibrating the Pumps’ on page 221
- ➦ Chapter 2.4.4 ‘Equipping the Ports with the Septum and Septum Collar’ on page 38

Autoclaving Inoculation Needles

Proceed as follows:

1. Carefully remove the protective caps from the inoculation needle.
2. Get the septum collar ready for equipping the port in the vessel top plate.
3. Connect the hose of the reagent bottle to the inoculation needle.
4. Secure all hose connections with cable ties.
5. Lightly cover the filter of the reagent bottle with aluminum foil.
6. Wrap the inoculation needle in aluminum foil.
8. Pinch off the hose with the hose clamp.
9. Autoclave everything together e.g. at 121 °C for e.g. 30 to 60 minutes.

Using Inoculation Needles

After in situ sterilization, proceed as follows:

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

Add a few drops of (70 %) ethanol to the septum to provide additional protection against contamination.

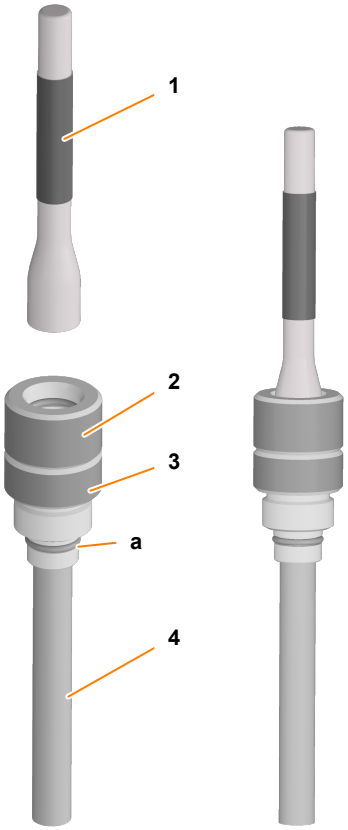
3. Remove the aluminum foil from the inoculation needle.
4. Immediately pierce the septum with the inoculation needle.
5. Screw the inoculation needle into the septum collar.
6. Open the clamp.
7. Fill the hose with the liquid to be pumped via the corresponding pump up to the visible inlet in the inoculation needle (➥ Chapter 8.8.4, page 224).
8. Start the cultivation (➥ Chapter 8.9.7, page 239).

4.6.3 Specifications

Data	Value
Material in contact with medium	316L
Surface in contact with medium	Ra 0.8 µm, electropolished
Material O-ring	EPDM

4.7 Vessel Light

4.7.1 Setup and Function

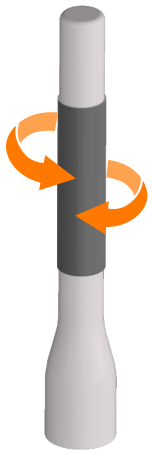


1 Torch
2 Hollow screw
3 Threaded housing with O-ring (a)
4 Glass lens

The vessel light consists of a torch and threaded housing with thread and O-ring with integrated glass lens for screwing into a 19 mm port in the vessel top plate. A hollow screw is screwed into the threaded housing and is thus used to affix the torch.

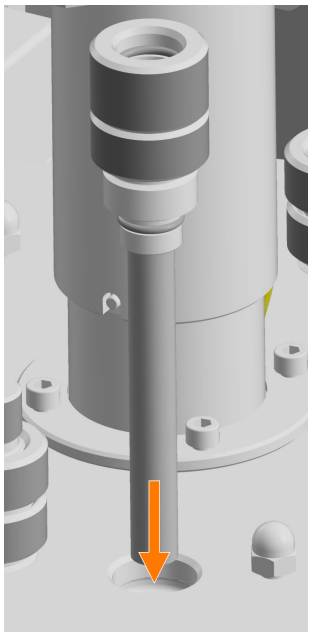
Switching the Vessel Light On and Off

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

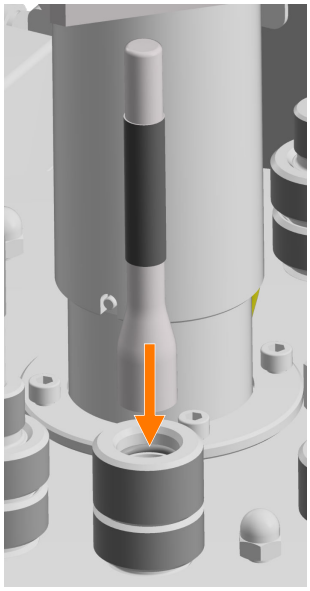


4.7.2 Mounting the Vessel Light

The vessel light is mounted in a 19 mm port in the vessel top plate. To do so, proceed as follows:



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



2. Place the torch in the hollow screw.

5 Transport and Storage

Inbound delivery and transport to the assembly location are performed only by INFORS HT employees or by persons authorized by INFORS HT. Nonetheless it is possible that the provider's personnel is entrusted with transport tasks in the context of on-site transport. In this case, observe the following notes.

5.1 Transport

⚠ WARNING

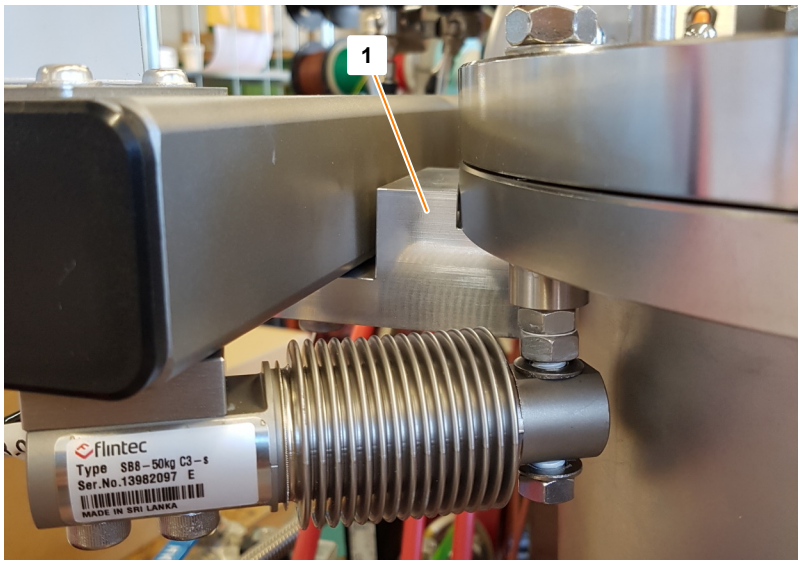
Improper transport, use of incorrect auxiliary tools and careless handling of the device may lead to injuries and significant damage to property.

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

- Before moving a device, all provided transportation safety devices must first be affixed to protect the device from damage.
- Always work at least in pairs and use suitable auxiliary equipment when transporting the device.
- Especially when using auxiliary tools, keep in mind that the device's center of gravity is not in the middle.

5.2 Transportation Safety Device

To protect the load cells from damage during transport, a transportation safety device is fitted to the weight measurement frame. This means that two plates (1) are screwed to the right and left on the underside of the frame.



The safety plates prevent the load from being applied to the load cells by the vessel. The safety plates are only removed when qualified personnel installs the device and are handed over for safekeeping. The transportation safety device must be mounted prior to any transport of the device.

5.3 Storage

- Decontaminate, thoroughly clean and dry the vessel and all accessories every time before placing them in storage.
- Maintain and store sensors produced by other manufacturers in accordance with their instructions.
- 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 humidity but protected against frost.
  - Storage temperature: 5 °C to 55 °C
  - Relative humidity, non-condensing: 10 % to 95 %
- Protect the device from aggressive media, direct sunlight and vibrations.

6 Installation and Commissioning

Only the manufacturer's qualified expert personnel or persons authorized by the manufacturer may install and initially commission the device.

After installation of the device, the temperature control circuit must be filled first. This then remains filled and is emptied only when repair or service work is performed. After connecting the motor cable, the basic functions of the bioreactor are tested briefly in a test run. Since these tasks must not be performed by the operator, they are not covered in this operating manual. Hence, the following section only lists the connection requirements and energies to be provided by the provider.

⚠ WARNING

Installation and initial commissioning require trained expert personnel with sufficient experience. Errors during installation may lead to dangerous situations or significant damage to property.

- Only the manufacturer's expert personnel or persons authorized by the manufacturer may install and initially commission the device.
- Contact the manufacturer if the device is to be placed in a different location.

6.1 Operating Conditions at the Installation Location

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

- The figures and ranges specified in the technical data must be observed (➥ Chapter 12.2 'Connections and Connection Values' on page 263 and ➥ Chapter 12.5 'Operating Conditions' on page 282).
- The device must only be installed inside a laboratory or a laboratory-like environment.
- The installation surface must be level, sufficiently stable and load-bearing.
- There must not be any sources of electrical interference in the vicinity.
- The working environment is equipped with a sufficient ventilation system, depending on the application.

6.2 Minimum Distances to the Device

The device must be positioned at least 150 mm away from walls, ceilings and other devices.

Furthermore, make sure that the vessel top plate with its built-in-parts can be easily lifted off and removed from the vessel. When calculating the distance between the device and the ceiling, this must be taken into account.

6.3 Requirements for the Mains Connection

To avoid dangers due to electrical current, the in-house mains connection must meet the following requirements:

- Constant power supply
- The power supply of the device must be secured on-site by means of an fault current protection switch (RCD – Residual Current Device) of RCCB type B.

In addition to that, ensure the following:

- The building's mains connection can be accessed at all times.
- The voltage values of the device match those of the local mains voltage. Note the information on the identification plate.

Refer to the technical data for the electric connection values.

6.4 Requirements for Connections and Interfaces

To ensure trouble-free operation of the device, certain conditions must be met by the provider. In addition to compliance with the connection pressures, these include further requirements for the supply and discharge of the various energies as well as for process gas and steam. These are listed in the following sections.

For further information on connection pressures and connection sizes, see ➦ Chapter 12.2 'Connections and Connection Values' on page 263.

Process Gas

- Process gases must be dry, clean, and free of oil and dust (recommended pre-filter: 10 µm).
- Compressed air as process gas: recommended compressed air quality as per DIN ISO 8573-1: Class 1,2,3,4

! NOTICE

Compressed air containing water or oil can lead to damage to the mass flow controllers.

Exit Gas

- The exit gas must be dissipated securely by means of a suitable, gas-tight hose.
- The exit gas line must be higher than the exit gas filter.

Water for Temperature Control Circuit

Water for the temperature control circuit must be of the following quality: $CaCO_3$-concentration 0 mmol L^{-1} to 1.5 mmol L^{-1}

NOTICE

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

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) mounted on the device can be used to manually switch between cooling water and tap water.

NOTICE

An incorrect position of the ball valves (tap water IN open/chilled water OUT open) for tap water/chilled water can lead to overfilling or overflowing of the cooling circuit!

Steam

The device's steam is supplied by the building or via an optional integrated steam generator.

The steam must be of clean steam quality and can be guided through a 5 µm filter.

Required Amount of Steam for each Vessel Size

Vessel size	Vessel & filters for inlet air und 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)

Water for the integrated steam generator must be of the following quality: $CaCO_3$ concentration 0 mmol L^{-1} up to a max. of 0.53497mmol 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 of the device and following the instructions therein.

Outlets

- All drains must be heat resistant (max. 100 °C).
- For safety reasons the drains must not be in the immediate vicinity of the operator.
- Contaminated liquids must be drained safely and disposed of in an environmentally friendly manner.

Hoses

Conditions for all hoses used:

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

6.5 Safety Valves

CAUTION

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

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

To ensure that, if the safety valve of the vessel or the temperature control system is triggered, escaping medium is discharged safely, the following must be ensured in the building:

- The outlet of the overpressure venting pipe of the safety valves are equipped with suitable gas-tight, heat-resistant and pressure-resistant hoses or piping. The inner diameters of the hoses/piping must not be smaller than the inner diameters of the overpressure venting pipes.
- The hoses/piping are routed in such a way that the content is discharged safely .
- The safety valve lines have no, or at most the following, backpressures:
  - Vessel safety valve: 15 % of the set pressure
  - Temperature control system safety valve: 10 % of the set pressure

7 Cultivation

This chapter describes the work necessary for preparing, performing and finalizing a cultivation. It also describes how the vessel is sterilized again, cleaned and prepared for a new cultivation.

7.1 Preparing the Bioreactor

CAUTION

Uncontrolled rolling away of the device poses a risk of injury and damage to property.

- Always block the swivel castors.
- Before you start work, ensure that the device stands securely and cannot roll away.

NOTICE

Using tools when mounting/removing built-in-parts including blanking plugs on the vessel and top plate can damage these and result in screw connections that can no longer be removed.

- Mount/remove built-in-parts by hand.
- Insert (hand-tight) and remove the 19 mm blanking plug with the hexagon socket wrench provided.

The following check list contains all activities for preparing the vessel for cultivation. The order of the activities corresponds to the typical procedure for preparing the bioreactor.

The checklist serves only as an example. The company's internal specifications regarding the activities to be carried out and their sequence must always be observed!

1. Checking and Filling the Vessel

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 motor must be uncoupled, and 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/piping on the overpressure venting pipe of the safety valve installed by the operator, however, this might have to be removed.

No.	Activity	Additional Information	☑
1.1	Uncouple the motor.	➦ Chapter 2.7.2, page 52	☐
1.2	Remove the exit gas cooler with filter.	➦ Chapter 2.10.2, page 66	☐
1.3	Remove the inlet air filter.	➦ Chapter 2.9.2, page 63	☐
1.4	Remove the vessel top plate.	➦ Chapter 2.4.2, page 35	☐
1.5	Check impellers, baffles and top plate seal.	➦ Chapter 2.4.3, page 37	☐
1.6	Mount the vessel top plate.	➦ Chapter 2.4.2, page 36	☐
1.7	Check the lubrication of the mechanical seal, lubricate if necessary.	➦ Chapter 2.7.3, page 54	☐
1.8	Mount the exit gas cooler and filter. Check the twist valves on the exit gas filter: ▪ Twist valve with connected hose is open. ▪ Unused twist valve is closed.	➦ Chapter 2.10.2, page 67	☐
1.9	Mount the inlet air filter. Check the twist valves on the inlet air filter: ▪ Twist valve with connected hose is open. ▪ Unused twist valve is closed.	➦ Chapter 2.9.2, page 63	☐
1.10	Couple the motor.	➦ Chapter 2.7.2, page 53	☐

2. Preparing and Mounting Built-in-parts

After the vessel has been checked and closed again, all required built-in-parts must be mounted and accessories such as inoculation needles, reagent bottles, etc. prepared.

No.	Activity	Additional Information	☑
2.1	Mount the manometer.	➦ Chapter 2.6.2, page 48	☐
2.2	Mount the safety valve.	➦ Chapter 2.14.4, page 83	☐
2.3	If available: mount the vessel light.	➦ Chapter 4.7.2, page 125	☐

No.	Activity	Additional Information	☑
2.4	If necessary, calibrate the pumps. This makes it possible to display the actual volume pumped in mL or g. The calibration of the pumps must be performed before autoclaving the reagent bottles.	➦ Chapter 8.8.2, page 221	☐
2.5	Equip the reagent bottles and autoclave them with the addition utensils (inoculation needle, push valve, antifoam sensor).	➦ Chapter 4.4.2, page 114	☐
2.6	If available: prepare inoculation needles for use and autoclave them together with the reagent bottles.	➦ Chapter 4.6.2, page 122	☐
2.7	If available: autoclave the push valves together with the reagent bottles and mount them.	➦ Chapter 4.5.2, page 118	☐
2.8	If available: prepare the resterilizable feed line for use: ▪ Autoclave the block valve *13.16.02* / *13.16.04* with the reagent bottle ▪ Mount the block valve *13.16.01* / *13.16.03* in situ.	➦ Chapter 3.3.2, page 91	☐
2.9	Connect pumps to reagent bottles and fill the hoses of the reagent bottles.	➦ Chapter 2.3.2, page 28	☐
2.10	If required: equip the ports with the septum and septum collar.	➦ Chapter 2.4.4, page 38	☐
2.11	Close unused ports and nozzles.	➦ Chapter 2.4.5, page 39	☐

3. Preparing the Sensors

Before in situ sterilization, all necessary sensors must be prepared, calibrated if necessary, and mounted.

No.	Activity	Additional Information	☑
3.1	Prepare the antifoam sensor for use. The antifoam sensor cannot be sterilized in situ and therefore has to be autoclaved separately with the corresponding reagent bottle.	➦ Chapter 2.13.2, page 77	☐
3.2	Mount the temperature sensor.	➦ Chapter 2.8.2, page 58	☐
3.3	Calibrate the pH sensor.	➦ Chapter 8.6.3.5, page 201 ➦ Chapter 8.6.3.3, page 196	☐
3.4	Mount and connect the pH sensor.	➦ Chapter 2.11.2, page 72	☐
3.5	Calibrate the pO_2 sensor.	➦ Chapter 8.6.3.8, page 208 ➦ Chapter 8.6.3.7, page 205	☐
3.6	Mount and connect the pO_2 sensor.	➦ Chapter 2.12.2, page 74	☐

No.	Activity	Additional Information	☑
3.7	Prepare all additional (optional) sensors (e.g. level, pressure, turbidity, redox, pCO_2, permissiveness or O_2 / CO_2 in the exit gas). This is described in the chapter of the respective sensor in the main chapter “Options”.		☐

7.2 In Situ Sterilization

For in situ vessel sterilization, there must be enough liquid in the vessel for sufficient steam to form. The exact evaporation loss during a vessel sterilization cannot be determined precisely. A part of the liquid evaporates via the inlet air or exit gas line. A part of the shortfall is compensated for by the inoculum (inoculation culture). Further shortfalls can be compensated for by adding more water before sterilization or by adding separately sterilized medium or sterile water after sterilization.

In principle, there are various possible sterilization methods, but sterilization is always carried out according to the operator’s specifications. The following two strategies are commonly used and listed as general examples:

Sterilizing the Vessel with Culture Medium Method

- Fill culture medium into the vessel.
- Sterilize the vessel.
- Fill sterile water into the vessel in a sterile manner to compensate for evaporation losses. Add any non heat-stable components in a sterile manner.

Sterilizing the Vessel without Culture Medium Method

- Fill the vessel with water, add basal salts if needed.
- Sterilize the vessel.

  Either drain the water that remains after sterilization or take it 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.

For detailed information on the programmed sterilization processes, see ➦ Chapter 8.9 ‘Processes’ on page 226.

7.3 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, set the pO_2 concentration and the pH. The time required for this depends on the working volume.

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.

7.4 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 analyzes carried out by the operator.

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

If the optional sample valve *17.13.01* mounted in one of the Ingold nozzles is not available, 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 on the function and use of harvest/sample valves, see ➦ Chapter 2.5.1 ‘Harvest/Sample Valve (Bottom Valve)’ on page 42.
- For details on the function and use of the optional sample valve, see ➦ Chapter 3.2.1 ‘Sample Valve’ on page 88.

7.5 Inoculation

Requirements

Check and ensure the following before inoculation:

- Medium has been filled.
- Heat-labile, separately sterilized substances have been added.
- The reagent bottles are connected with the pumps and the vessel, and are filled with a sufficient amount of reagent and nutrient solution for the duration of the 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 correct (or not yet activated).
- Utensils for the inoculation and vessels with inoculum are ready.

Methods

There are different methods for adding inoculum. The exact method depends on the internal guidelines and on the system used and is defined by the operator.

7.6 Harvest

The culture can be harvested at the end of the cultivation. For example, get a suitable vessel ready or connect a hose to the harvest valve.

There are generally two methods for doing this:

- using gravity (0 bar)
- overpressure (1.0 bar) – if optional pressure control is available

For information on the function and use of the harvest valve, see ➦ Chapter 2.5.1 'Harvest/Sample Valve (Bottom Valve)' on page 42.

7.7 Emptying the Vessel

Depending on the user specifications, the vessel can be emptied either before or after repeated sterilization. A vessel that has been emptied beforehand and only filled with water for sterilizing facilitates its subsequent cleaning.

For emptying the vessel, the same options as for harvesting are available, see ➦ Chapter 7.6 'Harvest' on page 139.

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

7.8 Sterilization after Cultivation

Depending on internal regulations, after completion of cultivation, some accessories such as reagent bottles, hoses, inoculation needles, etc. are then autoclaved separately before subsequent cleaning. The vessel is also once again sterilized in situ. This is particularly necessary as it is relevant to safety when processes are carried out with potentially dangerous, pathogenic or genetically modified microorganisms.

In any case, the exact procedure depends on the operator's requirements and can therefore differ from the one described here.

Proceed as follows:

1. Use pumps to completely empty all hoses of the reagent bottles.
2. Disconnect the hoses and remove them from the pumps.
3. If in use: remove the inoculation needles from the ports in the vessel top plate under sterile conditions and close the ports with blanking plugs before in situ sterilization.
4. If in use: close the push valves and then sterilize them in situ together with the vessel and then autoclave separately.
5. 

   We recommend thoroughly rinsing the reagent bottles with water after emptying and before autoclaving. Depending on the operator's specifications, the hoses are disposed of in an environmentally friendly manner and new ones are used for the next cultivation.

   If necessary, dispose of residual liquid from the reagent bottle in an environmentally friendly manner.
6. Autoclave all components together (reagent bottle, hoses and inoculation needle).

   ➡ After the sterilization process is completed successfully, these components will be sterile and no longer carry a risk of microbial contamination.
7. Repeat in situ sterilization.

8 Operation

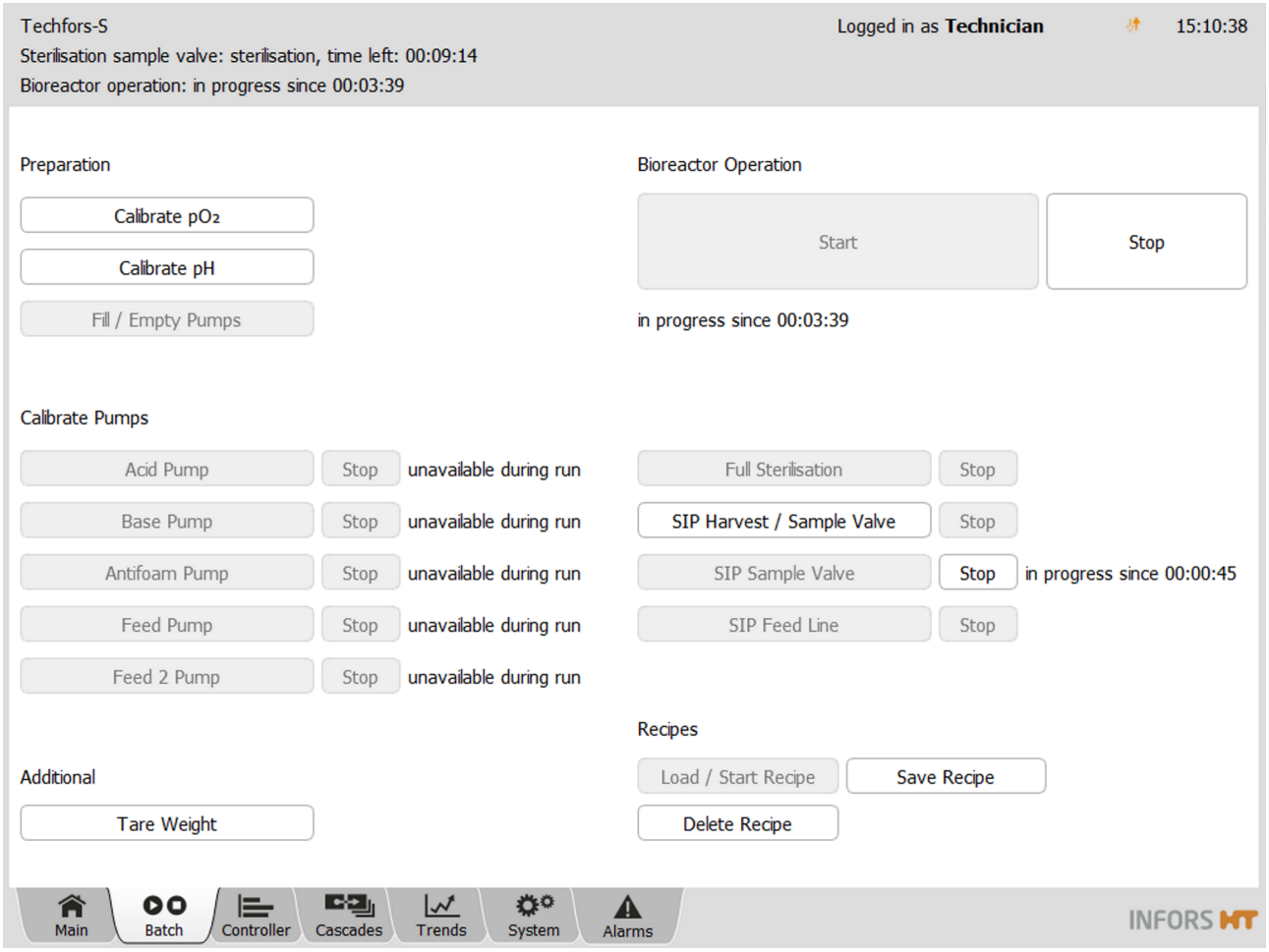
This chapter describes all touch screen software functions accessible to the operator in detail. It also describes the emergency shut-off and restarting after an emergency shut-off.

NOTICE

Changes to settings in the touch screen software by unqualified or untrained personnel can lead to malfunctions.

Most of the illustrations of the various menus, dialog boxes and tab pages of the touch screen software in this manual correspond to the view of a user of the *Technicians* user group and serve as examples. For more information on user groups and access rights, see ➦ Chapter 8.3.2.2 ‘User Groups’ on page 159 and chapter ➦ Chapter 8.3.2.3 ‘Access Rights’ on page 160.

8.1 Overview Screen, Menu Navigation and Control Elements



Sections

Title bar	Shows the device name, operating states, warning messages, login status and time. If an external software like eve® accesses the OPC XML DA server of the touch screen software, this is indicated by two vertically opposed arrows in the title bar. These flash while data is being transmitted.
Main section	Shows the main menus and submenus. Inputs are only made in the main section.
Footer	The footer consists of 7 tabs that provide access to the 7 main menus. The tab of a selected main menu is displayed with a light grey background.

Main Menus

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

- *Main*: shows parameters and their values, pumps or individual valves of the bioreactor.
- *Batch*: this is where the cultivation and all sterilization processes are started and stopped, and sensors and pumps are calibrated.
- *Controller*: lists the process parameters and makes it possible to change values.
- *Cascade*: allows serial, parallel or parallel serial (mixed) cascaded control of one or more parameters.
- *Trends*: shows trend lines of the parameters, time spread between 15 min and 2 days.
- *System*: provides access to the submenus *Valves*, *Security*, *Settings*, *Wipe Screen* and *Shutdown*.
- *Alarms*: shows parameter and system alarms.

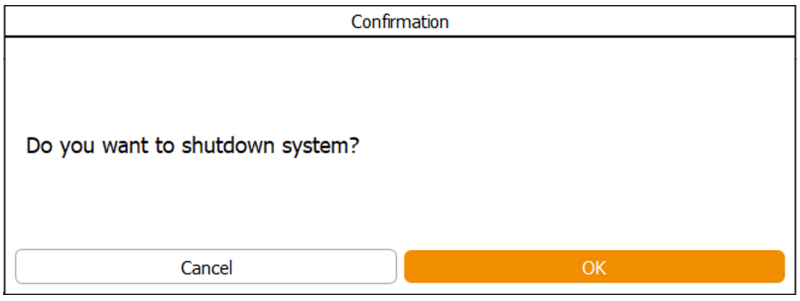
Buttons

Different buttons are displayed depending on the selected main menu or submenu and access rights. Pressing buttons opens submenus, dialog boxes or tab pages. Available buttons have a white background, buttons that are not available appear grey.

Buttons that are intended to be the next logical step are highlighted in orange color, see figure in next section.

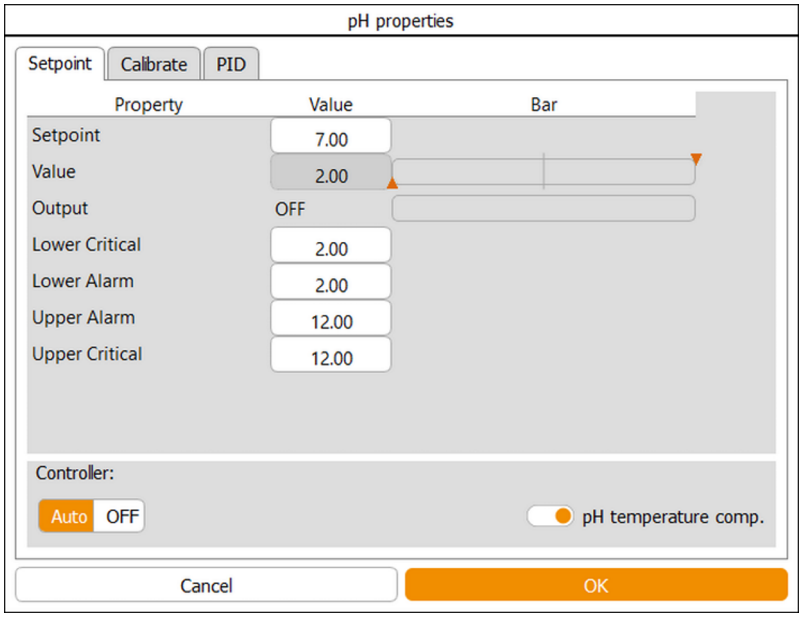
Dialog Boxes and Tab Pages

A dialog box can contain instructions, notes, warnings and general information.



A dialog box can also contain additional buttons, input fields or view boxes as well as tab pages. Example: dialog box *pH properties* with tab pages that lead to the parameter options.

Operation

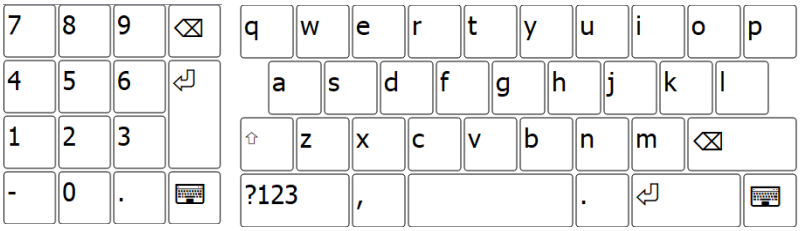


Input Fields and View Boxes

Input fields and view boxes are included in various menus, dialog boxes and tab pages. They require numeric or alphanumeric values to be entered or display these.

Numeric Keypad and Alphanumeric Keyboard

Numeric values are entered using a numeric keypad and alphanumeric values are entered using an alphanumeric keyboard. After pressing an input field, the corresponding block for the input appears, depending on the type of field.



ON/OFF Switch

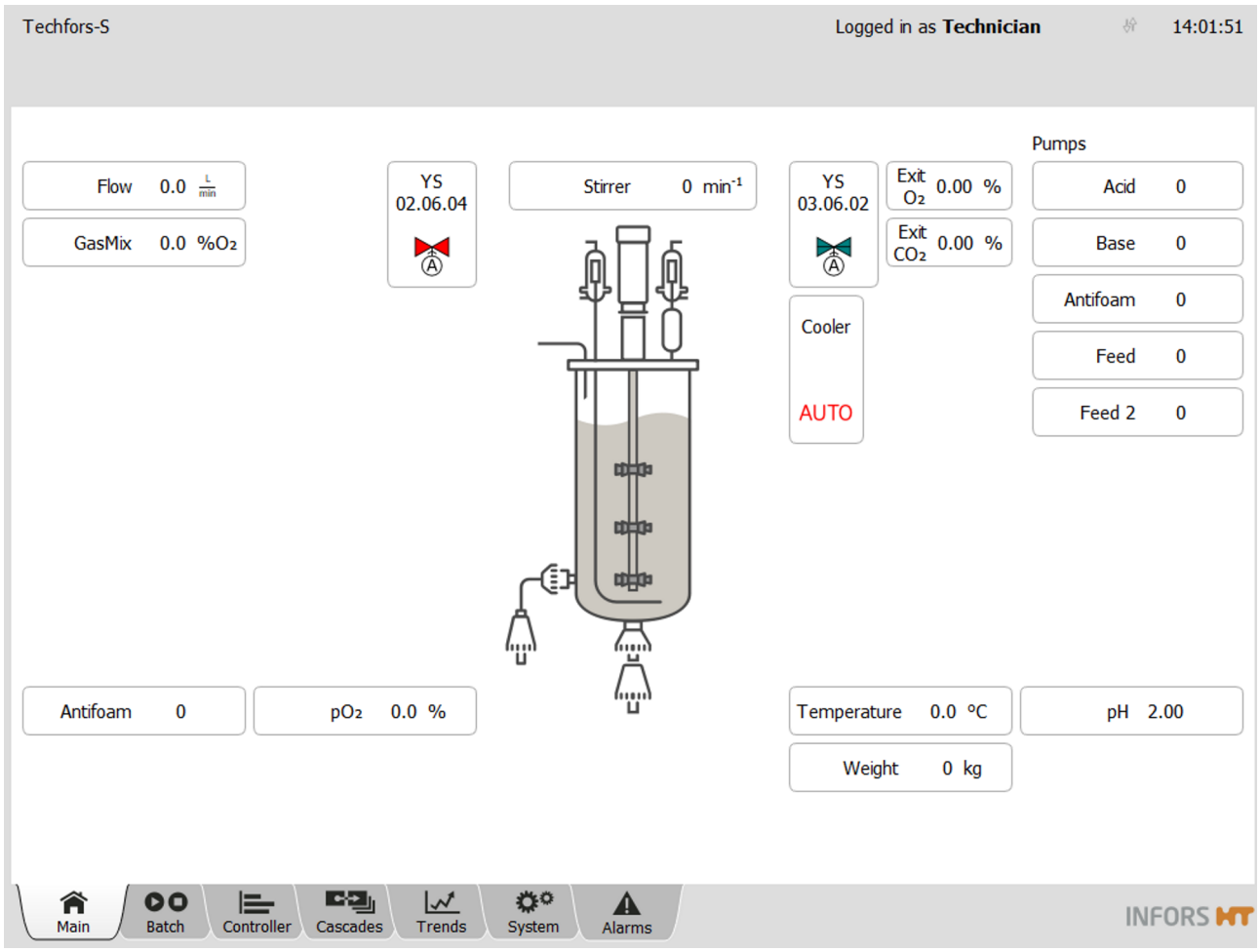
The **ON/OFF** switch is used for activating or deactivating a function.

ON: the switch is orange.

OFF: the switch is white.

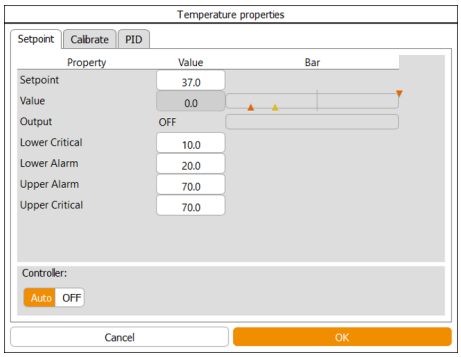
8.2 Main Menus

8.2.1 Main – Overview



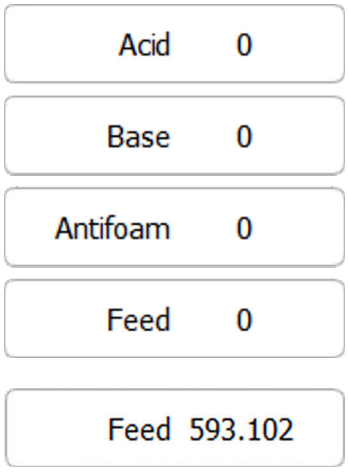
The *Main* menu depicts the bioreactor and some of its valves graphically and provides an overview of the process parameters and pumps, which vary depending on the device configuration.

Parameter



Controlled process parameters and their actual values are displayed in the form of buttons. Pressing the button of a parameter leads to the parameter options. Example on the left: *Temperature* parameter, *Setpoint* option.

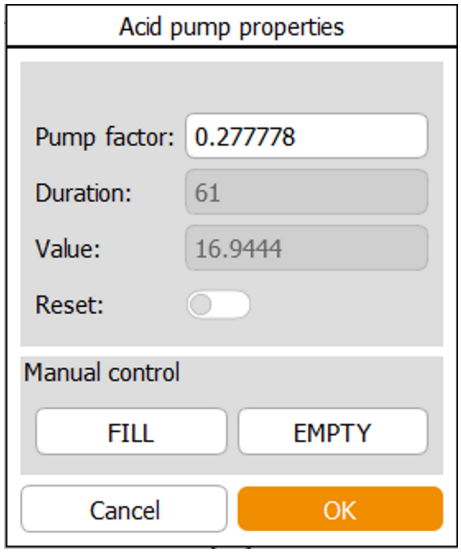
Pumps



The right part of the screen depicts all integrated peristaltic pumps of the bioreactor in the form of buttons. By default, four pumps are available.

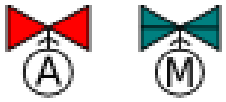
- *Acid*
- *Base*
- *Antifoam*
- *Feed*

The quantity conveyed (in mL) of the calibrated pump is continuously displayed during a cultivation. This number is visible on the button of the corresponding pump. For non-calibrated pumps the number of rotations is displayed.

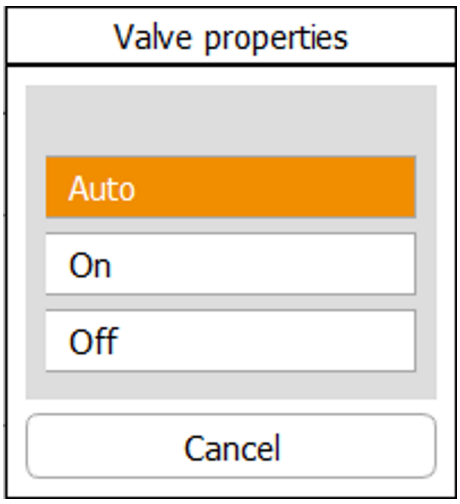


Pressing one of the pump buttons opens the *pump properties* dialog box of the selected pump in which the number of revolutions can be reset to zero. The pump factor calculated during a pump calibration is also shown here and can be changed manually. In addition, the **FILL** / **EMPTY** buttons enable manual filling or draining of the pump hose.

Valves



- The red color indicates a closed valve.
- The green color indicates an open valve.
- The letter *A* indicates that the valve is in automatic mode.
- The letter *M* indicates that the valve is in manual mode, i.e. in a "forced" state.

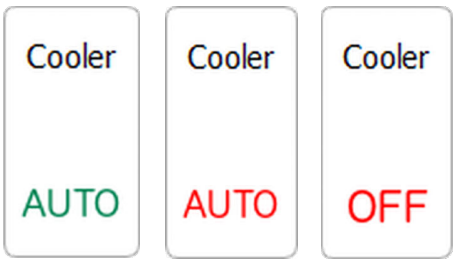


Pressing a valve button opens a dialog box where you can use **On**, **Off**, or **Auto** to change the valve status for diagnostic purposes.

NOTICE

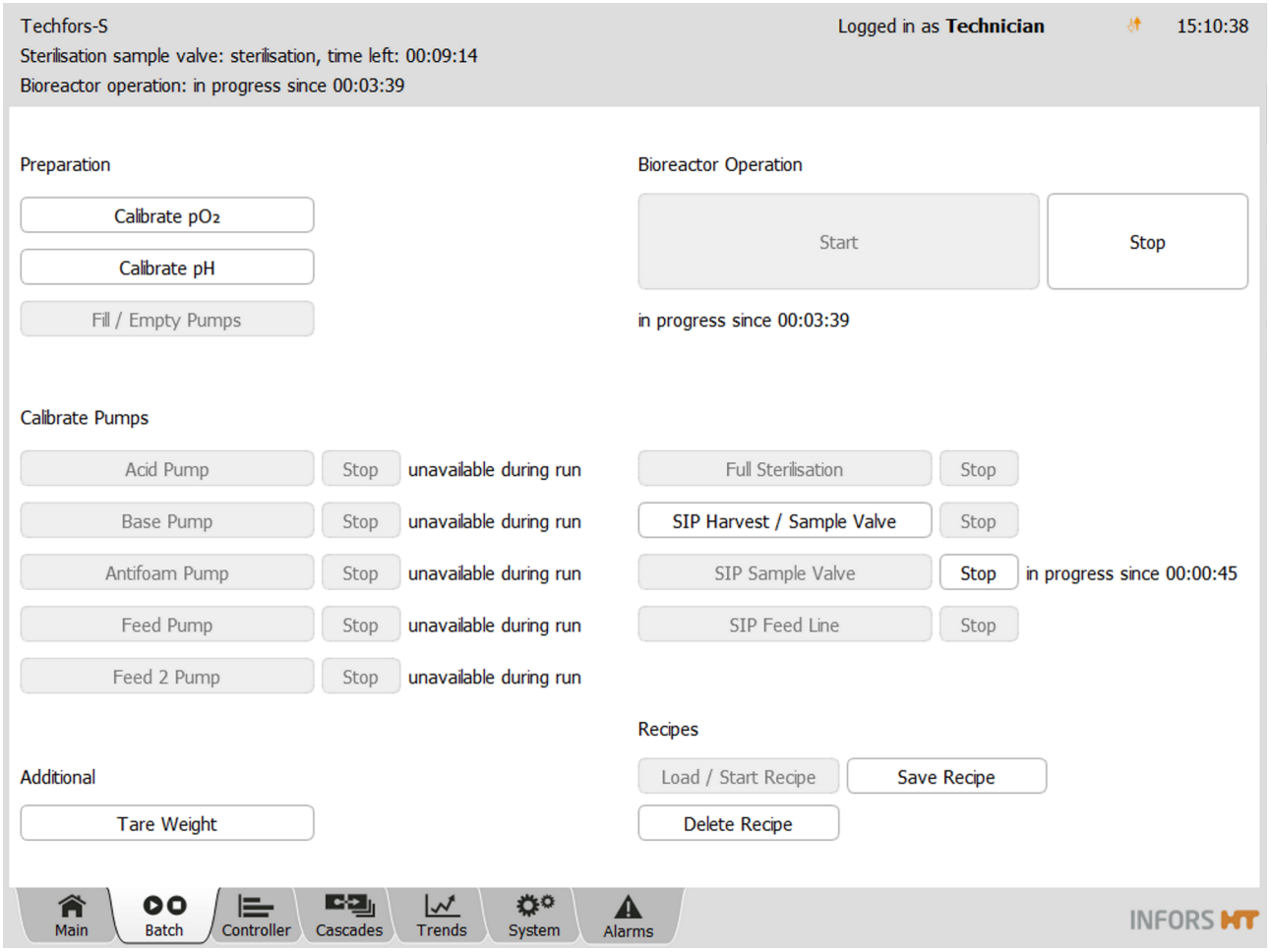
Ex-factory, all valves are switched to automatic mode (*Auto*). These settings must not be changed.

Exit Gas Cooler



The **Cooler** button signals the *01.06.06* valve for the water feed to the exit gas cooler. In automatic mode, the valve opens during an running cultivation and during full sterilization it opens in the cool down phase. For a manually switched valve, no water can be fed in, the valve remains closed. This is signalized with *OFF* in a red font.

8.2.2 Batch – Start Menu

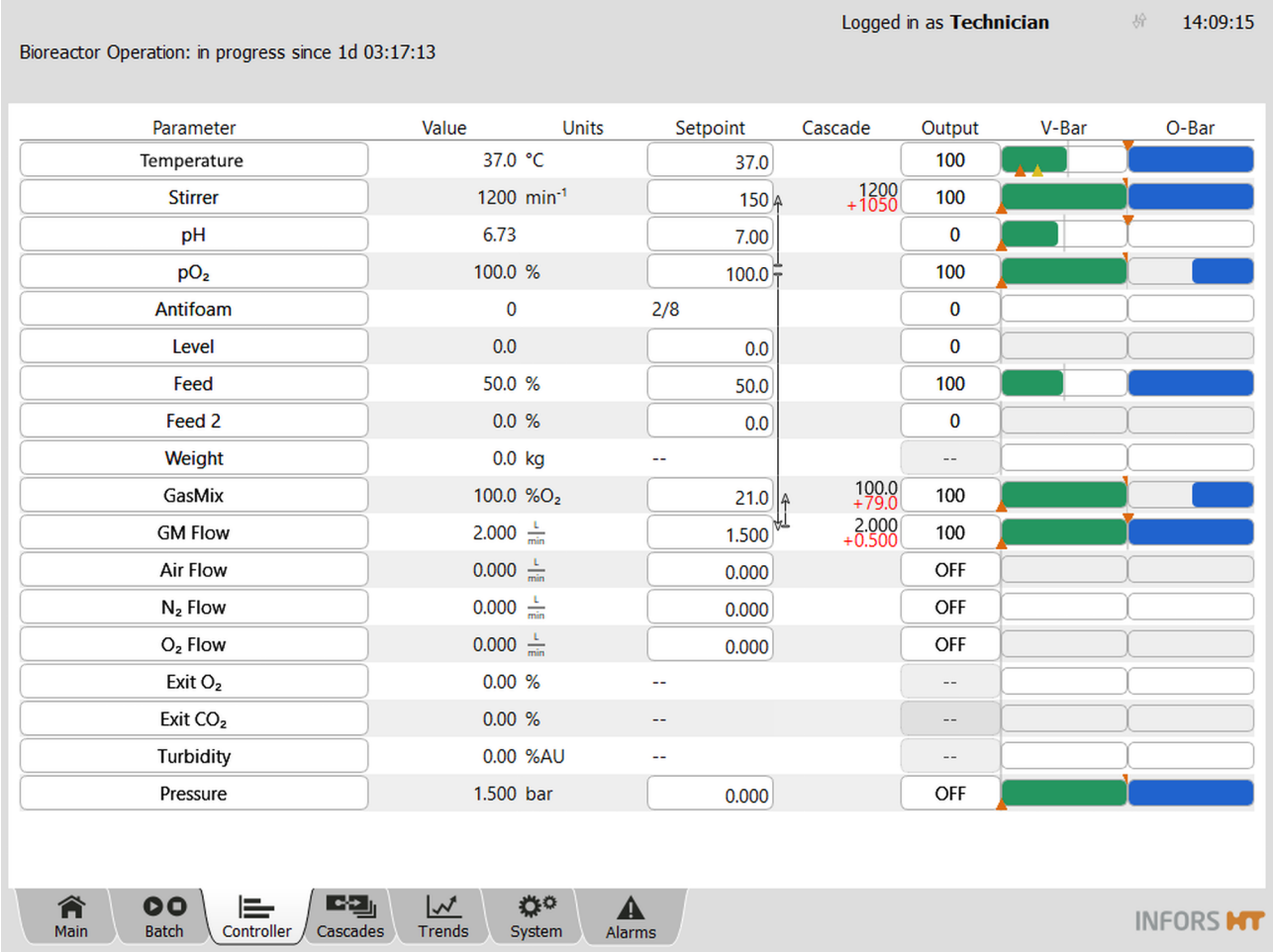


In the *Batch* main menu, the following activities can be performed.

- Starting and stopping the processes.
- Calibrating the pH und pO_2 sensors and pumps.
- Filling/emptying the pump hoses.
- Saving, loading and deleting recipes.
- Taring the weight display (only if the optional vessel weighing system is available).

Depending on the device configuration, the access rights of the operator and the operating status of the bioreactor, more or fewer functions are available and executable. Detailed descriptions of the various functions and processes are available in the corresponding chapters in this manual.

8.2.3 Controller – Value Display



The *Controller* main menu shows the actual values, setpoints and control outputs of the parameters of the bioreactor. Parameter settings can be adjusted here.

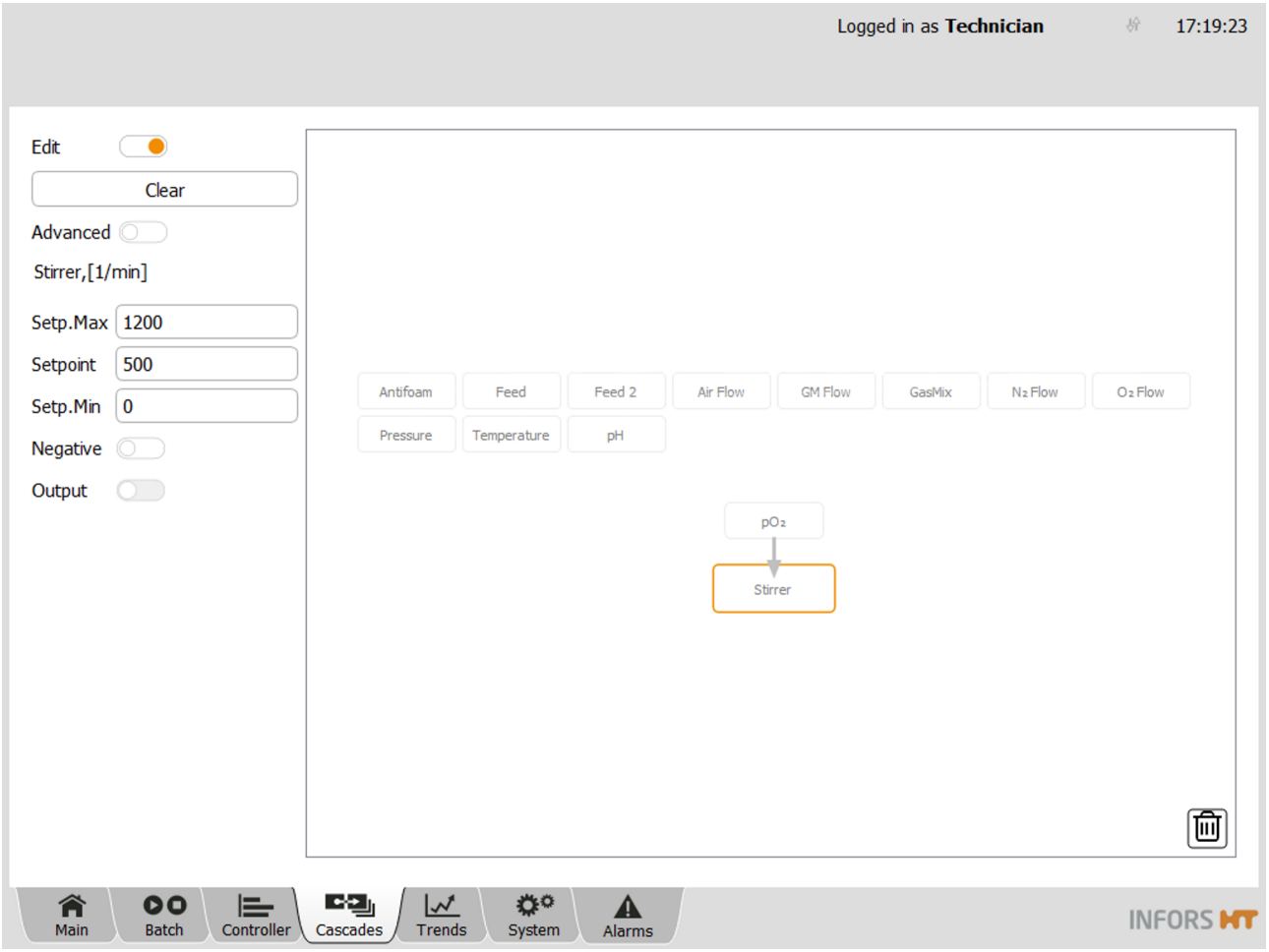
Menu Overview

Designation	Description
Parameter	Lists the parameters. Pressing a parameter button calls up its setting menu (➥ Chapter 8.6, page 190).
Value	Shows the actual value of the parameters.
Units	Shows the unit of the parameters.
Setpoint	Enter/change parameter setpoints (➥ Chapter 8.6.2.2, page 192).

Designation	Description
Cascade	Shows whether and which cascade control is active and which process parameters are used. Settings for cascade control are made in the *Cascade* main menu (➦ chapter 8.7, page 215).
Output	Displays the controller output of a parameter in %. A deactivated parameter is indicated with the word *OFF*. If no process is running, all parameters are automatically deactivated. While a cultivation is running, parameters can be activated or deactivated by pressing the controller output button (**.. %**) or **OFF** provided automatic mode is set in the *Setpoint* parameter option (➦ Chapter 8.6.2.2, page 192).
V-Bar (value bar)	Graphically displays the comparison between the actual value, setpoint and alarm limit: ■ Grey continuous marking: set setpoint ■ Yellow marking: set alarm limits (*lower alarm* / *upper alarm*) ■ Red marking: set critical values (*lower critical* / *upper critical)* ■ Green bar: actual value is within alarm limits. ■ Yellow bar: actual value has exceeded the upper alarm limit or fallen below the lower alarm limit. ■ Red bar: actual value has exceeded the critical upper value or fallen below the critical lower value.
O-bar (controller output bar)	Graphically displays the current controller output in %. Two-sided controlled parameters (e.g. pH and temperature) are displayed as two-part bars.

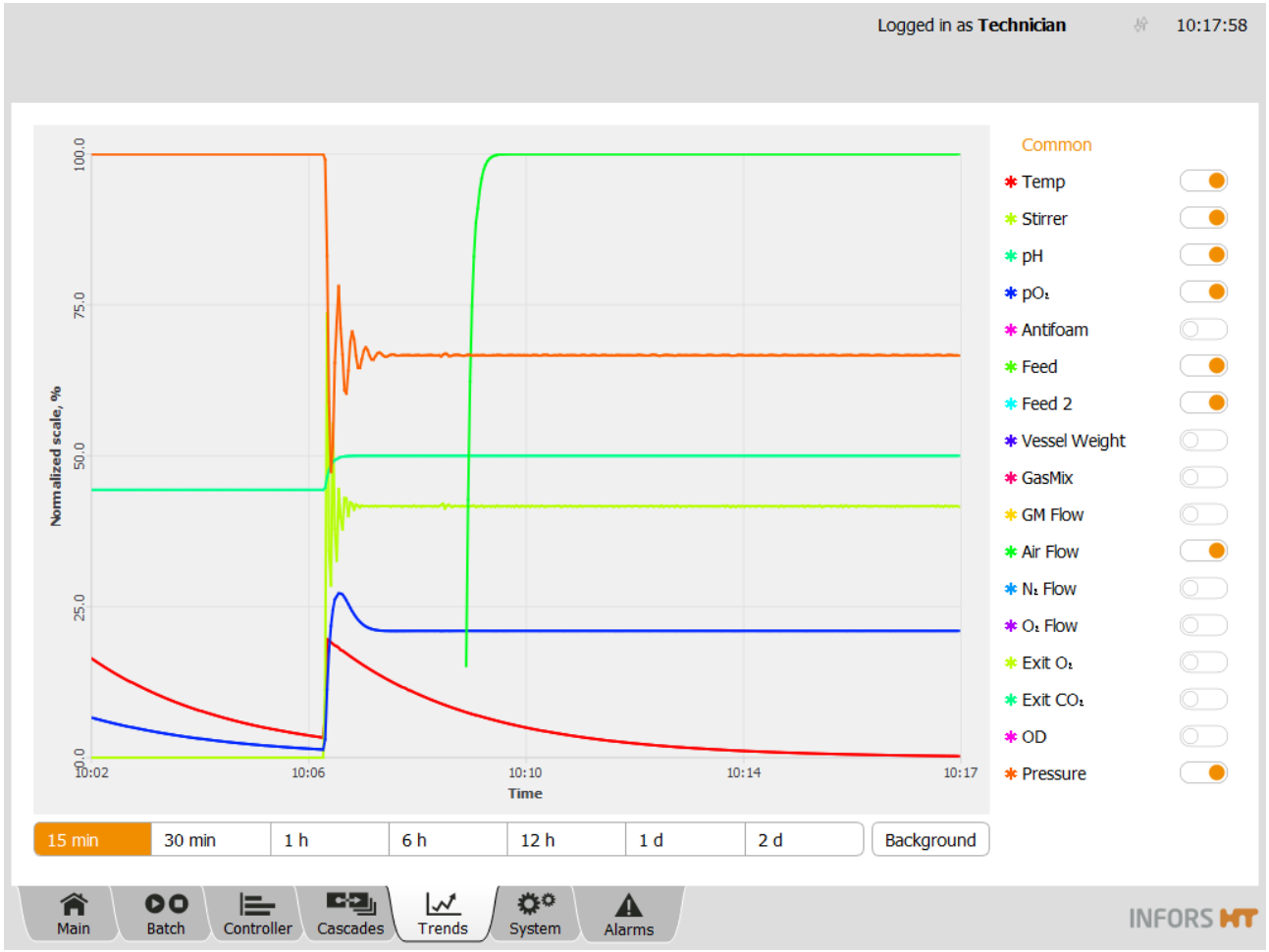
Changed settings in the *Controller* main menu only apply to the running cultivation. A cultivation is always started with the settings in the configuration dialog.

8.2.4 Cascades



The *Cascades* main menu provides the option of setting up a serial, parallel or mixed cascade control of a parameter. This function is mainly used for pO_2 control. 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 (➥ Chapter 8.7, page 215).

8.2.5 Trends – Trend Lines



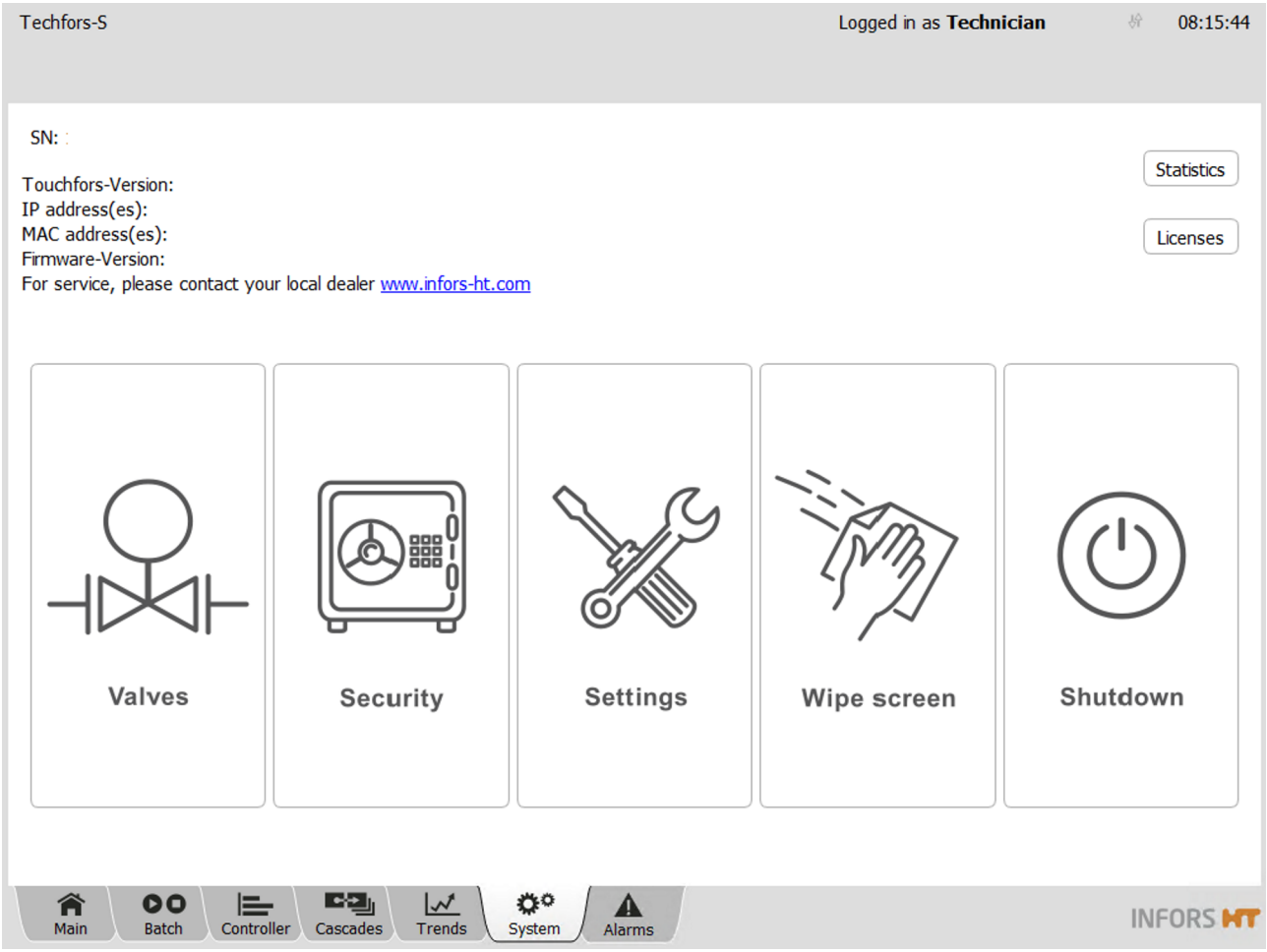
The touch screen operating panel keeps the actual values of the parameters in a buffer memory and displays them continuously as a diagram in the *Trends* main menu. This data cannot be archived, edited or exported. However, this data can be transferred to a computer connected via a network, for example, by using eve®, and then be archived there.

The parameters are displayed on the right side of the screen. The trend lines can be shown or hidden by using the **ON/OFF** switches.

- Y-axis: if the *Common* view is selected (press *Common* above the parameter list), all trend lines of the parameters are displayed on a normalized scale. This means that minimum and maximum permissible values are displayed as 0 % and 100 %.

  If a parameter is selected in the list (press the parameter name), the Y-axis label changes to the value range in the parameter's unit.
- X-axis: the time spread of the diagram display can be set from 15 min to 2 days using the buttons below the diagram.
- **Background**: to set the background color in white, grey or black.

8.2.6 System – System Settings



Device Information

The *System* main menu shows the following information on the device:

- Serial number
- Software version
- IP address(es) of the system
- Device address (*MAC address*)
- Firmware version
- Internet address (domain) of the manufacturer

Buttons

The top right of the screen has two buttons:

- **Statistics**: makes it possible to view some statistics of the software communication with the control board, or hardware. The only purpose of this function is to assist the manufacturer's technical support with troubleshooting.
- **Licenses**: opens a menu with licenses of the software libraries used.

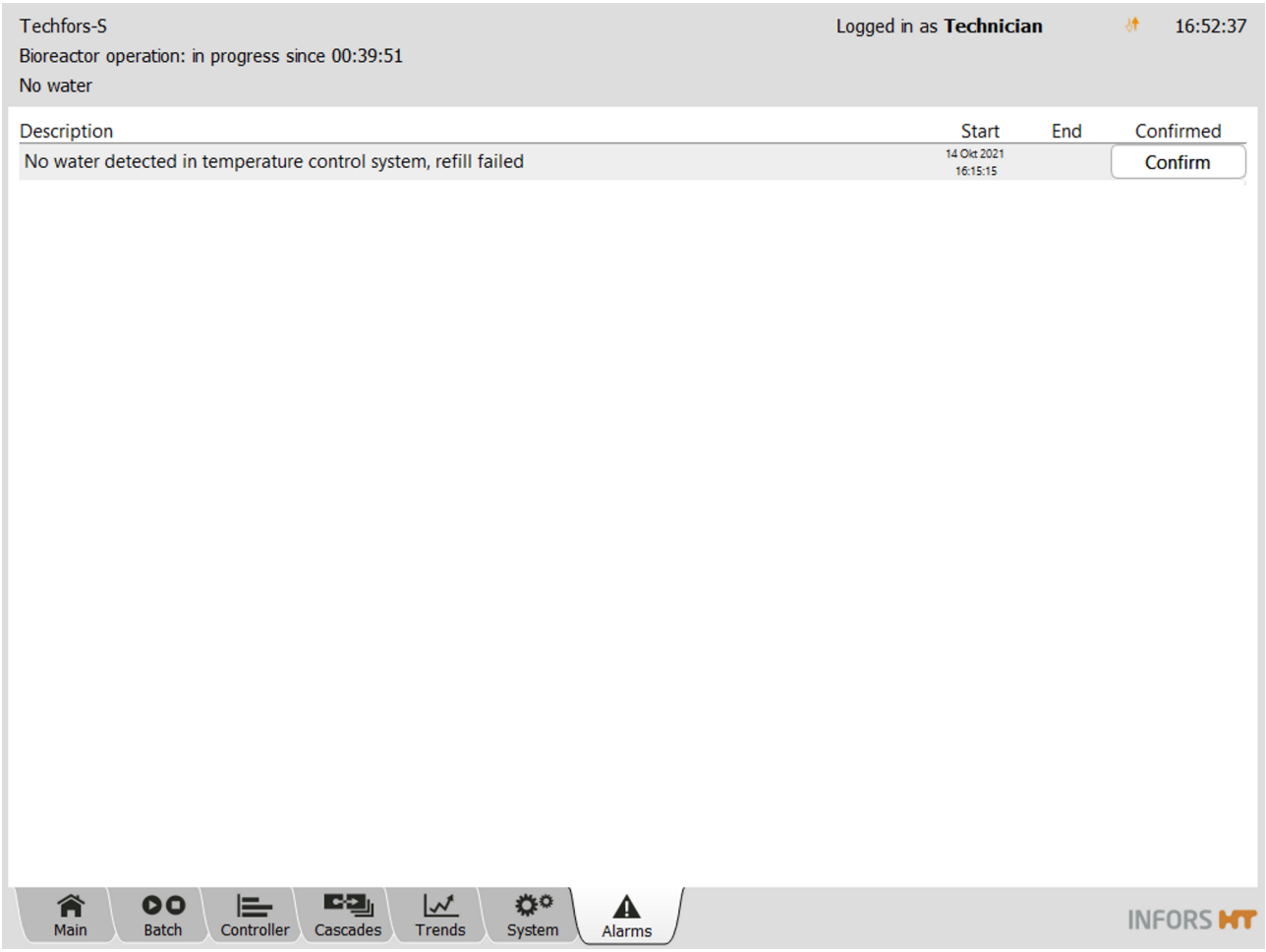
Submenus

The menu has 5 buttons, which lead to different submenus:

- *Valves*: shows the status of the digital outputs
- *Security*: for system login and logout, passwords and user management
- *Settings*: for system and basic settings of the device.
- *Wipe Screen*: lock the screen for 20 seconds e.g. to clean the screen
- *Shutdown*: for shutting down the system.

8.2.7 Alarms – Alarm Display

8.2.7.1 Menu Overview



The Alarms main menu lists all process parameter alarms by time of occurrence. All system alarms are also displayed here.

Alarm Display

An alarm is indicated by the alternately light red-dark red flashing *Alarms* tab.

The screen has the following columns:

- *Description*: describes the alarm.
- *Start* and *End*: shows the start and end of the alarm with date and time.
- *Confirmed*: uses **Confirm** to display alarms with date, time and user.

8.2.7.2 Parameter Alarms

A parameter alarm occurs as soon as the actual value of a parameter is outside the set alarm limits or critical values.

Example

- Displayed alarm: *pO_2: lower (14.3 < 15)*
- Meaning: the actual value of the parameter pO_2 (= 14.3 %) has fallen below the lower alarm limit (= 15 %).

The values in brackets always refer to the actual value compared to the set alarm limit or critical value.

8.2.7.3 Overview of System Alarms

The following system alarms can occur.

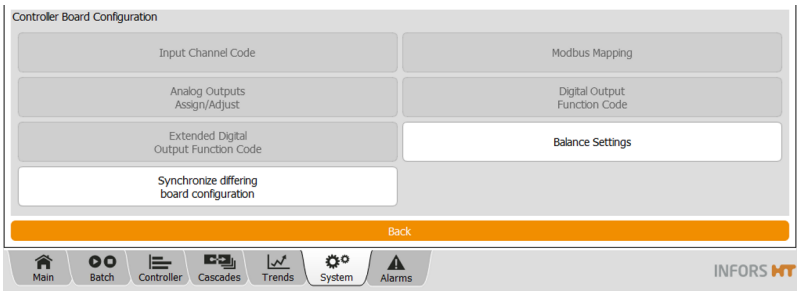
System Alarm	Short Description	Additional Information
Password Expiry	The password expires. The alarm for password expiry appears during the 10-day period leading up to the expiry. The password validity period is set when a new user login is created.	➥ Chapter 8.3.2.10, page 169
Difference in board configuration	Different control board configuration(s) detected.	➥ Chapter 8.2.7.3, page 157
Invalid modbus map for Parameter xy	Invalid modbus setting for parameter xy.	This alarm can only appear if changes have been made in the modbus settings. Modbus settings can only be changed by the *Service* user group.
Requested specialized configuration not installed	An error occurred while restoring backed up data via **Restore** or installing software updates via **Update**.	➥ Chapter 8.2.7.3, page 157
No communication	No communication between the control board and the operating panel.	➥ Chapter 9.1.1, page 244
System restarted after power failure	System restart after power failure.	➥ Chapter 9.1.10, page 253

System Alarm	Short Description	Additional Information
No water detected in temperature control system, refill failed	No water detected in temperature control system.	➦ Chapter 9.1.3, page 246

System Alarm *Difference in board configuration*

A backup of the control board configuration is stored in the touch screen for the device. After a firmware update/control board or touch screen swap, the *Difference in board configuration* alarm might appear. This means that the back up does not match the current configuration.

To be able to select the corresponding configuration, the *Settings* submenu, *Controller Board Configuration* area now shows the **Synchronize differing board configuration** button.



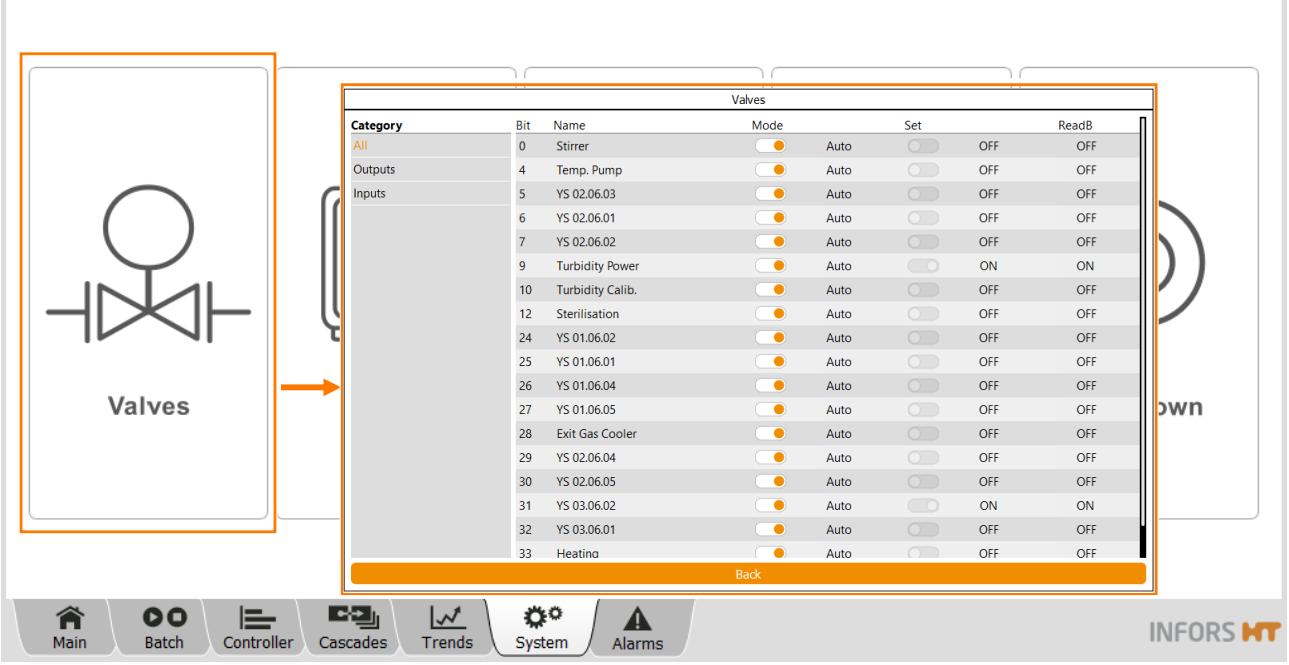
When this function is selected (by pressing the button), the menu appears with two options:

- **Use board configuration**: replace the backup in the touch screen with the current configuration of the control board. This option is useful after changing the touch screen.
- **Use stored board configuration**: the configuration of the control board is overwritten with that from the backup. This option is useful after a firmware update or changing the control board.

  The alarm disappears as soon as the selection function has been executed.

8.3 Submenus

8.3.1 Valves – Digital Controller Outputs

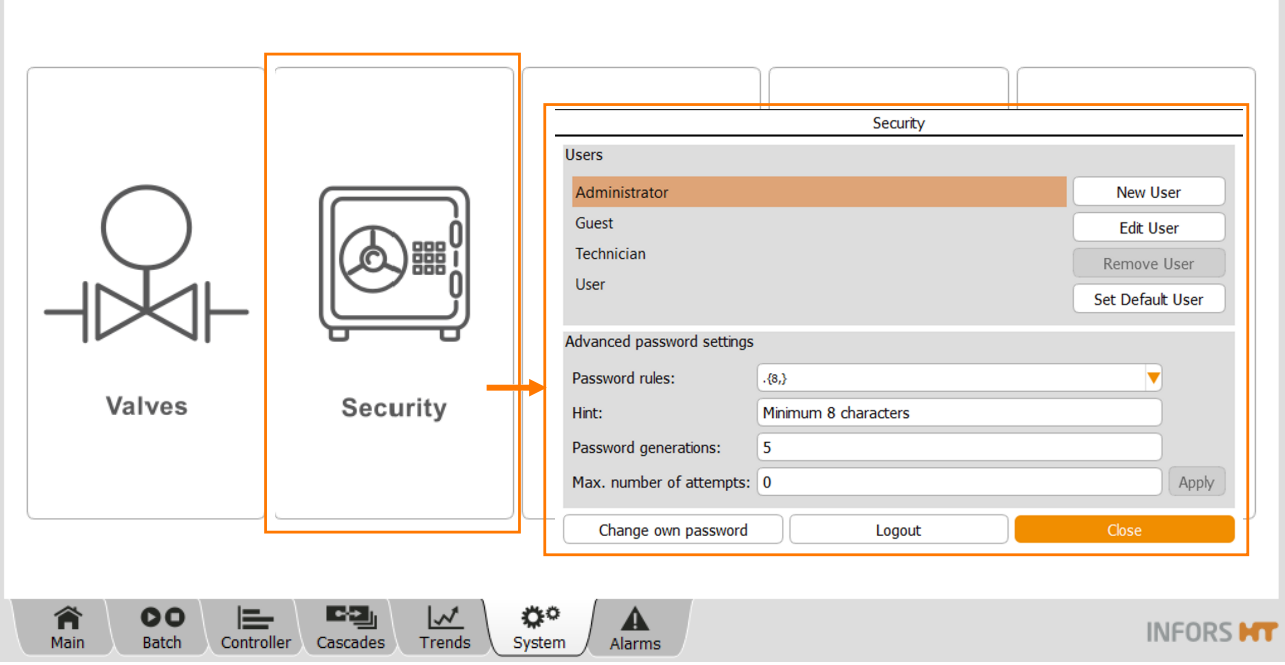


The submenu *Valves* displays the digital outputs and inputs of the control board. The overview is predominantly used for fault diagnosis. All valves and digital outputs are set to automatic mode (*Auto*) ex-factory. These settings must not be changed! The view of all (*All*) digital inputs and outputs or only the display of the inputs or outputs can be selected in column (*Category*). The main column contains:

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*.		

8.3.2 Security – User Administration

8.3.2.1 Menu Overview



The *Security* submenu is used for logging on and off to and from the system. Users can also be added or deleted here, passwords can be set and access rights can be assigned. The number of functions available depends on the authorisation of the user that is logged on:

- **Login/Logout**: log in to/out of the system.
- **Change own password**: change your own password.
- **New User**: add a new user.
- **Edit User**: edit user settings.
- **Remove User**: delete user.
- **Set Default User/Clear Default User**: set/delete automatic user login.
- *Advanced password settings*: define password rules for password security.

The different user groups, access rights and functions are described in the following chapters.

8.3.2.2 User Groups

There are five user groups (*Groups*) with different access rights. Ex-factory, a user has been created for each of the groups, except for the *Service* group.

User groups	User	Password
Guest [1]	*Guest*	No password
Users	*User*	qwertyuiop
Technicians	*Technician*	qwertyuiop
Administrators	*Administrator*	qwertyuiop
Service [2]	--	--

[1] *Without access rights, is logged on automatically if no other user is logged on.*

[2] *Can only be accessed by qualified INFORS HT service technicians and is blocked for all other users.*

The passwords defined ex-factory should be changed and administrated by the authorized person (*Administrator*) during initial commissioning.

8.3.2.3 Access Rights

Legend

- V (= View) = visible, function cannot be executed. Depending on the function, visible means that only the button or the menu/ dialog box is visible.
- E (= Execute) = visible and function can be executed.
- Blank field = neither visible nor can the function be executed.

CULTIVATION (*Bioreactor Operation*)	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Start / Stop (**Start**/**Stop**)	V	E	E	E	E

STERILIZATION	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Default: full sterilization (**Full Sterilisation**)	V	E	E	E	E
Default: sterilization harvest/sample valve (**SIP Harvest / Sample Valve**)	V	E	E	E	E

STERILIZATION	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Option: sterilization sample valve (**SIP Sample Valve**)	V	E	E	E	E
Option: sterilization feed line (**SIP Feed Line**)	V	E	E	E	E

RECIPES (*Recipes*)	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Load / **Start**	V	E	E	E	E
Save	V	V	E	E	E
Delete	V	V	E	E	E

PUMPS	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Calibrating (*Calibrate Pumps*)	V	E	E	E	E
Resetting the counter (*Reset*)	V	E	E	E	E
Manually setting the pump factor	V	E	E	E	E
Filling/emptying hoses (**FILL**/ **EMPTY**)	V	E	E	E	E

PARAMETER options	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Setpoint input (*Setpoint*)	V	E	E	E	E
Alarm values and critical values (*Upper/Lower Alarm, Upper/Lower Critical*)	V	E	E	E	E
Activating and deactivating parameters (*Output active ON / OFF*)	V	E	E	E	E
Calibrating the pH sensor (**Calibrate pH**)	V	E	E	E	E

PARAMETER options	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
pH analog: changing *Slope* and/or *Offset* (calibration mode **Manual**)		E	E	E	E
Calibrating the pO_2 sensor (**Calibrate pO_2**)	V	E	E	E	E
pO_2 analog: **Use As Setpoint** function in calibration menu		E	E	E	E
Use As Setpoint function (if available) in all other calibration menus				E	E
Calibrate, all except the ones mentioned above			V	E	E
Calibration, manual (calibration mode **Manual**), all except the ones mentioned above				E	E
Option: turbidity sensor, calibrating the zero point (*Turbidity, Calibrate*)	V	E	E	E	E
Option: taring the vessel weight display (**Tare Weight**)	V	E	E	E	E
PID			E	E	E
Options					E

CASCADES (*Cascades*)	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Setting a cascade	V	E	E	E	E
Setting an advanced cascade (*Advanced*)			E	E	E

TREND LINES (*Trends*)	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Changing the display settings	E	E	E	E	E

ALARMS (*Alarms*)	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Confirming an alarm (**Confirm**)	V	E	E	E	E

SYSTEM (*System*)	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Viewing the statistics of the communication software with the bioreactor hardware (**Statistics**)	E	E	E	E	E
Viewing licenses for software libraries (**Licenses**)	E	E	E	E	E

DIGITAL INPUTS/OUTPUTS (*System, Valves*)	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Switching inputs/outputs manually (*Outputs / Inputs*)	V	V	E	E	E

USER ADMINISTRATION (*System, Security*)	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Logging in (**Login**)	E	E	E	E	E
Logging out (**Logout**)		E	E	E	E
Changing the password (**Change Password**)		E	E	E	E
Setting password rules (*Advanced password settings*)				E	E
Adding a new user (**New User**)		V	V	E	E
Removing a user (**Remove User**)		V	V	E	E
Changing user settings (**Edit User**)		V	V	E	E
Setting a default user (**Set Default User**)		V	V	E	E
List of all users (*Users*)				V	V

SYSTEM SETTINGS (*System/ Settings*)	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Network settings (**IP Settings**)	V	V	V	E	E
Changing the date and time (**Change Time**)	V	V	V	E	E
Saving data (**Backup**)			V	E	E
Restoring data backups (**Restore**)			V	E	E
Service menu		V	V	V	E
Exporting log files (**Export Logs**)		E	E	E	E
Setting codes for input channels (**Input Channel Code**)			V	V	E
Assigning/changing analog outputs (**Analog Outputs Assign/Adjust**)			V	V	E
Setting extended function codes for digital outputs (**Extended Digital Output Function Code**)			V	V	E
Synchronizing different board configurations (**Synchronize differing board configuration**)			E	E	E
Modbus settings (**Modbus Mapping**)			V	V	E
Setting function codes for digital outputs (**Digital Output Function Code**)			V	V	E
Balance Settings	V	V	V	E	E

SCREEN LOCK (*System, Wipe Screen*)	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Activating a temporary screen lock (**Wipe Screen**)	V	E	E	E	E

SYSTEM SHUTDOWN (*System, Shutdown*)	**User groups**				
	Guests	**Users**	**Techn.**	**Admin.**	**Serv.**
Shutting down the system (**Shutdown**)	V	E	E	E	E

8.3.2.4 Login/Logout – Logging in to/out of the System

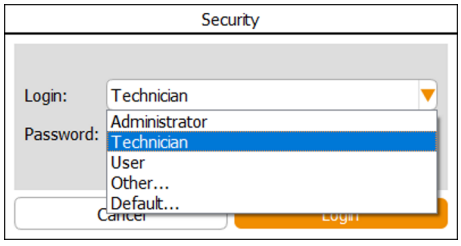
To log in to the system, proceed as follows:

1. Call up the *System* main menu and press **Security**.

   ➡ The *Security* submenu appears.

   The drop-down list in the *Login* field contains all users that are pre-set ex-factory and can be selected:

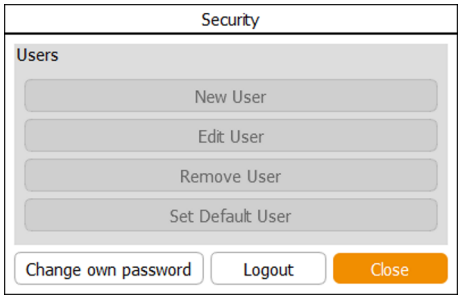
   - *User*
   - *Technician*
   - *Administrator*
   - *Other*: only for INFORS HT service staff
   - *Default*: automatic user login without password input, if previously configured via **Set Default User**.



2. Select the desired user, e.g. *Technician*.
3. Enter the password, and press **Login**.

   ➡ The user is logged in.

   ➡ The *Security* menu now lists the different functions as buttons.



Change own Password (change your own password), **Logout** (log out of the system) and **Close** (leave menu) are available to all users (except for the *Guest* user).

For the *Administrators* user group, all password rules can also be set here, see ➦ Chapter 8.3.2.10 'Password Security – Setting Password Rules' on page 169.

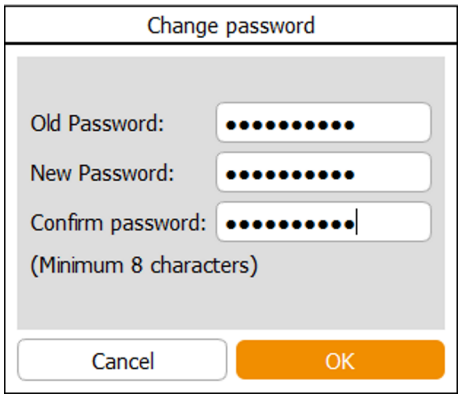
8.3.2.5 Change Own Password – Changing the (Own) Password

Users of all user groups can change their own password. To be able to change their password, the user must be logged in to the system.

To change the own password, proceed as follows:

1. Call up the *Security* submenu and press **Change own password**.

   ➡ The *Change password* dialog box appears.



2. Enter the old password.
3. Enter the new password and confirm by entering it again.
   ➡ All inputs are displayed as dots.

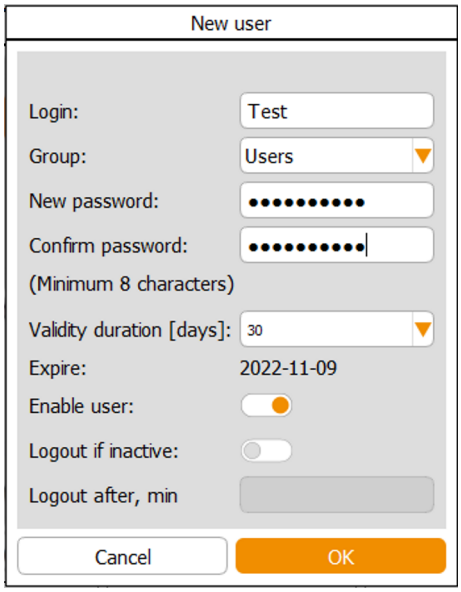
> Depending on the password rules set, the password must meet various conditions. Password rules can be configured by *Administrator* users.

4. Press **OK**.
   ➡ The dialog box disappears, the password is saved.

8.3.2.6 New User – Adding a New User

To add a new user, proceed as follows:

1. As *Administrator* call up the *Security* submenu and press **New User**.
   ➡ The *New User* dialog box appears.



2. Enter the new user (*Login*).
3. Select the user group in the *Group* drop-down list.
4. Enter the password in *New password* and confirm it by entering it again in *Confirm password*.

> Depending on the password rules set, the password must meet various conditions. Password rules can be configured by *Administrator* users.

5. Select the validity period of the password in the *Validity duration [days]* drop-down list, by choosing between "unlimited", 30, 100 and 365 days.
   ➡ The corresponding expiry date is then shown in *Expire*.
6. Activate or deactivate the new user's access rights (*Enable user*); these are activated by default.

> If the function is deactivated, the user has no access rights and a password cannot be assigned.

7. Activate or deactivate the automatic user logout (*Logout if inactive*) after expiry of a defined time period of screen inactivity, and set a time limit (*Logout after, min*) if necessary.

8. Press **OK**.

   ➡ The dialog box disappears, the new user appears in the user list of the *Security* submenu.

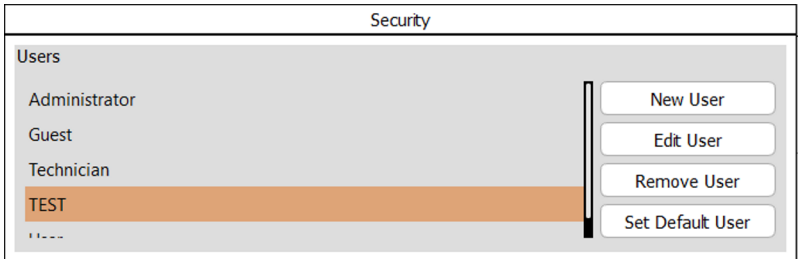
8.3.2.7 Edit User – Changing User Settings

Edit User can be used to change the following settings of an existing user:

- Assign a new user group.
- Change the password.
- Set automatic user logout on screen inactivity after a predefined time in minutes. The lowest user group *Guests* is then set automatically.

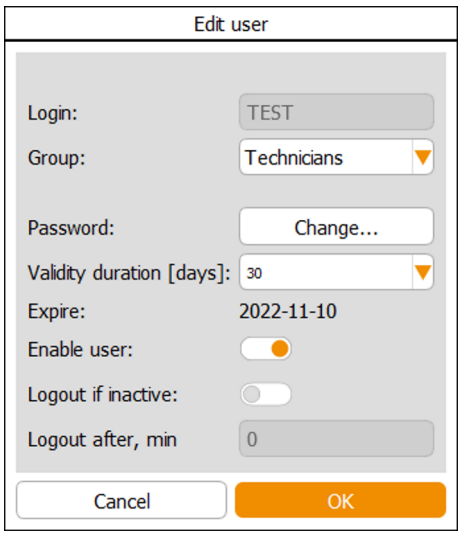
To make changes, proceed as follows:

1. As *Administrator* call up the *Security* submenu.



2. Select the desired user (here: *TEST*) from the selection list and press **Edit User**.

   ➡ The *Edit User* dialog box appears with almost identical options to those for entering a new user.



3. Make the desired settings.

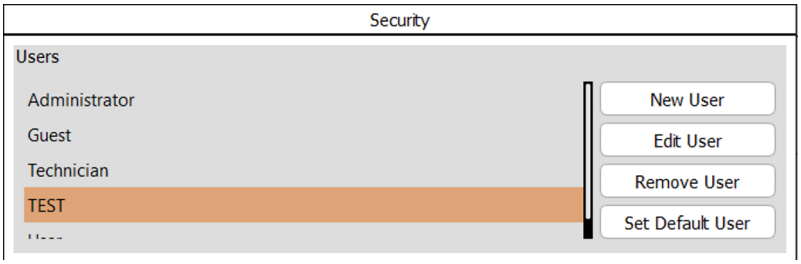
4. Press **OK**.

   ➡ The settings are applied, the dialog box disappears.

8.3.2.8 Remove User – Deleting a User

To delete a user, proceed as follows:

1. As *Administrator* call up the *Security* submenu.



2. Select the desired user (here: *TEST*) from the selection list and press **Remove User**.

   ➡ The *Confirmation* dialog box appears with information and the prompt to confirm the deletion of the user.

3. Press **OK** to confirm the deletion.

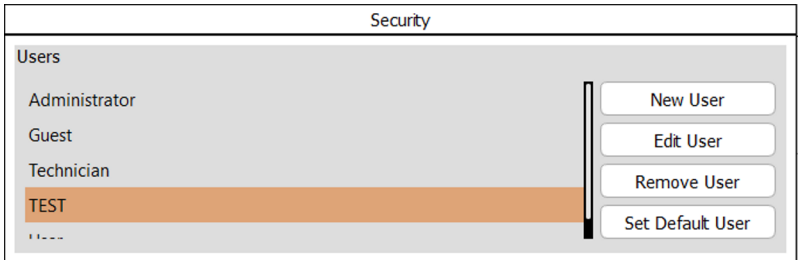
   ➡ The dialog box disappears, the *TEST* user has been deleted.

8.3.2.9 Set / Clear Default User – Setting up Automatic User Login

Set Default User is used to set up an automatic user login. That is, a user can be defined, which will be logged in automatically by the system next time it is switched on. This setting can be deleted via **Clear Default User**.

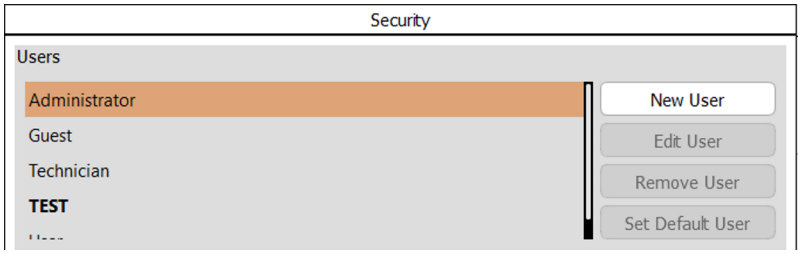
To do so, proceed as follows:

1. As *Administrator* call up the *Security* submenu.



2. Select the desired user (here: *TEST*) from the selection list and press **Set Default User**.

   ➡ The defined user for automatic user login is now displayed with a bold font, the **Set Default User** button is still visible but no longer available.



By selecting any other user, all buttons become available for changes again.

By selecting the defined user with automatic user log in, the **Clear Default User** button becomes available instead of **Set Default User**.

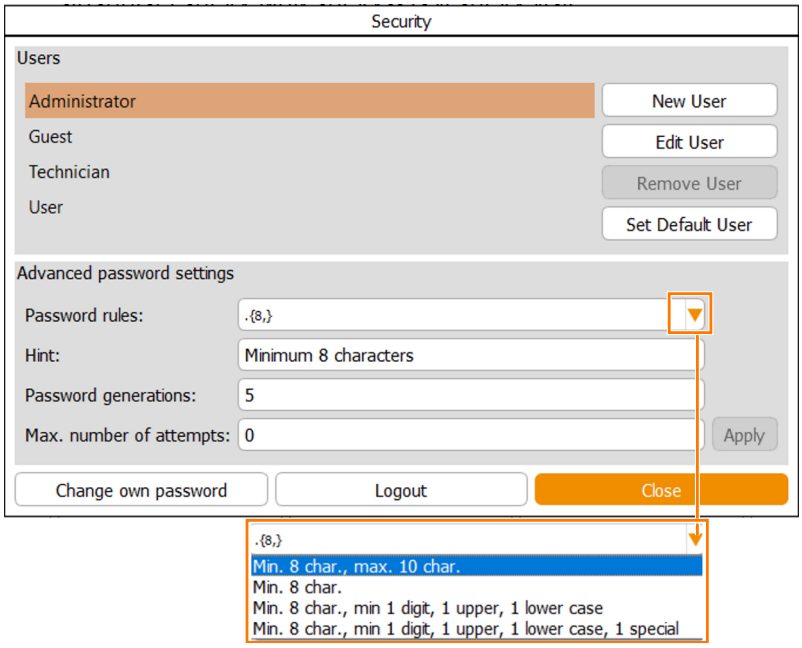
8.3.2.10 Password Security – Setting Password Rules

As *Administrator* user, the conditions for creating new user passwords can be configured in the *Security* submenu.

To do so, proceed as follows:

1. As *Administrator* call up the *Security* submenu.

   ➡ The lower menu section *Advanced password settings* is now visible and available.



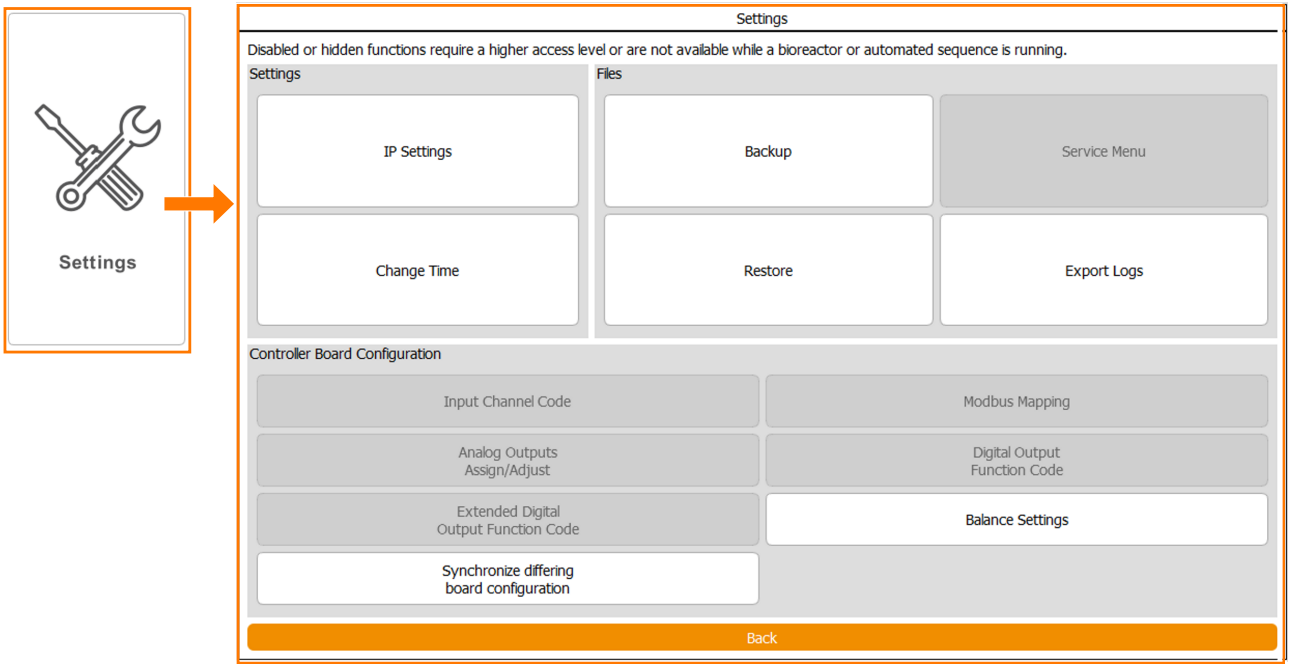
- *Password rules*: a drop-down list with four password rules is available (see figure above). The password must contain at least:
  - 8 characters, which have to include at least 1 number, 1 upper case letter and 1 lower case letter
  - 8 characters, which have to include at least 1 number, 1 upper case letter, 1 lower case letter and a special character
  - 8 characters
  - 8 to a maximum of 10 characters
- *Hint*: when a password is being created, this shows the rules that have to be observed.
- *Password generations*: specifies the number of new passwords to be created before a password may be reused.
- **Apply**: apply the rule for new passwords to be created from now on.

2. Select the rule and enter the number of new passwords to be created.
3. Press **Apply**.

   ➡ The rule is saved and is displayed accordingly when the next password is to be created.
4. Close the *Security* submenu via **Close**.

8.3.3 Settings – Basic Settings of the Device

8.3.3.1 Menu Overview



The basic settings of the device are made in the *Settings* submenu. The number of buttons visible and available in this menu depends on the authorisation of the user that is logged on. The figure above shows the menu for an *Administrator* user. The menu is divided into three sections with different functions.

Settings

- **IP Settings**: network settings.
- **Change Time**: setting the time and date.

Files

- **Backup**: save data.
- **Restore**: upload saved data to the system.
- **Service Menu**: accessible only to INFORS HT service technicians or authorized licensed dealers.
- **Export Logs**: export log files.

Controller Board Configuration (Control Board Configuration)

- **Input Channel Code**: set codes for input channels.
- **Analog Outputs Assign/Adjust**: assign/change analog outputs.

- **Extended Digital Output Function Code**: set functions codes for extended digital outputs.
- **Synchronize differing board configuration**: synchronize differing board configuration.

This button only appears if a corresponding alarm (*Difference in board configuration*) has been triggered after a firmware update/change of control board or touch screen replacement and is displayed in the *Alarms* main menu.

- **Modbus mapping**: make modbus settings.
- **Digital Output Function Code**: set function codes for digital outputs.

This manual does not provide any further details on all the functions concerning inputs and outputs, function codes and modbus mappings. Only INFORS HT service technicians or authorized licensed dealers have access to these functions.

- **Balance Settings**: balance settings.

8.3.3.2 IP-Settings – Network Settings

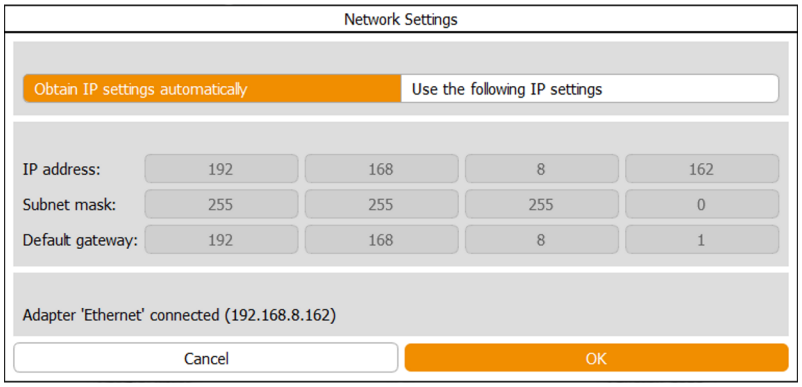
IP-Settings can be used to configure a network connection. This can be done automatically or manually.

Settings can only be made if a network cable is connected. This manual does not cover how a network is set up or a network connection is established.

To call up this menu, proceed as follows:

1. As *Administrator* call up the *Settings* submenu.
2. Press **IP-Settings**.

   ➡ The *Network Settings* menu appears.



- **Obtain IP settings automatically**: automatically apply IP settings (default settings). Prerequisite: a DHCP server [1] is available in the network.
- **Use the following IP settings**: use the following IP settings. An entry can only be made in the following fields after pressing this button.
  - *IP address*: IP address or enter IP address manually.
  - *Subnet mask*: shows the current subnet mask or lets you enter one manually.
  - *Default gateway*: shows the default gateway or lets you enter one manually.

A status message ending with *...connected* indicates that the network connection has been established correctly. If that is not the case (no signal) the error message *No active LAN connection* appears.

[1] *Dynamic Host Configuration Protocol*

8.3.3.3 Change Time – Changing the Date and Time

Change Time is used to adjust the date and time to the system's location. Ex-factory, the system is set to automatic synchronization with the time server. That is, it is displayed according to the selected time zone. Alternatively, settings can also be made manually.

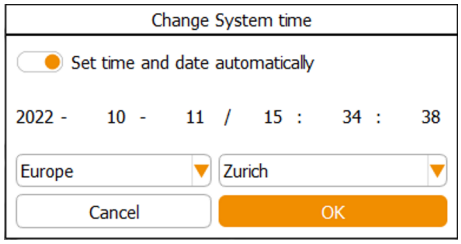
To make settings, proceed as follows:

1. As *Administrator* call up the *Settings* submenu.

2. Press **Change Time**.

➡ The *Change System time* dialog box appears with the configuration set ex-factory:

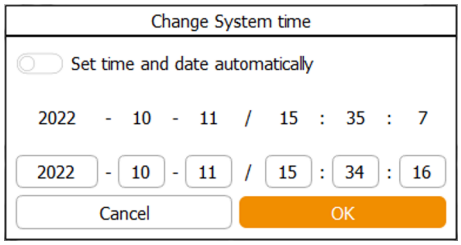
- *Set time and date automatically*: activate or deactivate automatic time and date setting. This function is activated by default. This makes it possible to select the time zone and the cities assigned accordingly.
- Drop-down lists for selecting time zones and cities: *Europe* and *Zurich* are set as the default.



To make manual settings, proceed as follows:

3. Deactivate automatic time and date setting.

➡ Instead of the drop-down lists, input fields for year/month/day and hours/minutes/seconds appear now.



4. Set the desired values and use **OK** to confirm.

➡ The entries are saved and the dialog box disappears.

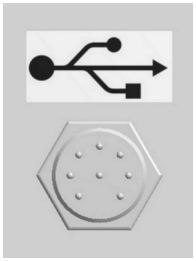
8.3.3.4 Backup – Saving Data

The *Backup* function is used to save all settings of the touch screen software and the control board. This data can then be restored using the *Restore* function.

Please note:

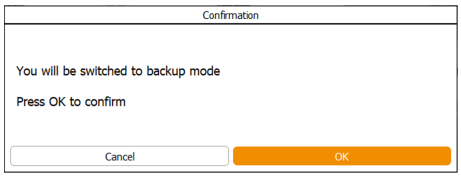
- Data can be backed up to internal storage or a USB stick.
- A data backup can only be executed when all processes have stopped.
- Skip step 1 in the following description if you are not backing up the data onto a USB stick.

To back up data, proceed as follows:



1. Connect the special cable supplied by the device manufacturer to the connection socket on the back of the operating panel and connect the USB stick.

2. As *Administrator* call up the *Settings* submenu.

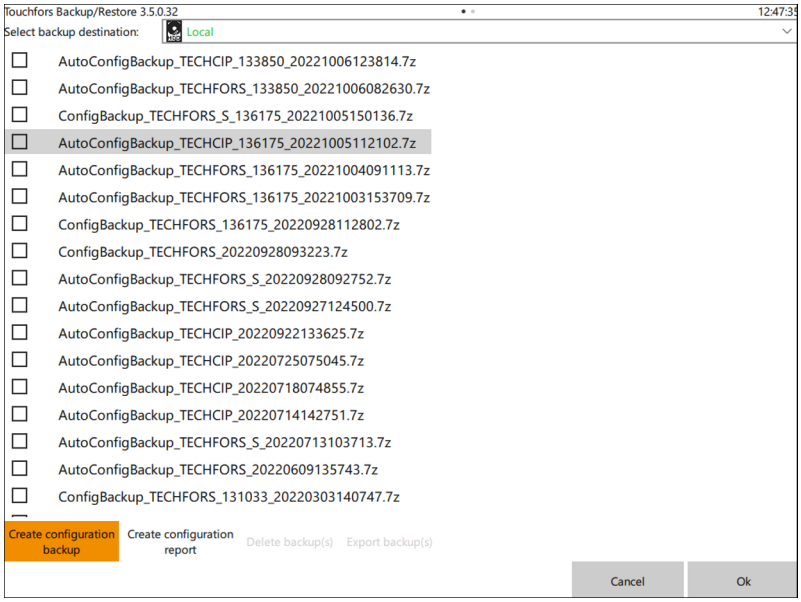


3. In the *Files* section, press **Backup**.

   ➡ The *Confirmation* dialog box appears with a note and a prompt for switching to backup mode.

4. Press **OK**.

   ➡ The data backup menu appears.



   - *Select backup destination*: choose a storage location, either *local* o *external* (on the connected USB stick).
   - **Create configuration backup**: create a backup file of the current configuration.
   - **Create configuration report**: output configuration data in a CSV file.
   - **Delete backup(s)**: delete saved backup file(s).
   - **Export backup(s)**: export the backup file(s) from the local storage location to the USB stick.

5. Select a storage location and press **Create configuration backup** to create the data backup.

   ➡ The configuration backup is stored as a 7zip file at the selected storage location.

6. Press **OK** to leave the menu.

7. Remove the USB stick, if you've used one.

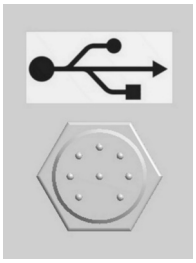
8.3.3.5 Restore – Restoring Data Backups

The *Restore* function enables loading data to the system, which were saved using the *Backup* function. Also factory settings can be restored.

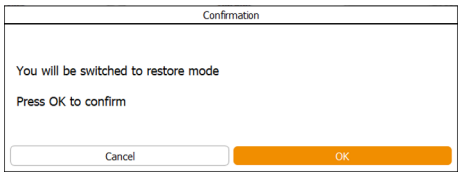
Please note:

- The data is loaded either from the internal storage or from a USB stick, see ➦ Chapter 8.3.3.4 ‘ Backup – Saving Data’ on page 174.
- The *Restore* function can only be executed when all processes are stopped.
- Skip step 1 in the following description if you are not loading the data from a USB stick.

To load data backups to the system, proceed as follows:



1. Connect the special cable supplied by the device manufacturer to the connection socket on the back of the operating panel and connect the USB stick with the saved data (*Backup* data).
2. As *Administrator* call up the *Settings* submenu.



3. In the *Files* section, press **Restore**.

   ➡ The *Confirmation* dialog box appears with a note and a prompt for switching to *Restore* mode.

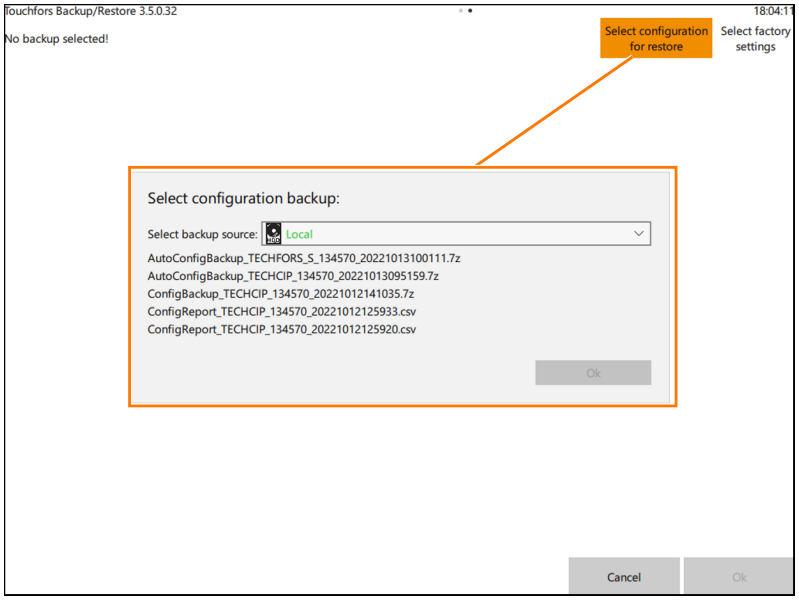
4. Press **OK**.

   ➡ The data backup/restore menu appears.

   - **Select configuration for restore**: select configuration data backup for restoring.
   - **Select factory settings**: select the factory setting.

5. Press **Select configuration for restore**.

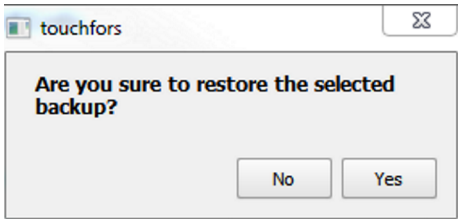
   ➡ The window for selecting the data source appears in the menu:



- *Local*: local, internal memory.
- XY/: (Drive): detected connected USB stick.

6. Select a data source and press **OK**.

➡ A dialog box with a confirmation prompt **No** or **Yes** for restoring the data appears.



7. Press **Yes**.

➡ The menu view changes, and the configuration comparison listing appears (not shown here).

The view of the differences within a file is primarily intended as information for the INFORS HT service technician. It represents the differences of the settings file to be restored compared to the version currently used in unified format (also unidiff).

8. Use **Cancel** to terminate the process or **OK** to execute the data restore.

9. Remove the USB stick, if applicable.

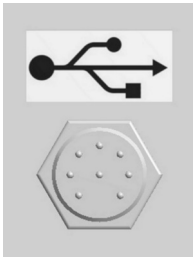
8.3.3.6 Export Logs – Exporting Log Files

The *Export Log* function can be used to store all log files as well as alarms and error messages on a USB stick.

Please note:

- A USB stick is required for the data export.
- A data export can only be executed when all processes have stopped.

To export the log files, proceed as follows:



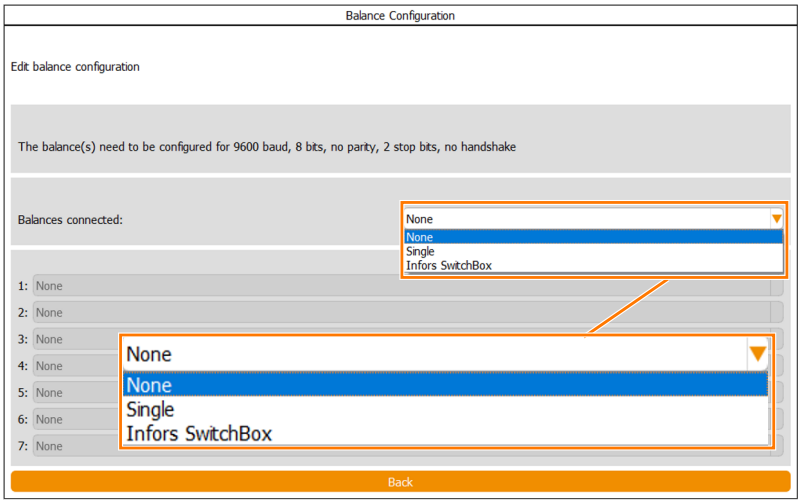
1. Connect the special cable supplied by the device manufacturer to the connection socket on the back of the operating panel and connect the USB stick.
2. As *Administrator* or *Technician,* call up the *Settings* submenu.
3. In the *Files* section, press **Export Logs**.
   ➡ The data export is started. As soon as this is done, an *Information* dialog box appears with the message that the log data has been successfully exported as a zip file (*Log files successfully exported to: xxxxx*).
4. Press **OK** to close the dialog box.

8.3.3.7 Balance Settings

The *Balance Settings* function is used to set up a maximum of 7 balances that can be connected (via the device manufacturer's Switchbox). Balances must be configured with the correct values. *Baud rate 9600 / 8 bits /* no parity */ 2 stop bits*.

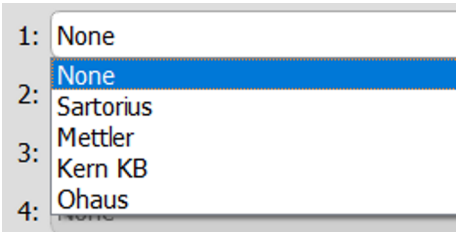
To make the settings, proceed as follows:

1. Connect the balance(s) or Switchbox.
2. As *Administrator* call up the *Settings* submenu.
3. Press **Balance Settings**.
   ➡ The *Balance Configuration* appears with the mentioned configuration values for scales and drop-down lists for selecting the number and type of connected scales.



4. Select the number of balances in *Balances connected*:

- *None*: none
- *Single*: one balance; this means that the first drop-down list in the menu area becomes available.
- *Infors Switchbox*: switchbox, this makes all 7 drop-down lists in the lower menu section available.

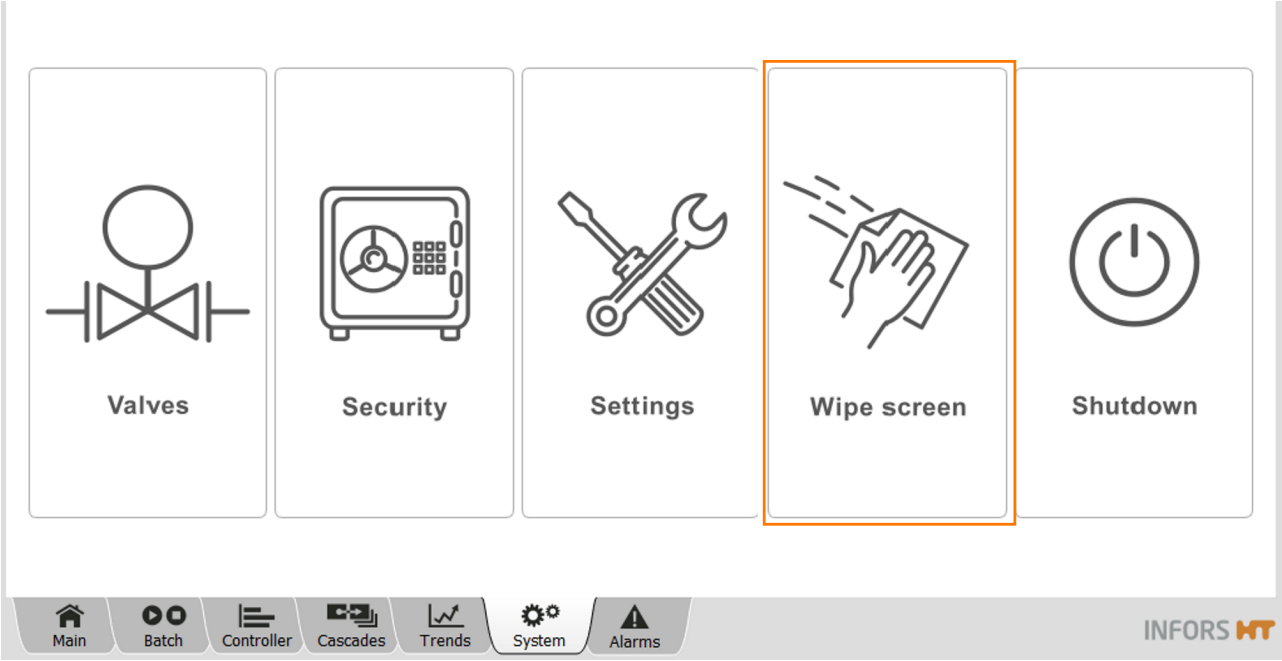


5. Select the type of balance(s) from the drop-down list(s).

6. Press **Back**.

➡ The settings are applied, the configuration menu disappears.

8.3.4 Wipe Screen – (Temporarily) Locking the Screen



The *Wipe Screen* submenu has only one function: it locks all input on the screen for 20 seconds. This enables you to clean the screen within 20 seconds, if required.

To activate the temporary screen lock, proceed as follows:

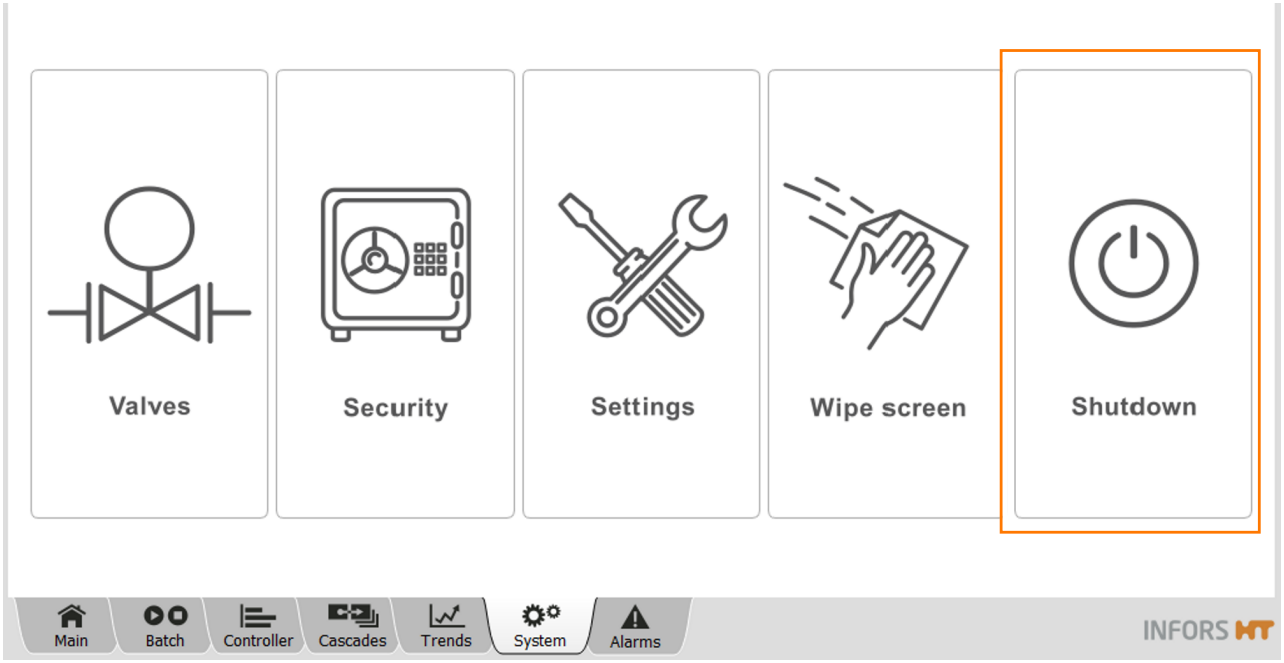
→ Press **Wipe screen**.

Wipe time left: 17 seconds...

➡ The screen turns blank, the remaining time (*Wipe time left*) is displayed.

➡ At the end of this time, the last screen display reappears automatically.

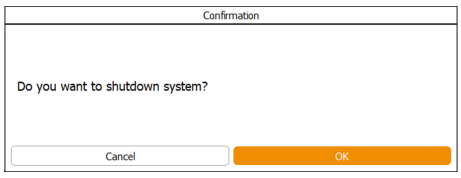
8.3.5 Shutdown – Shutting Down the System



The *Shutdown* submenu has only one function: it shuts down the system. This is only possible when all processes have stopped.

ALWAYS shut down the system first, then switch off the device on the main switch!

Proceed as follows:



1. Call up the *System* main menu and press **Shutdown**.

   ➡ The *Confirmation* dialog box appears with the query/prompt to confirm the shutdown.

2. Press **OK**.

   ➡ The system shuts down.

8.4 Recipes

8.4.1 General Information

The different buttons of the *Recipes* function in the *Batch* main menu can be used to load and start, store or delete what are referred to as recipes. That is, the parameter settings (including cascades) of a cultivation can be stored and reused when the same work processes occur again.

All parameter settings, cascade settings and sensor calibration data are stored. Pump calibration data is not stored. Sensor calibration data is not loaded.

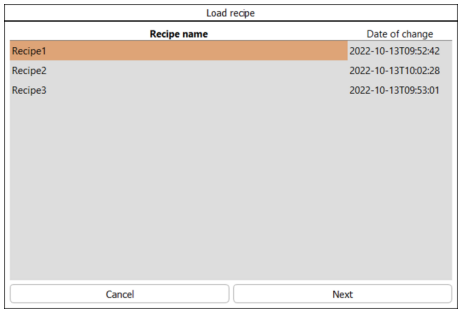
8.4.2 Save Recipe

Recipes can be saved when the cultivation is running or stopped.

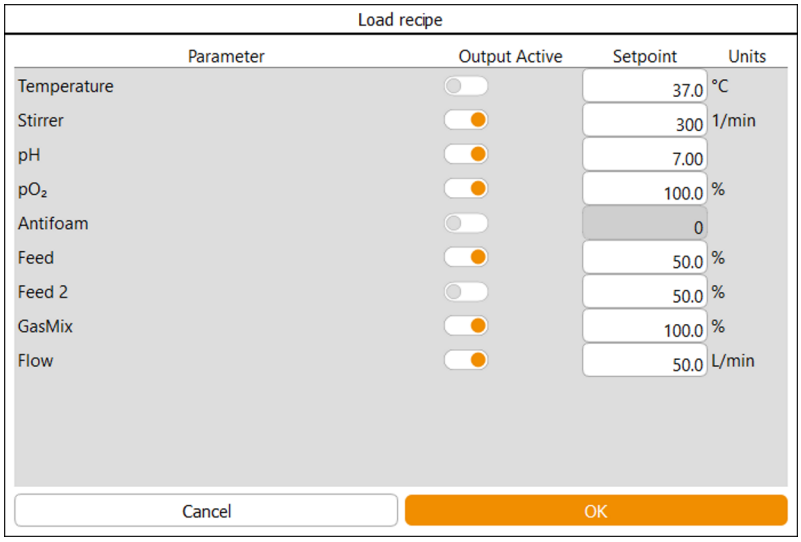
1. Log in to the system as *Technician* or *Administrator*.
2. Call up the *Batch* main menu and press **Save Recipe.**
   ➡ The *Save Recipe* dialog box appears for naming the recipe to be saved.
3. Enter a file name of your choice.
4. Press **OK**.
   ➡ The recipe has been saved.

8.4.3 Load/Start Recipe

Before loading and starting a recipe, all preparations for a cultivation should have been performed.



1. Call up the *Batch* main menu and press **Load/Start Recipe.**
   ➡ The *Load Recipe* dialog box appears, listing all saved recipes with date and time.
2. Select a recipe.
   ➡ The recipe is displayed highlighted in orange.
3. Press **Next.**
   ➡ The *Load Recipe* dialog box changes the view.



Here, all parameters used in the recipe are listed. Setpoints can be changed subsequently and parameters can be activated or deactivated. Use **OK** to start the cultivation.

4. If necessary, change the setpoint and/or activate/deactivate parameters.

5. Press **OK**.

➡ The cultivation is started.

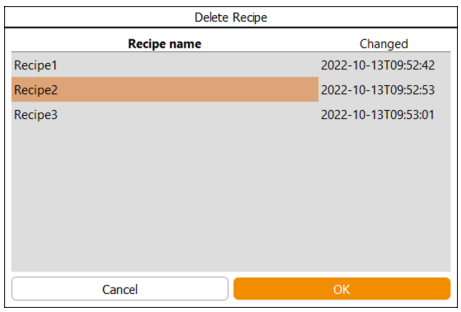
8.4.4 Delete Recipe

Recipes can only be deleted individually. A recipe can also be deleted during a running cultivation.

1. Log on to the system as *Technician* or *Administrator*.

2. Call up the *Batch* main menu and press **Delete Recipe.**

➡ The *Delete Recipe* dialog box appears, listing all saved recipes with date and time.

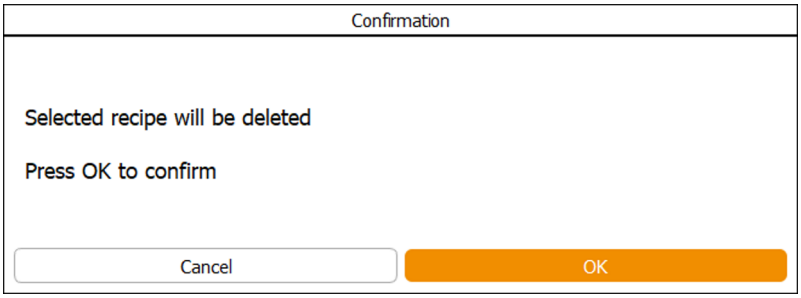


3. Select a recipe.

➡ The selected recipe is displayed highlighted in orange.

4. Press **OK**.

➡ The *Confirmation* dialog box appears to confirm the deletion process.



5. Press **OK**.

➡ The recipe has been deleted.

8.5 Parameters

This chapter contains brief descriptions of all parameters. In addition to all parameters that are available by default in every device configuration, this also includes those parameters that are only configured if the corresponding device option is available.

Temperature

Measures and controls the temperature in the vessel. Measurements in °C are recorded by a platinum resistance temperature sensor (Pt100 sensor).

Stirrer

Measures and controls the rotation speed of the stirrer shaft in min^{-1}. The rotation speed range depends on factors such as vessel volume, number of impellers (stirrers) and the viscosity of the culture.

pH

Measures and controls the pH. This is controlled via the two digital peristaltic pumps *Acid* and *Base*. Their activity is time-specific. This means that they always operate in start/stop mode at the same speed. Control takes place using a PID loop. A deadband can be used to prevent unwanted rapid dosing of the pumps.

Temperature compensation is a special function of the pH parameter when using the analog pH sensor by the manufacturer METTLER. This function must be switched on during cultivation so that the temperature dependency of the measurement principle is corrected.

pO_2

Measures and controls the saturation of dissolved oxygen. Unlike e.g. pH measurements, which are calibrated to absolute measurements, 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. The PID controller output from the *pO_2* parameter is generally cascaded in combination with other parameters such as *Stirrer*, *Flow*, *Feed* or *GasMix*.

Antifoam

Detects foam and controls the addition of antifoam agent. The antifoam pump is activated as soon as the antifoam sensor comes in contact with foam. The parameter output (*Output*) shows 100 % instead of 0 %. 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.

Level

Detects liquid in the vessel by means of the level sensor. As soon as liquid is detected, a signal is generated, and the parameter output (*Output*) shows 100 % instead of 0 %. This signal can be used as required for level control in the vessel. Configurations of this type are available on request.

Feed

Controls the corresponding analog peristaltic pump for adding nutrient solution. The speed of the pump is variably adjustable in %.

Parameter	Controlled pump
Feed	Feed
Feed 2	Feed 2
Feed 3	Feed 3

Flow Parameter

Measures and controls the volume flow of the process gases via one or more mass flow controllers. The measurement system is completely electronic and the measurements are displayed in L min^{-1}.

Parameter	
Flow	Measures and controls the volume flow of two or more process gases in the vessel via a single mass flow controller (thermal mass meter with integrated control valve). If the *Flow* parameter is available this means that the individual process gas lines are equipped with solenoid valves, which are switched using the *GasMix* parameter.
Air Flow, O_2 Flow and/or N_2 Flow	Measures and controls the volume flow of two or more process gases in the vessel via a mass flow controller for each gas.

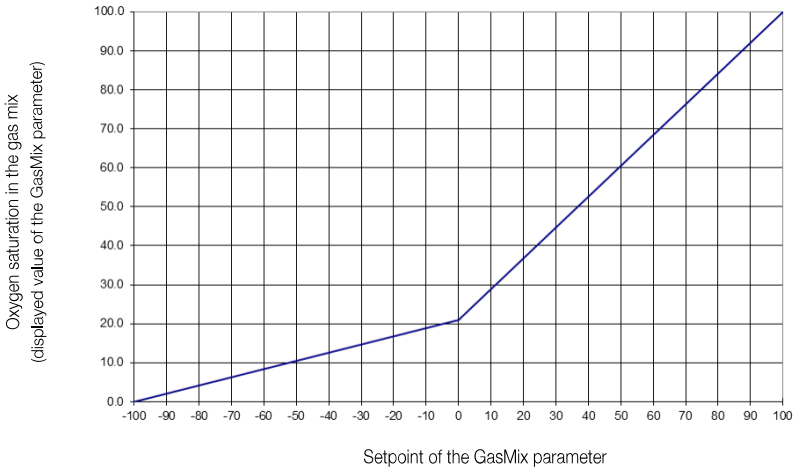
GasMix

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.

If the *GasMix* parameter and the *GM Flow* parameter and the *Air Flow*, *O_2 Flow* or/and *N_2 Flow* parameters have been installed and configured, the specified parameters in an advanced cascade for pO_2 control are preconfigured ex-factory by the device manufacturer.

The following applies to setpoint entry and value display in the touch screen software:

GasMix setpoint	Meaning	Value display
-100 %	Only nitrogen	0 % O_2
0 %	Only air	21 % O_2
100 %	Only oxygen	100 % O_2



Example of a 2-gas-mix system with Air und O_2 with solenoid valves

The solenoid valves are switched according to the pre-set cycle time in the *PID* parameter option of the *GasMix* parameter.

Settings:

- Cycle time: 10 seconds (visible in input field *Eval. Time (s)* in option *PID* of parameter *GasMix*)
- Setpoint in the *GasMix* parameter: 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 corresponds to 10 seconds
- Setpoint 20 corresponds to 2 seconds

For this described configuration, the oxygen portion of the gas mixture cannot fall below 20.95 %.

GM Flow

Sets the gas flow rate of the gas mixture (*GasMix* parameter). The *GM Flow* parameter can only be used and set in conjunction with the parameters *GasMix*, *Air Flow* as well as *O_2 Flow* or/and *N_2 Flow*.

The device uses the gas flow rate of the gas mixture (*GM Flow*) and the setpoints of the *GasMix* parameter to calculate the flow rates of the individual gases. Only a setpoint input for the *GM Flow* parameter is required, the values of the parameters specified above are automatically determined and controlled.

Pressure

Measures and controls the pressure in the vessel in bar. The measurement takes place using a piezo-resistive pressure sensor and control takes place using the control valve in the exit gas line.

Weight

Measures the weight of the vessel and its content in kg. The weight display is tared using **Tare Weight.**

Turbidity

This 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 measurement range and the measurand CU of the *Turbidity* parameter are set analogously to the measured value and range of the transmitter integrated into the sensor.

Exit CO_2 and Exit O_2

Measure the gas concentration of carbon monoxide (CO_2) and oxygen (O_2) in the exit gas stream of the bioreactor via a combined gas sensor and are used for exit gas analysis.

pCO_2

Measures the saturation of dissolved carbon dioxide (CO_2) in the culture using a digital CO_2 sensor with integrated temperature sensor. Measurements are displayed on the transmitter and in the touch screen software. The measurement range and the measurand CU of the pCO_2 parameter are set analogously to the measurement and range of the transmitter.

Redox

Measures the reduction/oxidation potential (redox) in the medium in mV.

Conductivity

If the bioreactor is equipped with an ABER FUTURA biomass sensor, this can also be used to measure conductivity (measurement mS cm^{-1}). Sensors of the ABER Futura system measure the permittivity (also: *Capacitance*) und *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.

Capacitance

Measures the capacity (measured in pF cm^{-1}) that correlates to the live biomass. This is measurement takes place using an ABER FUTURA biomass sensor. Sensors of the ABER Futura system measure the permittivity (also: *Capacitance*) und *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.

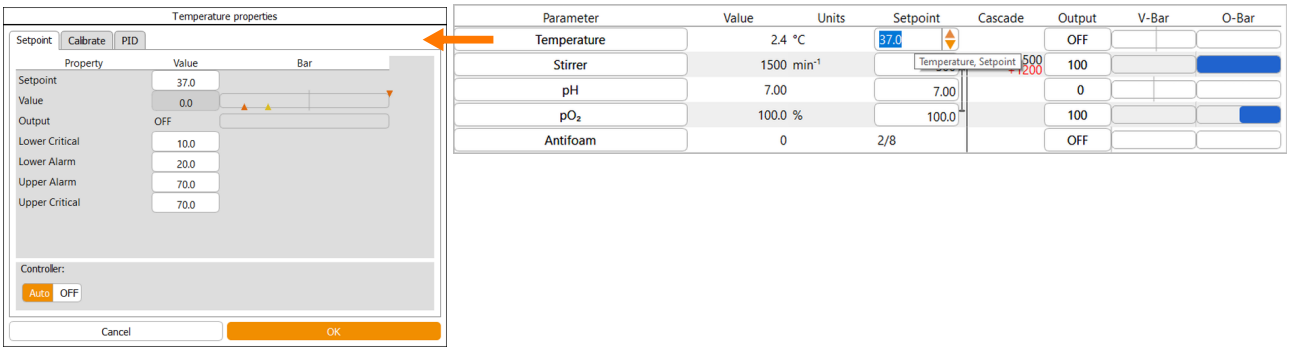
Ext. Pump

Controls an external (optional) pump. The speed is variably adjustable in %.

8.6 Parameter Options

8.6.1 Overview of Settings Menu

Parameter options are called up via the *Controller* main menu. The settings menus are displayed as tab pages in *Properties* dialog boxes of the selected parameter.



Each *Properties* dialog box has two buttons:

- **OK**: save the entries, close the dialog box.
- **Cancel**: close the dialog box without making any changes.

Depending on the access rights and type of the parameters, a greater or smaller number of options will be available:

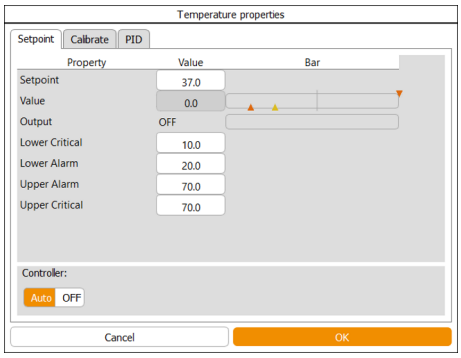
- *Setpoint*: this is where setpoints, alarm values and critical values are set, and parameters are activated and deactivated.
- *Calibrate*: this is where the measurements of the sensors are calibrated and the functionality of the measurement sections is checked.
- *PID*: this is where the controller settings are made.
- *Options*: only qualified INFORS HT personnel has access to this. This option is not available nor visible to any other user group.

If the weight measurement for the vessel is available, the weight display can be tared via **Tare Weight** in the *Batch* main menu. This function can only be executed there and is not available as an option in the *Weight* parameter.

The following chapters explain the individual setting menus. This is then followed either by detailed instructions for making the appropriate settings or a reference to the corresponding chapter.

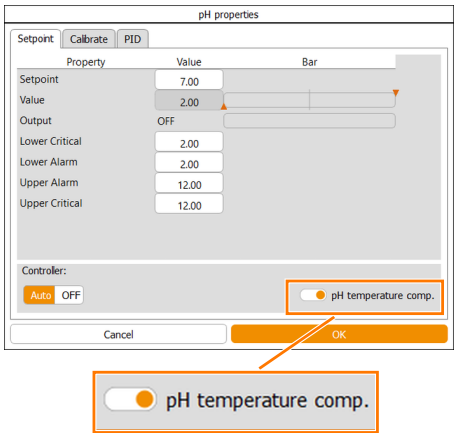
8.6.2 Setpoint

8.6.2.1 Menu Content



- *Setpoint*: set the setpoint.
- *Value*: shows the current measurement (actual value).
- *Output*: shows the controller output in % or *OFF*.
- *Lower Critical* and *Upper Critical*: set the lower and the upper critical value.
- *Lower Alarm* and *Upper Alarm*: set the lower and the upper alarm limit.
- *Controller* **AUTO**: activate the parameter, automatic mode. In this mode, the parameter can be activated or deactivated via the controller output (*Output*) in the *Controller* main menu at any time while a cultivation is running.
- *Controller* **OFF**: deactivate the parameter. This mode also deactivates the controller output in the *Controller* main menu.

Function for pH Temperature Compensation



In the pH measurement system with analog pH sensor, the *pH* parameter has the additional function *pH temperature comp.* (pH temperature compensation). In the digital pH measurement system, this function is integrated into the pH sensor. The pH temperature compensation must be activated during a cultivation so that temperature compensated values can be generated. That is, this is used to correct the temperature dependence of the measurement principle.

The pH of liquids is also temperature dependent, which is why the pH also reacts to temperature deviations when temperature compensation is switched on.

For calibration of the pH sensor with simultaneous temperature measurement of the pH buffer solution or manual entry of the temperature of the buffer solution, this function must also be activated. For more information on the calibration, see ➦ Chapter 8.6.3.5 ‘Calibrating an Analog pH Sensor’ on page 201.

8.6.2.2 Setting Setpoints, Activating and Deactivating Parameters

General Information

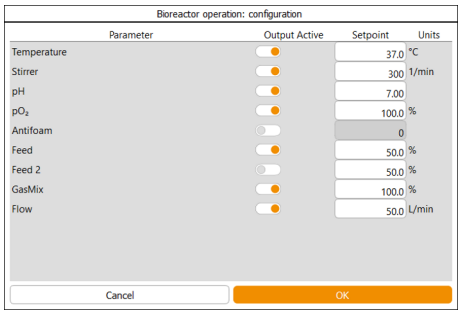
The setpoints of parameters are generally set in the configuration dialog of the cultivation. While the process is running, these can be changed via the *Controller* main menu.

The same applies for activating and deactivating parameters. For this, the controller output must be switched to automatic mode (Option *Setpoint*, *Controller* = **Auto**).

When the cultivation is stopped, all parameters are automatically deactivated.

The cultivation is started with the settings in the configuration dialog. Changes to these settings are saved and transferred into the next configuration dialog. Changes of parameter settings during the running process are only applied to the current cultivation.

Settings in the Configuration Dialog



Proceed as follows:

1. Call up the *Batch* main menu and press **Start.**

   ➡ The configuration dialog appears:

   - All controlled parameters are listed on the left. The number of available parameters depends on the respective device configuration.
   - On the right, there are switches for activating or deactivating the parameters and the start setpoints are listed in the corresponding input fields.

2. If necessary, change the setpoints and activate/deactivate parameters.

3. Press **OK**.

   ➡ The settings have been saved; the cultivation is started.

   ➡ Changed settings are transferred to the next configuration dialog.

Settings while the Cultivation is Running

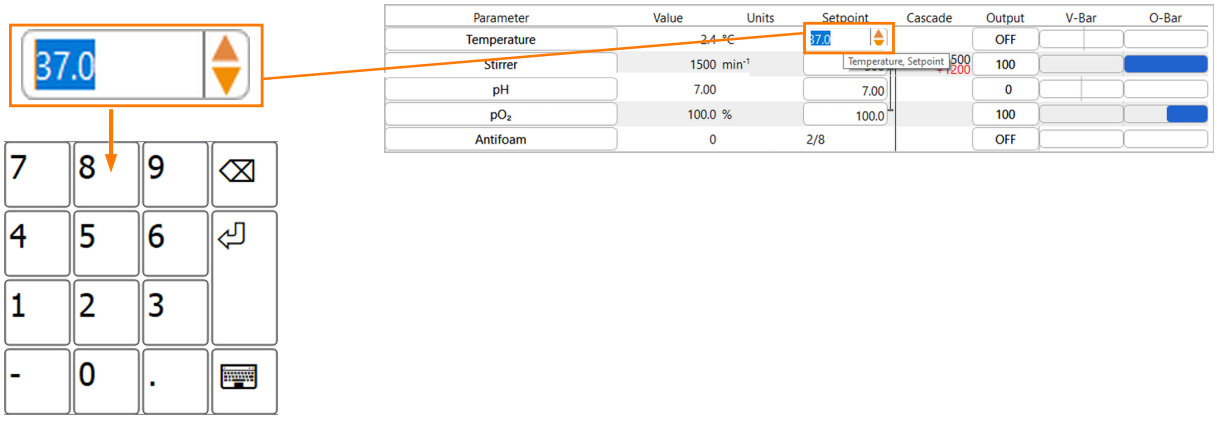
There are two options for entering settings while the cultivation is running:

- Variant A: directly via the *Setpoint* input field/view box and controller output button in the *Output* column
- Variant B: via the *Setpoint* option of the selected parameter in the parameter column

Changed settings are only applied to the cultivation that is currently running.

For variant A), proceed as follows:

1. In the *Controller* main menu, press the *Setpoint* input field/view box of the desired parameter, e.g. *Temperature*.



2. Set the setpoint via the numeric keypad.

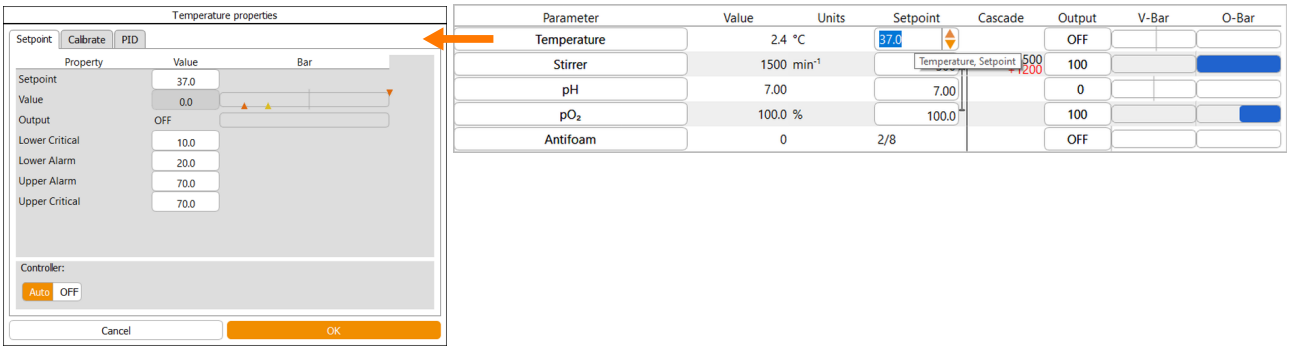
3. Activate the parameter via the controller output button.

➡ The controller output switches from **OFF** to the corresponding numerical value in percent.

The parameter can only be activated or deactivated here, if the controller output is switched to automatic mode (Option *Setpoint*, *Controller* = **Auto**); refer also to the procedure in variant B.

For variant B), proceed as follows:

1. In the *Controller* main menu, press the button of the desired parameter.



➡ The *Setpoint* tab page appears.

2. Set the setpoint and, if necessary, change alarm limits and critical values.

3. Ensure that the controller output is in automatic mode, if not, activate it.

4. Press **OK**.

➡ The settings have been saved.

8.6.2.3 Setting Alarm Limits and Critical Values

The alarm limits and critical values of a parameter can be set symmetrically or asymmetrically:

- Symmetric = the difference between the setpoint and the upper alarm limit or upper critical value = difference between setpoint and lower alarm limit or lower critical value.
- Asymmetric = the difference between the setpoint and the upper alarm limit or upper critical value ≠ difference between setpoint and lower alarm limit or lower critical value.

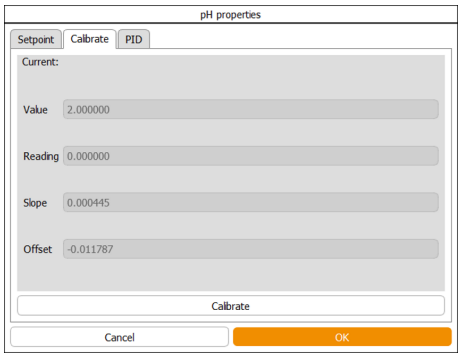
The upper alarm limits can be set as ≤ the upper critical values. The lower alarm limits can be set as ≥ the lower critical values.

A parameter alarm is triggered as soon as the value falls below the lower alarm limit or exceeds the upper alarm limit. For more information, see ➦ Chapter 8.2.7.2 ‘Parameter Alarms’ on page 156.

Alarm limits and critical values must be set in the *Controller* main menu via the *Setpoint* option of each parameter, irrespective of whether the cultivation is stopped or running. The procedure is the same as for setting the setpoints.

8.6.3 Calibrate

8.6.3.1 Menu Content



- *Reading*: shows the current measurement in digital units.
- *Value*: shows the current measurement, depending on the last calibration.
- *Slope*: shows the digital value of the calculated linear slope.
- *Offset*: describes the intersection of the calibration line with the x-axis.

  Reading, *Slope* and *Offset* are not relevant for measurement systems with digital pH and pO_2 sensors. These values are stored directly in the integrated electronic system of the respective sensor.
- **Calibrate**: open the calibration menu.

The calibration menus for pH and pO_2 can also be opened directly via the **Calibrate pO_2** and **Calibrate pH** buttons in the *Batch* main menu.

8.6.3.2 General Information on Calibrating

Sensors for measuring the pH, pO_2 and turbidity are usually calibrated before each cultivation.

- pH sensors: pH sensors must be calibrated before each sterilization. That is, this is done before mounting in the vessel.
- pO_2 sensors: as a rule, a 1-point calibration to 100 % is usually sufficient for exact measurement, and should be carried out before each cultivation. If necessary, 2-point calibration to 100 % and 0 % is also possible.

The prerequisites for exact calibration results are available in separate documentation from the sensor's manufacturer. The calibration conditions and how these can be met are specified by the operator and are not part of this operating manual.

Depending on the selected variant, the device is equipped and configured with a digital or analog pH and pO_2 measurement system.

8.6.3.3 Calibrating a Digital pH Sensor

General Information

The pH buffers and their temperature dependence are saved in the digital pH sensors and are automatically detected during calibration. It is therefore not necessary to carry out a separate temperature measurement of the buffer solution.

If a digital pH sensor has already been calibrated externally, the bioreactor will use this data and there is no need for calibration on the touch screen software.

Calibrating

Proceed as follows:

1. Connect the sensor cable.
2. Carefully remove the cap with the storage solution from the pH sensor and rinse the sensor with distilled water, do not rub it!

NOTICE

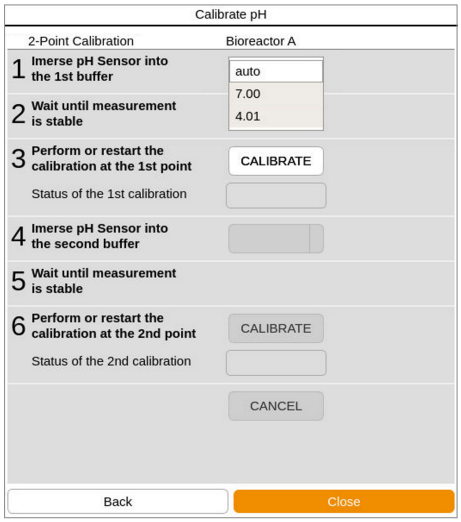
Wiping or rubbing the pH sensor after rinsing can generate an electrostatic charge. This can greatly increase the response time and generate incorrect measurements. At most, lightly dab the pH sensor after rinsing, NEVER wipe or rub.

Only sensor type Easyferm Plus ARC: an *ERROR Glass resistance too high* that might appear after initialization can be ignored. This can occur if the sensor is in contact with air or non-conductive liquid such as distilled water.

3. In the *Batch* main menu, press **Calibrate pH**.

➡ The calibration menu opens with four options:

- **1-Point Calibration** and **2-Point Calibration**: select 1-point or 2-point calibration.
- **Product Calibration**: select product calibration.
- **Show Sensor Status**: menu with dates and values that are output by the sensor manufacturer's firmware that is integrated in the sensor (➦ 'Sensor Status' on page 199).



4. Select 2-point calibration.

➡ The menu opens and guides you through the calibration step by step (1 to 6).

- Step 1 and 4: select the first or second reference value in drop-down lists. If the connected sensor allows the use of different calibration buffers or an automatic detection of the calibration buffer ("auto"), this can be selected. Otherwise, the calibration buffer to be used is displayed.
- Step 2 and 5: display of measurements, wait for stabilization.
- Step 3 and 6: use **CALIBRATE** to start the calibration process.

  As soon as the bar of the status display is filled and *Ready* is displayed, the button switches to **CONFIRM** to save the calibration point. **CANCEL** is available for aborting the calibration process.

  Status display *Ready*:

  – Variant METTLER ISM: measured value is stable, calibration point can be saved.

  – Variant HAMILTON Easyferm Plus ARC: calibration point ready to save, regardless of whether the measured value is stable.

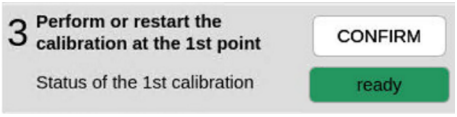
The calibration process can be continued from the last saved point at any time, if the menu was closed using **Close.** However, this does not apply if another calibration process is started.

5. Hold the pH sensor in the appropriate buffer solution of the first calibration point and, if possible, select reference value or automatic buffer recognition in drop-down list (step 1).

> HAMILTON Easyferm Plus ARC: Always start with the lower calibration buffer (4.01).

6. Wait until the measurement is stable (step 2).

7. Press **CALIBRATE** (step 3 a).



➡ The calibration process starts. The **CALIBRATE** button turns into **CONFIRM**. The status display turns green:

- Variant METTLER ISM: as soon as the status display is full, the calibration point can be confirmed.
- Variant HAMILTON Easyferm Plus ARC: the calibration point can be confirmed if the measured value in line 2 is defined as stable by the operator.

8. Press **CONFIRM** (step 3 b).

➡ The calibration point is saved.

> If the calibration process fails, an error message is displayed with a corresponding notice. In this case, restart the calibration.

If the calibration was successful, the drop-down list for selecting the second reference value and the **CALIBRATE** button become available for calibrating the second point.

The calibration process for the second point is the same as for the first point. After rinsing the pH sensor with distilled water, the same *Error...* might occur. This can also be ignored.

After the 2nd calibration point has been saved successfully via **CONFIRM**, calibration is complete and the menu can be closed using **CLOSE**.

Sensor Status

SHOW SENSOR STATUS is used to show data and values produced by the firmware of the sensor manufacturer integrated in the sensor. In addition to information on the sensor type and information on calibration, the following two values are displayed for METTLER ISM sensors:

- *ACT* (Adaptive Calibration Timer): adaptive calibration timer in days, determines the time of the next calibration to ensure that optimal measurement performance is guaranteed. After successful calibration, it is reset to its start value.
- *DLI* (Dynamic Lifetime Indicator): dynamic display of the lifetime. Shows the number of days remaining and is pre-set by the sensor manufacturer.

8.6.3.4 Product Calibration of a Digital pH Sensor

General Information

It is possible to adjust the calibration curve to the current process conditions using product calibration. This could be necessary if there is a possibility of drift of the displayed pH during a long-term cultivation, for example.

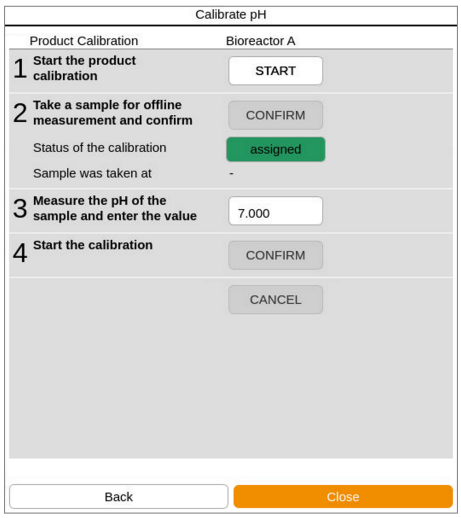
Product calibration can only be carried out and is only effective if the externally measured and entered pH value does not deviate from the original pH value by more than 2 pH units.

Calibrating

Proceed as follows:

1. Call up the calibration menu of the pH sensor and press **Product Calibration**.

   ➡ The menu for product calibration opens and guides you through the product calibration step by step (1 to 4):



- Step 1 and 2: confirm product calibration via **START** and 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 completed sampling can be generated via **CONFIRM**.
  - *measured*: time stamp has been generated.
  - *assigned*: last product calibration was successful and is active. A new product calibration can be performed.
  - *aborted*: last product calibration was aborted via **CANCEL** or was not successful; restart product calibration.
- Step 3 and 4: enter an external measurement and use **CONFIRM** to confirm in order to start the calibration.

The calibration process can be continued from the last saved point at any time, if the menu was closed using **Close.** However, this does not apply if another calibration process is started.

2. Press **START**.

3. Take a sample from the process.

There are two possible approaches:

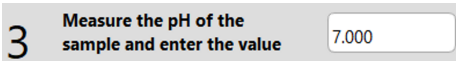
- Variant a): confirm the sampling (generate a time stamp), carry out a laboratory measurement of the pH value for the sample, enter the measurement and carry out product calibration.
- Variant b): confirm the sampling (generate a time stamp), leave the calibration menu by choosing **Close** and carry out the product calibration with an external measurement at a later time.

4. Choose **Close** to leave the menu.

An new product calibration or 1-point calibration or 2-point calibration cancels the active product calibration.

Details for Variant a)

After sampling:



1. Press **CONFIRM**.
   ➡ The status display changes to *measured*. The date and time of sampling are now displayed.
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 that is pH 7.0.
4. Press **CONFIRM** to start the calibration.
5. Wait until calibration is complete.
   ➡ That is, the status display changes to *assigned*. The status allows you to perform another product calibration or leave the menu.
6. Choose **Close** to leave the menu.

Details for Variant b)

After sampling:

1. Press **CONFIRM**.
   ➡ As in variant a), the status display changes to *measured*, and the date and time of sampling are displayed underneath. This indicates that sampling was carried out but product calibration is not yet active. If a sample is lost, step 1 can be repeated.
2. Leave the calibration menu using **Close** and carry out a laboratory measurement of the pH value for the sample at a later time.
3. To carry out product calibration, proceed as in Variant a) from step 2.

8.6.3.5 Calibrating an Analog pH Sensor

General Information

The correct temperature of the buffer solution must be measured to achieve extremely exact calibration results. This can be measured directly using the temperature sensor of the device[1)] during calibration. Another option is to measure the temperature externally and enter the value manually in the touch screen software. In both cases, the temperature compensation of the pH parameter must be activated. This is used to correct the temperature dependence of the measurement principle. If not measured or manually input, the buffer temperature is assumed to be 20 °C.

[1)] *Only possible with temperature sensor for vessel sizes 15 L and 30 L TV.*

Calibrating

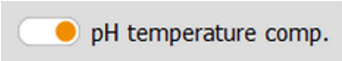
Proceed as follows:

1. Connect the sensor cable.

   Ensure the sensor cable is not buckled or twisted.

> **NOTICE**
>
> The screening on the sensor cable may become damaged if it is kinked or twisted. This may lead to faulty measurements.

If the externally measured temperature of the pH buffer solutions is to be entered or their temperature is to be measured using the temperature sensor:

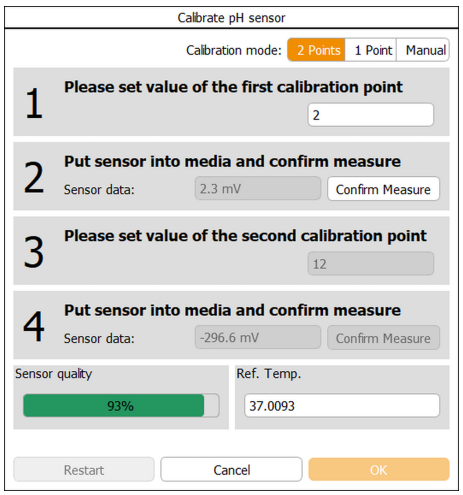


2. In the *Setpoint* parameter option, activate temperature compensation (*pH temperature comp.*).

3. Carefully remove the cap with the storage solution from the pH sensor and rinse the sensor with distilled water, do not rub it!

> **NOTICE**
>
> Wiping or rubbing the pH sensor after rinsing can generate an electrostatic charge. This can greatly increase the response time and generate incorrect measurements. At most, lightly dab the pH sensor after rinsing, NEVER wipe or rub.

4. In the *Batch* main menu, press **Calibrate pH.**



➡ The calibration menu opens and guides you through the calibration step by step (1 to 4).

2-point calibration mode is selected automatically. The *Ref. Temp* display/input field for temperature compensation is displayed.

> Without activating pH temperature compensation first, this display/input field is not visible.

The *Sensor quality* bar graphically depicts the quality of the sensor on a scale from 0 to 100 %

5. Enter the value of the lower (or upper) reference button in the input field in line 1.

The order in which the reference points are calibrated is irrelevant.

If temperature compensation is active:

6. Enter the temperature of the buffer solution in the *Ref. Temp* display/input field or hold the temperature sensor together with the pH sensor in the buffer solution at step 7.

7. Place the pH sensor in 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 lines 3 and 4 are now available.

The signal characteristics are asymmetric. In other words, the closer the signal comes to the real value, the slower the change. The calibration is not accurate, if the measurement is confirmed with **OK** before the sensor signal is completely stable. Wait a few minutes before confirming with **OK** and check the measurement again, if in doubt.

9. Rinse the pH sensor with distilled water, do not rub!

10. For the second calibration point, repeat the same steps as for the first point.

As soon as the second calibration value has been accepted:

11. Press **OK**.

➡ The dialog box disappears, the calibration values are stored.

12. Rinse the pH sensor with distilled water, do not rub!

8.6.3.6 Recalibrating an Analog pH Sensor

General Information

To compensate for a deviation (drift) of a measurement of an analog pH sensor during a long-term cultivation, a re-calibration is possible and sufficient. There are two different ways in which this can be done:

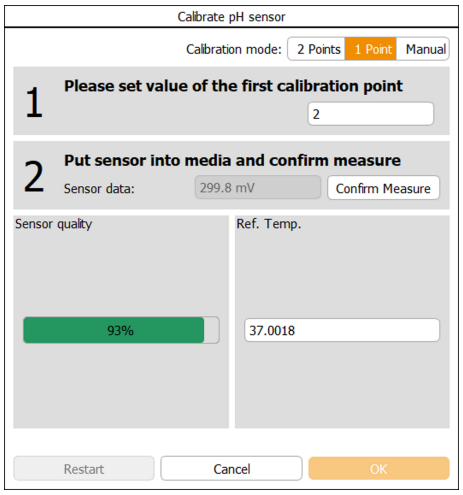
- 1-point calibration
- Manual correction of the "offset"

Calibrating

Proceed as follows:

1. In the calibration menu, use **1 Point** to select 1-point calibration mode.

   ➡ The menu view changes.



2. Enter the externally measured pH of a sample taken as a reference value in line 1.
3. Use **Confirm Measure** to confirm the value.

   ➡ The calibration value is accepted.

4. Press **OK**.

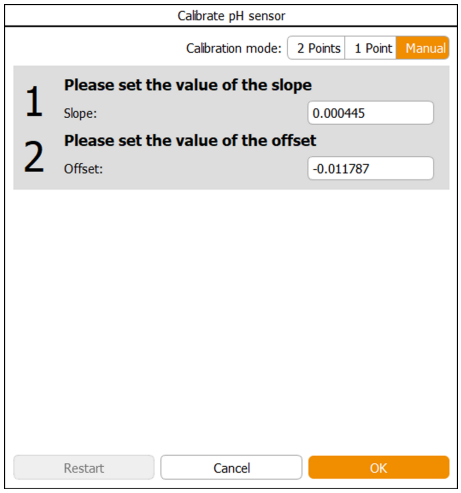
   ➡ The calibration menu disappears, the value is saved.

Manual Correction

Proceed as follows:

1. Determine the difference between the pH measured via an external measuring device and the pH of the culture measured via the connected pH sensor.
2. In the calibration menu, use **Manual** to switch to manual calibration mode.

   ➡ The menu view changes.



3. Depending on the difference between the two pH measurements, either add the result to the displayed "Offset" or subtract it and enter it.

4. Press **OK**.

➡ The calibration menu disappears, the value is saved.

8.6.3.7 Calibrating Digital a pO_2 Sensor

General Information

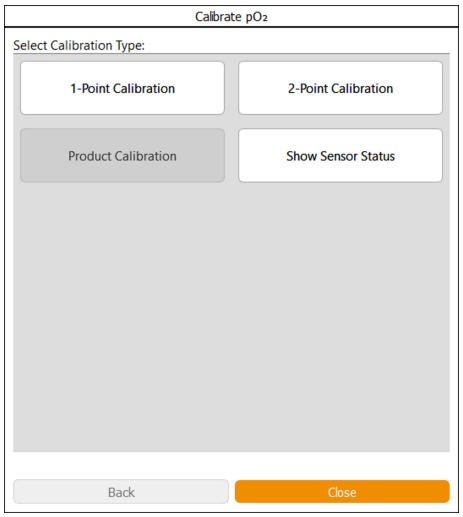
2-point calibration can only be performed in the correct sequence: 1st calibration point = 100 %, 2nd calibration point = 0 %. The following example describes a 2-point calibration.

Digital pO_2 sensors are preconfigured by the device manufacturer to the measurement %-sat.

Calibrating

As soon as the desired calibration conditions for 100 % calibration are reached, proceed as follows:

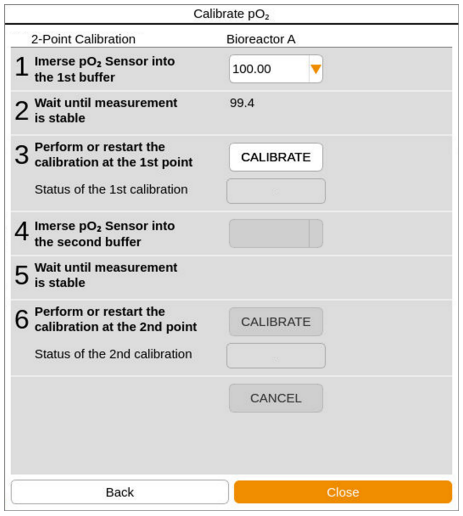
Operation



1. In the *Batch* main menu, press **Calibrate pO_2**.

➡ The calibration menu opens with three options:

- **1-Point Calibration** and **2-Point Calibration**: select 1-point or 2-point calibration.
- **Show Sensor Status**: shows dates and values that are output by the firmware that is integrated into the sensor.



2. Select 2-point calibration.

➡ The menu opens and guides you through the 2-point calibration:

- Step 1 and 4: select the first or second reference value in drop-down list. If the connected sensor allows the use of different reference values or an automatic detection of the reference value (“auto”), this can be selected. Otherwise, the reference value to be used is displayed.
- Step 2 and 5: display of measurements, wait for stabilization.
- Step 3 and 6: use **CALIBRATE** to start the calibration process.

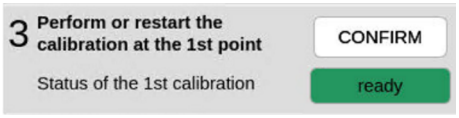
  As soon as the status display bar is filled and *Ready* is displayed, the button switches to **CONFIRM** to save the calibration point. **CANCEL** is available for aborting the calibration process.

  Status display *Ready*:

  – METTLER ISM: measured value is stable, calibration point can be saved.

  – HAMILTON Visiferm DO ARC / RS485-ECS: calibration point ready to save, regardless of whether the measured value is stable.

The calibration process can be continued from the last saved point at any time, if the menu was closed using **Close.** However, this does not apply if another calibration process is started.



3. If possible, select reference value *100* (= 100 %) in the drop-down list (step 1).
4. Wait until the measurement is stable (step 2).
5. Press **CALIBRATE** (step 3a).

   ➡ The calibration process starts. The **CALIBRATE** button turns into **CONFIRM**. The status display turns green:

   - Variante METTLER ISM: as soon as the status display is full, the calibration point can be confirmed.
   - Variante HAMILTON Visiferm DO ARC / RS485-ECS: the calibration point can be confirmed if the measured value in line 2 is defined as stable by the operator.

6. Press **CONFIRM** (step 3 b).

   ➡ The calibration point is saved.

   If the calibration process fails, an error message is displayed with a corresponding notice. In this case, restart the calibration.

   If the calibration was successful, the drop-down list for selecting the second reference value and the **CALIBRATE** button become available for calibrating the second point.

7. Establish correct calibration conditions for the 0 % calibration.

   Once these are met:

8. For the second calibration point for 0 %, proceed in the same way as described starting from step 4.

After the 2nd calibration point has been saved successfully via **CONFIRM**, calibration is complete and the menu can be closed using **CLOSE**.

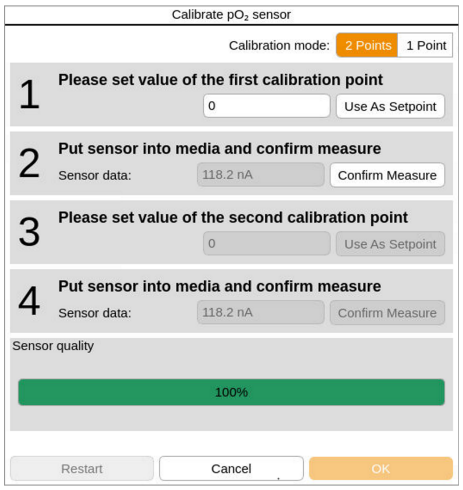
8.6.3.8 Calibrating an Analog pO_2 Sensor

General Information

Polarographic pO_2 sensors must be polarized for commissioning or after they have been disconnected from the power source. Otherwise, correct calibration is not possible. For detailed information on polarization, refer to the separate documentation provided by the sensor manufacturer.

2-point calibration of an analog pO_2 sensor can be performed in 2-point calibration mode or sequentially in 1-point calibration mode. The 2-point calibration must take place in the correct order. 1st calibration point = 0 %, 2nd calibration point = 100 %. The following example describes a 2-point calibration.

Calibrating



As soon as the desired calibration conditions for 0 % calibration are reached, proceed as follows:

1. Call up the *Batch* main menu and press **Calibrate pO_2**.
   - ➡ The calibration menu appears. 2-point calibration mode is selected automatically. The menu guides you through the calibration step by step.

   The **Use As Setpoint** button is only relevant and can only be used under certain circumstances (➥ 'Use As Setpoint Function ' on page 209).
2. In line 1, enter the value 0 (zero = 0 %) for the first calibration point.
3. Wait until the measurement (*Sensor data*, line 2) is stable.
4. Press **Confirm Measure**.
   - ➡ The value is accepted as 0 % oxygen.
5. Establish correct calibration conditions for the 100 % calibration.

   Once these are met:
6. In line 3, enter the value 100 (= 100 %) for the second calibration point.
7. Wait until the measurement (*Sensor data*, line 4) is stable.
8. Press **Confirm Measure**.
   - ➡ The value is accepted as 100 % oxygen saturation.

9. Press **OK**.

➡ The dialog box disappears, the calibration values are stored.

Use As Setpoint Function

Operators can use the **Use As Setpoint** buttons in the calibration menu of the analog pO_2 sensors under the following conditions:

- Configuration with GasMix air/O_2/N_2 is available.
- The GasMix parameter is configured in a cascade for the pO_2 control.

For all other parameters, the **Use As Setpoint** button is only relevant for INFORS HT service technicians.

How it works:

- 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), prior to entering the value 100: the input of 21 (%) in the input field of the second calibration point and pressing 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.

8.6.3.9 Calibrating the Turbidity Sensor

General Information

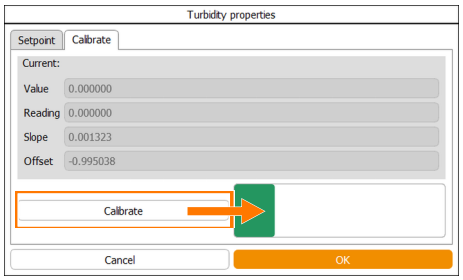
Turbidity sensors ASD25-N are pre-calibrated ex-factory. Inserts are available for reference measurement. Due to the different light absorption of different media, zero point calibration of the turbidity sensor should be performed before each cultivation process. This can be done either before or after in situ sterilization, depending on the application in question.

Conditions for zero point calibration of the sensor: the sapphire windows of the turbidity 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.

Calibrating

Proceed as follows to calibrate the zero point of the (optional, only for the Optek system) turbidity sensor:

1. Connect the sensor cable.
2. Call up the *Controller* main menu and wait until the measurement of the *Turbidity* parameter is stable.
3. Call up the *Calibrate* option of the parameter and press **Calibrate**.



   ➡ A display bar now briefly appears to the right of the **Calibrate** button, which graphically depicts the calibration progress. The progress is shown using a green color.

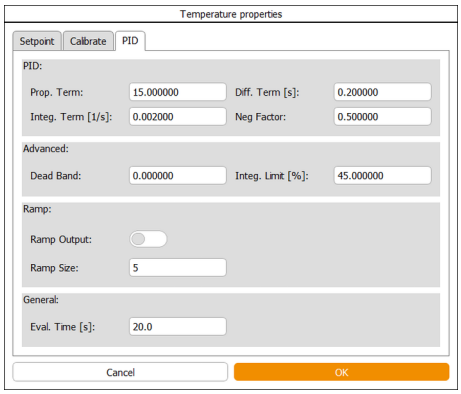
   If the bar disappears after a few seconds, the calibration is complete.

4. Press **OK**.

   ➡ The calibration is saved; the menu disappears.

8.6.4 PID Controller Settings

8.6.4.1 Menu Content



The *PID* menu contains input fields for setting up PID control (Proportional Integral Derivative control).

The table in the following chapter explains the functions of the setting value in more detail.

Please note the following points:

- If *Ramp Output* is deactivated, the value in *Ramp Size* is not relevant.
- For parameters that are not controlled but only measured, only the value in *Eval Time [s]* is relevant. This is always > 0 (zero).

8.6.4.2 Table with Settings for the PID Controller

Setting	Description
P (Prop. Term)	Proportional term: the greater the difference between setpoint and actual value, the greater the controller output.
I (Integ. Term [1/s])	The integral factor sums up all errors over the term. If the setpoint is not reached with the proportional factor, the integral factor successively adjusts the output until the setpoint is reached. If the integral factor is set too high, this leads to fluctuations of the control loop.

Setting	Description
D (Diff Term [s])	The differential quotient calculates the change in the actual value over time and counteracts this change.
Neg. Factor	The negative factor can be used to weight a two-sided control (+100 to -100 percent) (e.g. strong acid, weak base). Here, 1 is the balance and 0.5 or 2 the corresponding halving or doubling of the controller output. Example: nitrogen affects the pO_2 value less than oxygen, so a negative factor of 2 can rebalance the regulator's response.
Deadband	If a deadband value is entered, no control takes place within this value around the setpoint (symmetrical, +/-). That is, the controller output is = 0. The deadband is used for pH control.
I Limit (Integ. Limit [%])	To ensure that the integral factor cannot increase indefinitely, the integral influence is used. This limits the error summation. The integral influence is set between 0 % and 100 % of the controller output.
Ramp output	To make changes slowly and incrementally, a ramp can be activated. This makes sense, in particular, for the stirrer speed or a mass flow valve.
Ramp Size	Time period over which the setpoint of the controller is gradually brought up to the newly entered setpoint.
Eval Time [s]	The eval. time shows the intervals in seconds of the new calculation of the PID value. The controller speed is defined by this. 10 seconds is a good average value for the eval. time.

8.6.4.3 PID Control Explained

The PID function is based on the generic formula provided as the example:

$$Error_n = \frac{Set - Act}{Max.Value - Min.Value}$$

$$Output_n = P.Term * \left\{ Error_n + I.Term \cdot \int_{i=0}^{n} Error_i + D.Term \cdot (Error_n - Error_{n-1}) \right\}$$

The Formula Explained

- *Error*= deviation between setpoint and actual value
- *P* = proportional factor, also called slope, with which a setpoint is reached. The larger the value, the faster the control.
- *I*= Integral factor of the error in 1/second. A typical integral factor is < 0.05
- *D* = Differential quotient of the deviation (*Error*). This is set in seconds (mostly to 0).

The following has to be kept in mind in relation to the individual factors:

Factor	Explanation
Proportional factor	Changing the proportional factor has a big impact on a running process. Increasing it too much leads to oscillation of the control loop around the setpoint. Using the pH parameter as an example To reach the setpoint, a little acid is alternately added, then some base, acid again, then base, and so on. If the proportional factor is reduced too much, the controller hardly reacts to deviations and never reaches the setpoint.
Integral Term	The integral factor should have a small value and only be changed a little in small steps with very large pauses. Ideally, 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 be the reciprocal of two to four times the period of the system. The bigger the value, the less time in seconds remains for the control. Typically, a value greater than 0.05 does not make sense as it exceeds the minimum time required for the control. This leads to oscillations of the control circuit.
Differential quotient	The differential quotient is rarely required. It is set to 0 (zero) at the start. A high value is only necessary, if greater changes are taking place rapidly. It leads to a more rapid speed of response of the controller output for a given error value.

Example for Calculating the Integral Factor

The period of oscillation of the system is detected with 50 seconds from amplitude to amplitude. The integral factor is calculated as follows then:

$1 / (50 \text{ s} \times 2) = 0.01 \text{ s}^{-1}$

$1 / (50 \text{ s} \times 4) = 0.005 \text{ s}^{-1}$

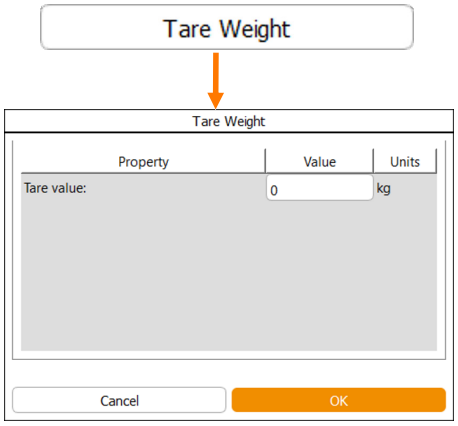
Integ. Term (integral factor)	Seconds
0.1	10
0.05	20
0.001	100
0.005	200

8.6.4.4 Tips for Readjusting a PID Controller

To readjust the PID controller, proceed as follows:

1. Write down the factory setting or ensure that these can be restored if need be.
2. Start by setting the proportional factor when readjusting a PID controller. Choose the proportional bandwidth as large as possible.
3. Set the integral factor and differential quotient to zero.
4. Increase the proportional factor until the controller causes oscillations of the actual value.
5. Measure the period of oscillation, e.g. with the bioprocess platform software eve® of the device manufacturer.
6. Halve the proportional factor and vary the integral factor between the reciprocal of twice and four times the period of oscillation.

8.6.5 Tare Weight Function - Taring the Weight Display



Tare Weight in the *Batch* main menu is generally used to define the zero point of the vessel weighing system. This sets the vessel weight to zero (tares it) so that only the weight of the vessel contents can be measured.

If certain applications require it, any numerical value can be entered as the tare weight instead of the value 0.

Keep in Mind

Before setting the weight display to zero, the vessel must be fully equipped and all hoses (e.g. reagent hoses) must be filled with liquid. Otherwise, the weight displayed in the *Weight* parameter will not correspond to the amount of liquid in the vessel.

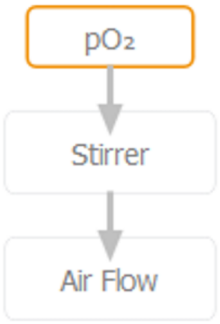
After taring, any change to the vessel, e.g. by dismantling built-in-parts, emptying hoses, etc., also means a change in weight. As a result, the weight measurement is falsified.

8.7 Cascade Control

8.7.1 Cascade Control Explained

The *Cascade* main menu provides the option of setting up a cascade control of a process parameter, usually pO_2. This means that the controller output (= *Output*) of the primary parameter (e.g. pO_2) is used as the reference variable for the secondary parameter(s) in the cascade.

Serial Cascade

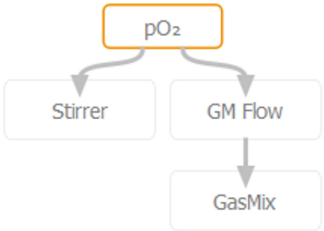


The *Stirrer* parameter is activated as the first one in the cascade to control the pO_2 parameter. The *Air Flow* parameter is only activated when the setpoint of the pO_2 parameter has not been achieved by the *Stirrer*.

Parallel Cascade

The parameters *Stirrer* and *Air Flow* are activated at the same time to control the pO_2 parameter.

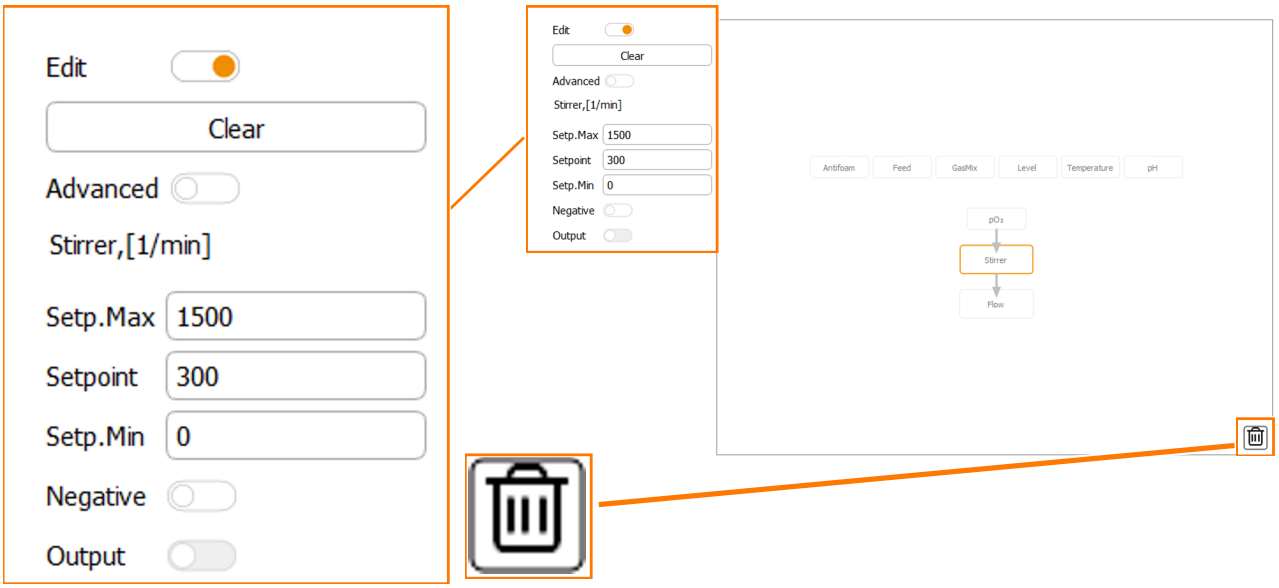
Parallel Serial Cascade



The parameters *Stirrer* and *GM Flow* are activated at the same time to control the pO_2 parameter. The *GasMix* parameter is only activated when the setpoint of the *pO_2* parameter has not been achieved by the *Stirrer* and the *GM Flow*

8.7.2 Setting a Cascade

8.7.2.1 Menu and Functions



Overview

The various cascade settings are made in the left menu area. To activate the view of the existing process parameters in the main area and to be able to make settings, the edit function (*Edit*) at the top left must be activated.

In the main area, the process parameters can then be combined into a cascade using drag & drop or removed individually from the cascade (recycle bin).

Each parameter can generally only be used once in a cascade. A selected parameter is visually highlighted to distinguish it from the other parameters. At the same time, its settings menu becomes visible to its left.

Settings

Input / Function	Description
Edit	Activate or deactivate the edit function.
Clear	Delete a (simple) cascade.

Input / Function	Description
Advanced	Activate or deactivate the setting mode for an advanced cascade. Advanced cascades are used for customer-specific device configurations. They are set exclusively by the device manufacturer ex-factory. In this case, their settings and change options are created for the specific device and can be requested from the manufacturer.
Setp. Max. and *Setp. Min.*	Values set ex-factory. These define the value range of the selected parameter, in which the cascade can change the setpoint to control the setpoint of the primary parameter. These values can be changed within this predefined value range.
Setpoint	Setpoint of the parameter. ■ For the primary parameter: the setpoint to be controlled. ■ For the secondary parameter: the initial setpoint of the parameter from which the setpoint can be varied by the cascade within the value range of *Setp. Min.* to *Setp. Max.* . We generally recommend setting the setpoint for seondary parameters to the lower end of the value range (*Setp. Min.*).
Negative	Activate or deactivate the Negative function of the cascade. The Negative function causes a change in sign of the controller output. This means that a negative controller output causes the addition of a positive value for the setpoint of the cascaded parameter and vice versa. The function can be used for secondary parameters if an increase in the setpoint of the secondary parameter results in a decrease in the actual value of the primary parameter.

8.7.2.2 Cascade Progress Display

Overview

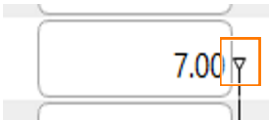
A cascade and its progress can be seen in the *Controller* main menu.

Parameter	Value	Units	Setpoint	Cascade	Output	V-Bar	O-Bar
Temperature	37.0	°C	37.0		100		
Stirrer	1500	min^{-1}	500	1500 +1000	100		
pH	7.00		7.00		0		
pO_2	100.0	%	100.0		100		
Antifoam	0		2/8		OFF		
Level	0.0		0.0		0		
Feed	100.0	%	100.0		100		
Weight	0	kg	--		--		
GasMix	100.0	$\%O_2$	100.0		100		
Flow	20.00	$\frac{L}{min}$	15.00	20.00 +5.00	100		
Turbidity	0.00	CU	--		--		

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 specified in the relevant parameter unit.

Negative Function Display

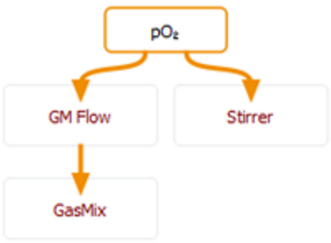
The fact that the Negative function is active is indicated by the triangle symbol on the arrow that indicates the direction of the cascade control.



This arrow shape can be seen in the *Controller* menu.

Color Scheme

The color of an added/subtracted setpoint in the *Controller* menu and the name of the parameter in the *Cascade* menu indicates the progress of the cascade. According to the following scheme, it shows how much leeway of the cascade remains in the value range of a secondary parameter in order to control the primary parameter:



Color	Value range utilisation
Grey	Inactive
Green	0 to 90 %
Yellow	90 to 99 %
Red	100 %
Blue	0 %

Calculation Example

The *Stirrer* parameter is used as the example for secondary parameter from the setpoint to the max. setpoint.

- Setpoint max: 1200 min^{-1}
- Setpoint: 500 min^{-1}
- Difference (=value range): 700 min^{-1}

Conversion:

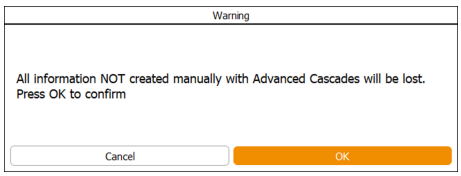
- 700 min^{-1} = 100 %
- 630 min^{-1} = 90 %

This results in a setpoint of 1130 min^{-1} (500 + 630), from which 90 % of the value range is reached. For this display according to the aforementioned color scheme, this means:

- Green: up to 1130 min^{-1}
- Yellow: up to 1193 min^{-1}
- Red: at 1200 min^{-1}

8.7.2.3 Deleting a Cascade

To delete all settings of a cascade (does not apply to extended cascades), proceed as follows:

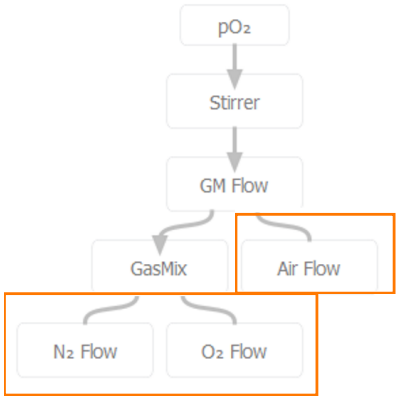


1. In the *Cascade* main menu, press **Clear**.
   ➡ A dialog box appears with the warning that all settings that were NOT made in *Advanced* cascade mode will be deleted.
2. Press **OK**.
   ➡ The cascade is deleted.

8.7.2.4 Special Configurations

For bioreactors with the "High-End" gassing strategy (configuration with several mass flow controllers and GasMix), the gases to be used, e.g. *Air Flow*, *N_2 Flow* and *O_2 Flow* must be assigned to the two gas mix controlling parameters *GasMix* and *GM Flow* in the cascade configuration. To do so, set up the following cascades in addition to the desired cascade configuration, provided the corresponding parameters are available:

- The *Air Flow* parameter as the secondary parameter for the *GM Flow* parameter
- The *O_2 Flow* parameter as the secondary parameter for the *GasMix* parameter
- The *N_2 Flow* parameter as the secondary parameter for the *GasMix* parameter



If both *O_2 Flow* and *N_2 Flow* are available, they will form a parallel cascade under the GasMix parameter.

To distinguish the assignment of these parameters from regular cascade elements, the connections are shown without an arrow.

8.8 Pumps

8.8.1 Control and Settings

Control

The peristaltic pumps are controlled in accordance with the respective parameters:

Pump	Parameter
Acid (digital)	*pH*
Base (digital)	*pH*
Antifoam (digital)	*Antifoam*
Feed (analog)	*Feed*
Feed 2 / *Feed 3* (analog, optional)	*Feed 2* / *Feed 3*

Digital pumps and time-depending and always operate at the same speed in start/stop mode. Analog pumps run continuously at a speed that can be set. Both digital and analog pumps are controlled within a range of 0 % up to 100 %.

Example

- Analog: 50 % of the maximum flow rate = pump runs at half speed.
- Digital: 50 % of the maximum flow rate = pump runs half the time.

Settings

The following settings can be made for the pumps:

- Feed pump(s): set the speed in 0.1 % increments in the range of 0 % to 100 %.
- Antifoam pump: set the dose/wait time in s.
- Calibrate the pumps.
- Manually reset the pump counter to zero.
- Fill and empty pump hoses manually or in a time-controlled manner.

8.8.2 Calibrating the Pumps

Calibration of the pumps enables display and recording of the actual pumped volume. The quantity conveyed is stated in mL.

Operation

Tools

Provide the following tools:

- Graduated measuring cylinder/cup or balance and empty vessel.
- Reagent bottle equipped with silicone hose and filled with the reagent to be pumped or equally viscous liquid.

For very precise results, the reagent bottle should be placed on a balance that can also be connected to the bioreactor or a PC with the eve® bioprocess platform software installed.

Requirements

Please note the following points:

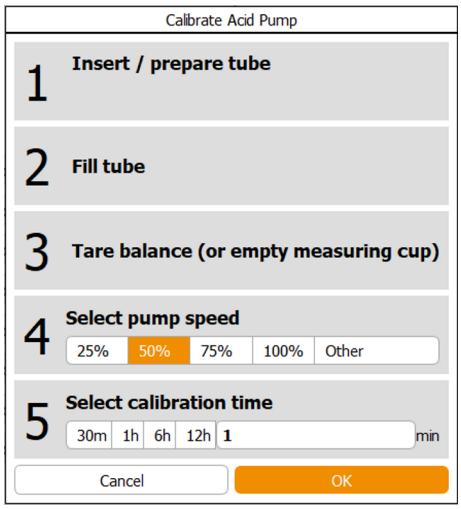
- Always use similar hoses with the same dimensions for calibrating and conveying the media.
- For calibration, use the same or equally viscous liquid as that used for conveying during the process.

Calibration

To calibrate a pump, e.g. the acid pump (*Acid*), proceed as follows:

1. Connect the reagent bottle to the pump.
2. Hang the output side of the hose into the measuring cylinder/beaker or place the reagent bottle on the balance and tare to zero, hang the output side of the hose in the empty vessel.
3. Fill the hose completely.
4. Call up the *Batch* main menu and press **Acid Pump**.

   ➡ The *Calibrate Acid Pump* dialog box appears and guides you through the calibration step by step.



5. At step 4 (*Select pump speed*) select the pump speed in percent or manually enter a value via the **Other** option.

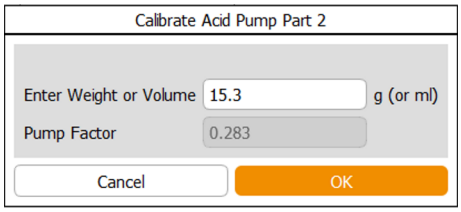
   For best results, the pump should be calibrated at the speed expected during operation.

6. At step 5 (*Select calibration time*) select the calibration time or set it manually.

7. Press **OK**.

➡ Calibration starts. The remaining time (*time left:...*) in h/min/s is displayed next to the **Stop** button that is now available.

As soon as this time has expired, the second dialog box appears (*Calibrate Acid Pump Part 2*).



8. Enter the pumped liquid in mL or g (*Enter Weight or Volume*).

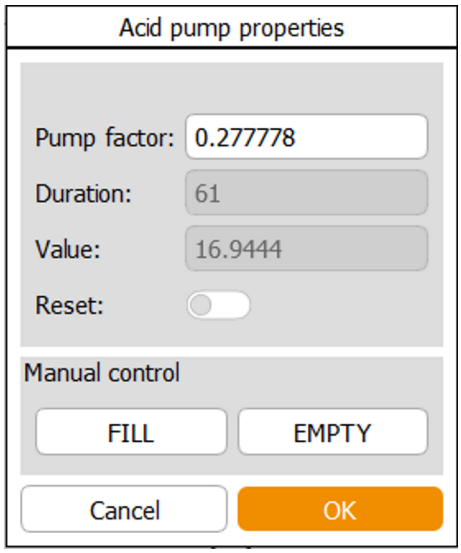
➡ After entering the pumped quantity, the automatically calculated pump factor is displayed. For a calibrated pump, the pump factor is always ≠ 1.

9. Press **OK**.

➡ The dialog box disappears, the calibrated value is saved. *Completed at* with date and time next to **Stop** shows that the pump has been calibrated as well as when this happened.

8.8.3 Resetting the Pump Counter to Zero

The number of revolutions (pump not calibrated) or the quantity conveyed in mL (pump calibrated) of the peristaltic pumps are continuously displayed during a cultivation. After the end of the process, this display continues until a new cultivation is started.



However, the counter can also manually be reset to zero:

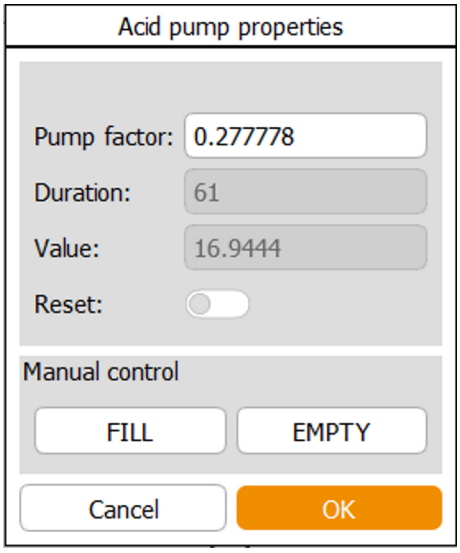
Press a pump button in the *Main* menu to open the pump dialog box, in the example on the left, this is the acid pump (*Acid*). The displayed number of revolutions (*Duration*) and quantity conveyed in ml (*Value*) can be reset here via *Reset*.

By manually changing the pump factor (*Pump factor*) the previously performed calibration is discarded. For a calibrated pump, the pump factor is always ≠ 1.

8.8.4 Filling and Emptying the Pump Hoses

The pump hoses can be filled and emptied either in a time-controlled manner or manually. Time controlled filling or emptying of the pump hoses is only possible only when the cultivation is stopped.

Manual Filling and Emptying



Press a pump button in the *Main* menu to open the pump dialog box e.g. *Acid* with **FILL** for filling and **EMPTY** for emptying. The pump runs as long as the corresponding button is pressed.

The pump hoses can also be filled and emptied manually via the rocker switches on the instrumentation cabinet, see ➦ Chapter 8.8 'Pumps' on page 221.

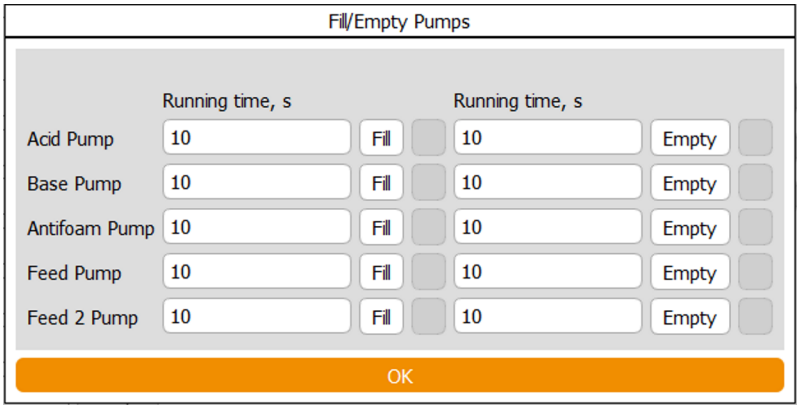
Time-Controlled Filling and Emptying

Automatic time-controlled filling or emptying of the pump hoses is possible when the cultivation is stopped.

Please note the following points first:

- Test the pumping time of a pump in advance with the liquid having the same or similar viscosity as the liquid to be pumped.
- Observe the hose lengths and hose sizes of the pumps and, if necessary, test the pumping time of each pump individually, taking into account the condition mentioned above.

Fill/Empty Pumps in the *Batch* main menu opens the *Fill/Empty Pumps* dialog box.



Here, an individual filling duration and empty duration in seconds can be defined for each pump.

The filling and emptying process is started via **Fill** and **Empty**. Next to each of these buttons is a button for immediately stopping the current fill / empty procedure.

If a filling or emptying procedure is active, the remaining filling or emptying time is displayed. The menu cannot be closed while at least one filling or emptying procedure is active.

8.9 Processes

8.9.1 General Information

The following processes can be performed with the bioreactor:

- Full sterilization (default)
- Sterilization of the harvest/sample valve (default)
- Sterilization of the sample valve (option)
- Sterilization of the feed line (option)
- Cultivation (default)

When equipped with an appropriately designed vessel, the bioreactor is CIP-enabled. However, the CIP process is controlled via the separate TechCIP mobile CIP unit of the INFORS HT device manufacturer. The instructions for this are available in the separate operating manual of the mobile CIP unit.

Process Configuration and Start

All processes are started and executed with the value set in the configuration dialog of the process [1]. The order in which the processes are performed can be selected freely and is specified by the operator. Whether and when processes can run in parallel or be started is predefined and recorded in a process compatibility chart (“interlock list”) in the separate technical documentation.

[1] *Only during cultivation can process parameter settings be changed while the process is running.*

Process Sequence and End

All processes [2] run through with predefined steps until the end, or until the "holding phase" (full sterilization). In addition to the running process sequence, the active process step as well as the running time...*in progress since in h:min:s* are displayed. If manual operator interactions are required during a process, this is indicated by means of corresponding instructions in dialog boxes.

[2] *Exception: cultivation*

In the “hold phase”, a full sterilization must be actively terminated using **Stop**. Alternatively, it can also be terminated by starting (**Start**) the cultivation. The cultivation must be actively terminated using **Stop**.

Process Abortion

There are two different types of process abortions:

- Automatic process abortion triggered by the system due to a faulty system state.
- Manual process abortion, triggered by the operator via **Stop**.

In any case, a safe abortion defined via the system takes place. A process abortion is shown as *aborted at* with date and time.

Process Descriptions

The following chapters describe each process and its sequence in table form with status displays and dialog boxes in the touch screen software (chapter "Process Sequence"). The parameters with value ranges that can be set for a process are listed in the respective "Process configuration" chapter. Prerequisites and instructions for carrying out the process follow afterwards (chapters "Before Starting the Process" and "Executing the Process"). If necessary, correspondingly named chapters follow with additional information on the end of the process or a manual process abortion. For more information on process sequences, refer to the "Process Sequences" document in the separate technical documentation of the bioreactor.

8.9.2 Safety Notes

WARNING

The vessel of the bioreactor is under pressure during the full sterilization. This can also be the case during other operations.

Removing built-in-parts or the vessel top plate may result in liquid splashing out or leaking and/or gases escaping. This can lead to severe burns, burns or poisoning.

Always make sure that the vessel is free of pressure before manipulating built-in-parts and the vessel top plate.

CAUTION

Risk of burns due to contact with the hot surfaces! The vessel, piping and associated components of the bioreactor can get hot. Touching these components can lead to burns.

8.9.3 Full Sterilization

8.9.3.1 Process Sequence

For full sterilization, the water in the vessel jacket is heated by feeding in steam. The steam generated by the liquid in the vessel also sterilizes the inlet air and exit gas filters at the same time.

Process step	**D = Dialog box, user interaction required** **S = Status display, no user interaction**	
Configuration	D	*configuration* for process configuration
User interaction	D	*user interaction required* with instruction(s)
Delayed start	S	*starting inhibitor* + *time left* in h:min:s
	Step is skipped if function is deactivated.	
Heating up to degassing temperature	S	*heating up to degassing temperature* + set temperature in °C + current temperature display
	Step is skipped if value for degassing time = 0.	
Degassing at degassing temperature	S	*degassing at degassing temperature* + set temperature in °C + *time left* in h:min:s
	Step is skipped if value for degassing time = 0.	
Heating up to sterilization temperature	S	*heating up to sterilisation temperature* + set temperature in °C + current temperature display
Sterilization at sterilization temperature	S	*sterilising at sterilisation temperature* + set temperature in °C + *time left* in h:min:s
User interaction	D	*user interaction required* with instructions
	The dialog box only appears if a resterilizable feed line (option) is used.	
Cooling down to 95 °C	S	*cooling down to 95 °C* + current temperature display
Cooling down to 70 °C	S	*cooling down to 70 °C* + current temperature display
	From a temperature of < 70 °C, an immediate process abortion is possible.	
Cooling down to holding phase temperature +10 °C	S	*cooling down to holding phase temperature +10 °C* set temperature in °C + current temperature display
Cooling down to holding phase temperature	S	*cooling down to holding phase temperature* + set temperature in °C + current temperature display
Holding phase	S	*holding phase* + set temperature in °C

Process step	D = Dialog box, user interaction required S = Status display, no user interaction	
	Holds holding phase temperature until cultivation is started or full sterilization is stopped.	
Full sterilization complete	S	*completed at* with date and time in h:min:s

Degassing

If the medium is heated too quickly, foaming may occur due to escaping gases. During the "degassing" phase, a specified temperature is therefore maintained for a defined time to allow gases to escape in a controlled manner. The time and temperature are set in the configuration dialog.

8.9.3.2 Process Configuration

Input field		Value range	Unit
Stirrer (rotation speed stirrer)		20 to 1000	min^{-1}
Degassing temperature		up to 95	°C
Degassing time		10 to 120	min
Sterilisation temperature		110 to 125	°C
Sterilisation time		10 to 120	min
Cooling flow (air flow during cooling phase to prevent vacuum in the vessel) (Only with mass flow controller, otherwise manual control using rotameter)	15 L TV	10.0 to 20.0	L/min
	30 L TV	20.0 to 40.0	L/min
	42 L TV	30.0 to 60.0	L/min
Holding phase temperature		up to 79	°C
Holding phase flow (air flow in holding phase) (Only with mass flow controller)	15 L TV	0 / 0.2 to 20.0	L/min
	30 L TV	0 / 0.4 to 40.0	L/min
	42 L TV	0 / 0.6 to 60.0	L/min
Holding phase pressure (pressure in holding phase) (Only with optional pressure control)		0 to 1.5	bar
Heating up time max.		90 to 300	min

Input field	Value range	Unit
Start inhibitor (activate or deactivate start delay)	*No* / *Yes*	
Hours	0 to 99	h
Minutes	0 to 59	min
(Start process in ... hours and ... minutes)		

8.9.3.3 Before 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 (➥ chapter 2.7.3, page 54).
- The antifoam sensor has been removed.
- If available: the inoculation needles have been removed.
- If available: the push valves are closed.

8.9.3.4 Executing the Process

To execute the process, proceed as follows:

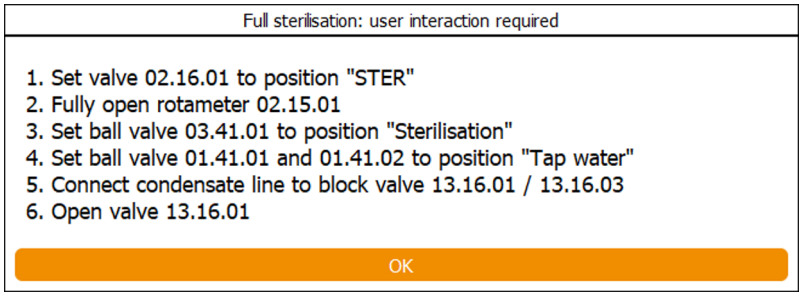
1. In the *Batch* main menu, press **Full Sterilisation.**

   ➥ The configuration dialog appears with more or fewer input fields depending on the device configuration.

2. Enter the setpoints.

3. Press **OK**.

   ➥ The dialog box for user interaction appears with more or fewer procedures to be performed depending on the configuration of the bioreactor.



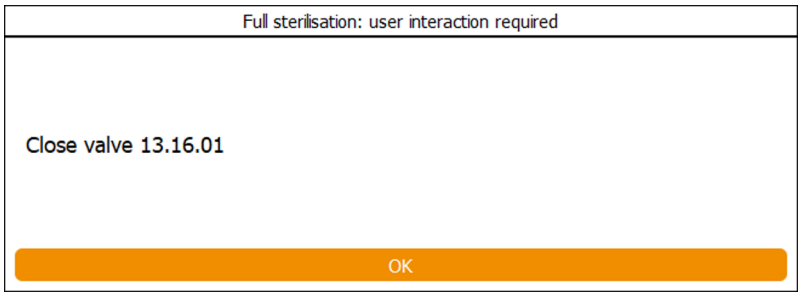
The figure shows, as an example, the dialog box of a device with a rotameter, gas sensors for exit gas analysis, ball valves for switching from tap water to chilled water and a resterilizable feed line.

4. Execute all the steps of the procedure in sequence.
5. Press **OK**.

➡ The process now runs automatically until the holding phase is reached. [1)]

If the sterilization temperature falls below the set setpoint, this is indicated by *temperature is low*. The countdown is stopped until the temperature has reached the setpoint again. The process is then continued.

[1)] With a resterilizable feed line, a second dialog box appears first after the set sterilization time has elapsed:



1. Execute the step.
2. Press **OK**.

➡ The process runs automatically until the holding phase is reached.

8.9.3.5 Terminating the Process

The holding phase temperature is maintained until the cultivation is started via **Start** or the process is stopped via **Stop** next to **Full Sterilisation.**

8.9.3.6 Aborting the Process

For safety reasons, an immediate process abortion is only possible at a temperature of < 70 °C. That is, at ≥ 70 °C the cool down phase is initiated first.

8.9.4 SIP Harvest/Sample Valve – Sterilization Harvest/Sample Valve

8.9.4.1 Process Sequence

The combined harvest/sample valve *05.12.01* can be sterilized any number of times, irrespective of a full sterilization. Between sterilization and sampling, you should wait long enough to allow the valve to cool down.

The process is started and terminated in the touch screen software, and the sterilization time is set in the configuration dialog. The addition of steam is controlled via valve *05.10.01* on the hose line on the harvest/sample valve.

Process step	**D = Dialog box, user interaction required** **S = Status display, no user interaction**	
Configuration	D	*configuration* for process configuration
User interaction	D	*user interaction required* with instructions
Sterilization	S	*sterilisation* + *time left* in h:min:s
User interaction	D	*user interaction required* with instructions
Sterilization of harvest/sample valve complete	S	*completed at* with date and time in h:min:s

8.9.4.2 Process Configuration

Input field	**Value range**	**Unit**
Sterilisation time (sterilization duration)	10 to 60	min

8.9.4.3 Before Starting the Process

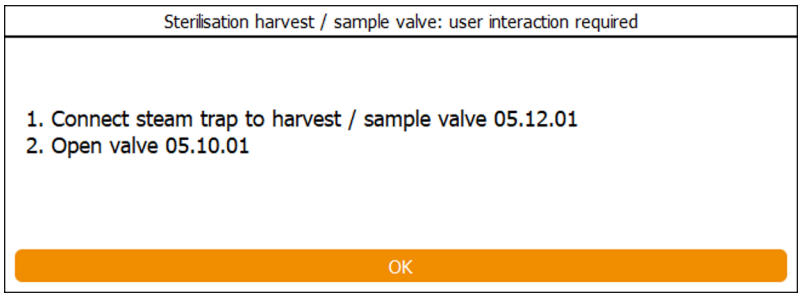
Before starting the process, check and ensure that:

- All required services are available and activated.
- All services have the correct connection pressure.
- The harvest/sample valve *05.12.01* is closed.
- The steam hose is connected.
- The container and/or hose for discharging the condensate is ready.

8.9.4.4 Executing the Process

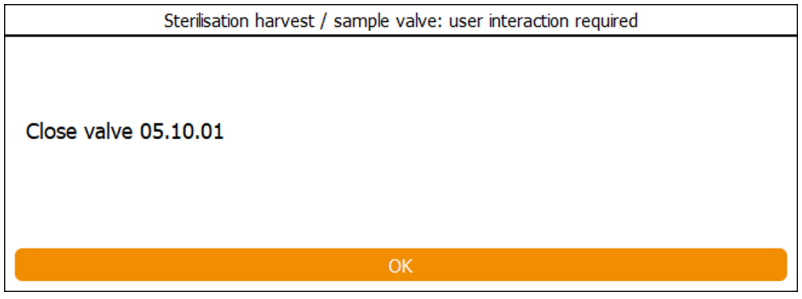
To execute the process, proceed as follows:

1. In the *Batch* main menu, press **SIP Harvest / Sample Valve.**
   ➡ The configuration dialog appears.
2. Enter the desired sterilization time.
3. Press **OK**.
   ➡ The dialog box for user interaction appears with instructions.



4. Execute the steps of the procedure in the order listed.
5. Press **OK**.
   ➡ The process starts.

   As soon as the set sterilization time has elapsed, the second dialog box appears with instructions.



6. Execute the step.

7. Press **OK**.

➡ The process is finalized.

8.9.4.5 Aborting the Process

The process can be aborted at any time. The same dialog box appears as for the normal process end.

8.9.5 SIP Sample Valve – Sterilization Sample Valve

8.9.5.1 Process Sequence

The (optional) sample valve *17.13.01* can be sterilized any number of times, irrespective of a full sterilization. Between sterilization and sampling, you should wait long enough to allow the valve to cool down. The process is started and terminated in the touch screen software, and the sterilization time is set in the configuration dialog. The addition of steam is controlled via valve *17.10.01* on the hose line on the sample valve.

Process step	**D = Dialog box, user interaction required** **S = Status display, no user interaction**	
Configuration	D	*configuration* for process configuration
User interaction	D	*user interaction required* with instructions
Sterilization	S	*sterilisation* + *time left* in h:min:s
User interaction	D	*user interaction required* with instructions
Sterilization of sample valve complete	S	*completed at* with date and time in h:min:s

8.9.5.2 Process Configuration

Input field	**Value range**	**Unit**
Sterilisation time (sterilization duration)	10 to 60	min

8.9.5.3 Before Starting the Process

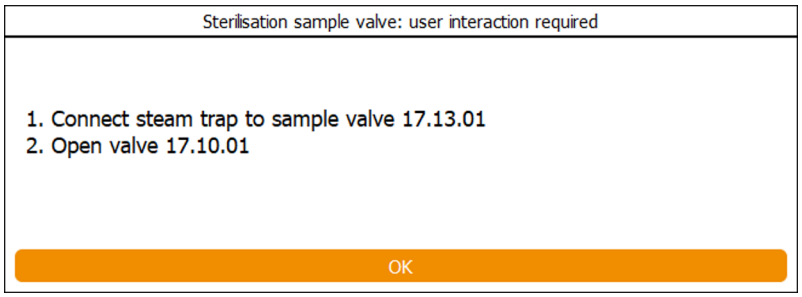
Before starting the process, check and ensure that:

- All required services are available and activated.
- All services have the correct connection pressure.
- Sample valve *17.13.01* is closed.
- The steam hose is connected.
- The container and/or hose for discharging the condensate is ready.

8.9.5.4 Executing the Process

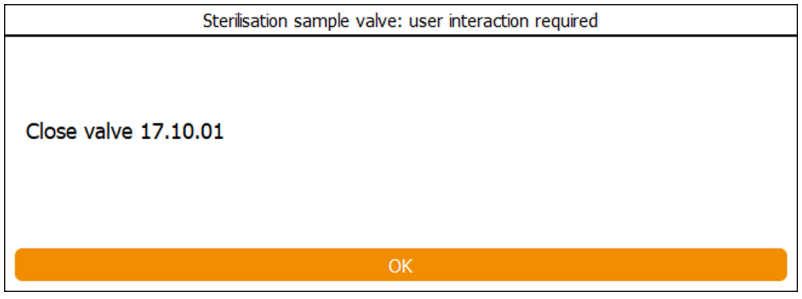
To execute the process, proceed as follows:

1. In the *Batch* main menu, press **SIP Sample Valve.**
   ➡ The configuration dialog appears.
2. Enter the desired sterilization time.
3. Press **OK**.
   ➡ The dialog box for user interaction appears.



4. Execute the steps of the procedure in the order listed.
5. Press **OK**.
   ➡ The process starts.

   As soon as the set sterilization time has elapsed, the second dialog box appears with instructions.



6. Execute the step.

7. Press **OK**.

➡ The process is finalized.

8.9.5.5 Aborting the Process

The process can be aborted at any time. The same dialog box appears as for the normal process end.

8.9.6 SIP Feed Line – Sterilization Feed Line

8.9.6.1 Process Sequence

The (optional) resterilizable feed line is first autoclaved and sterilized in additional sub-steps. For more information on this subject, see ➦ Chapter 3.3.1 'Resterilizable Feed Line' on page 90 The process is started and terminated in the touch screen software, and the sterilization and ventilation time is set in the configuration dialog. All valves of the feed line are opened and closed manually.

Process step	**D = Dialog box, user interaction required** **S = Status display, no user interaction**	
Configuration	D	*configuration* for process configuration
User interaction	D	*user interaction required* with instructions
Sterilization	S	*sterilisation* + *time left* in h:min:s
User interaction	D	*user interaction required* with instructions
Ventilation	S	*ventilation*+ *time left* in h:min:s
User interaction	D	*user interaction required* with instructions
Sterilization of feed line complete	S	*completed at* with date and time in h:min:s

8.9.6.2 Process Configuration

Input field	**Value range**	**Unit**
Sterilisation time	10 to 60	min
Ventilation time	0 to 60	min

8.9.6.3 Before Starting the Process

Before starting the process, check and ensure that:

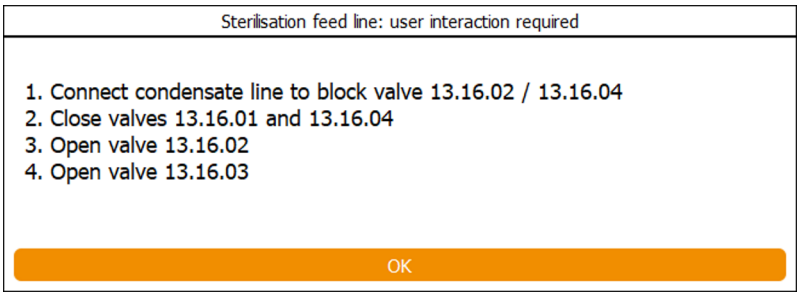
- All required services are available and activated.
- All services have the correct connection pressure.
- Block valve *13.16.02* / *13.16.04* is connected.
- The steam hose is connected.

To be able to start the process while a cultivation is running, the *Feed* parameter must be deactivated.

8.9.6.4 Executing the Process

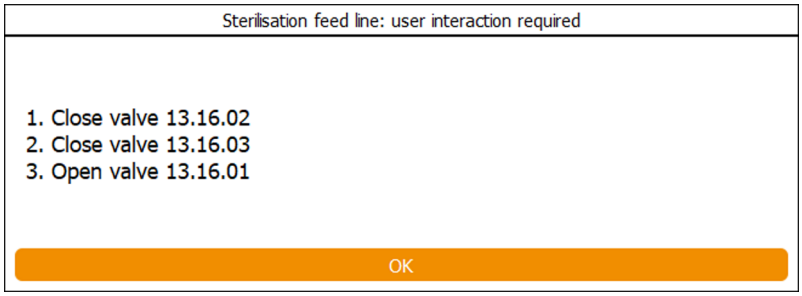
To execute the process, proceed as follows:

1. In the *Batch* main menu, press **SIP Feed Line.**
   ➡ The configuration dialog appears.
2. Enter the desired sterilization and ventilation time.
3. Press **OK**.
   ➡ The first dialog box for user interaction appears with instructions.



4. Execute the steps of the procedure in the order listed.
5. Press **OK**.
   ➡ The process starts.

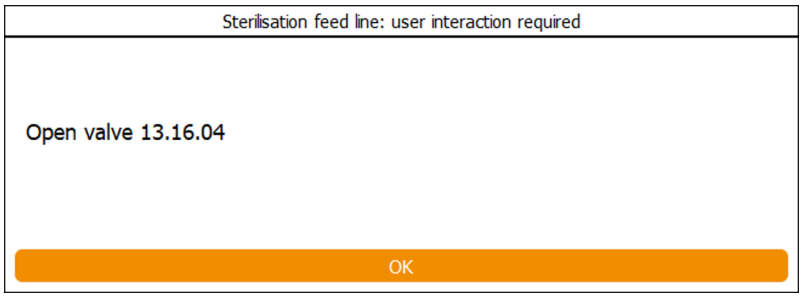
   As soon as the set sterilization time has elapsed, the second dialog box appears with instructions.



6. Execute the steps of the procedure in the order listed.
7. Press **OK**.

   ➡ Ventilation starts.

   As soon as the set ventilation time has elapsed, the third dialog box appears with instructions.



8. Execute the step.
9. Press **OK**.

   ➡ The process is finalized.

8.9.6.5 Aborting the Process

The process can be aborted at any time.

The valves of the feed line must be returned to their original position. To do this, follow the instructions in the dialog boxes.

8.9.7 Bioreactor Operation – Cultivation

8.9.7.1 Process Sequence

Process step	D = Dialog box, user interaction required S = Status display, no user interaction	
Configuration	D	*configuration* for process configuration
User interaction	D	*user interaction required* with instructions
Cultivation running	S	*in progress since* + running time in h:min:s
User interaction	D	*user interaction required* with instructions
Cultivation stopped	S	*stopped after* + cultivation time with date and time in d:h:min:s

8.9.7.2 Process Configuration

Input field		Value range	Unit
Temperature		0 / 20 to 79	°C
Stirrer (rotation speed stirrer)	15 L TV	0 / 20 to 1500	min^{-1}
	30 L TV	0 / 20 to 1200	min^{-1}
	42 L TV	0 / 20 to 1200	min^{-1}
pH		2 to 12	--
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 / *Air Flow* / *O_2 Flow* / *N_2 Flow* / *GM Flow* (Gas flow)	15 L TV	0 / 0.2 to 20.0	L/min
	30 L TV	0 / 0.4 to 40.0	L/min
	42 L TV	0 / 0.6 to 60.0	L/min
Pressure [1)]		0 to 1.5	bar

[1)] *Option*

[2] *The setting range depends on the type and number of gases used (air, O_2, N_2).*

[3] *Depending on the selected gassing strategy and the number of gases, more or fewer Flow parameters exist and are configured.*

8.9.7.3 Before 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 (➥ Chapter 2.7.3, page 54).

8.9.7.4 Starting the Process

To start the cultivation, proceed as follows:

1. In the *Batch* main menu, press **Start.**

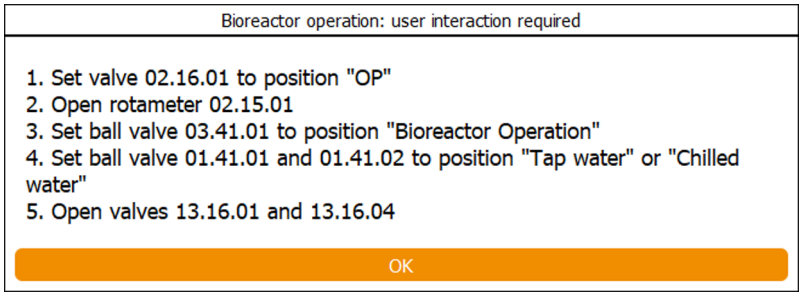
➡ The configuration dialog appears with more or fewer parameters depending on the device configuration. The setpoint settings of the parameters from the last cultivation are visible here.

The cultivation is started with the settings in the configuration dialog. Changes to these settings are saved and transferred into the next configuration dialog. Changes of parameter settings during the running process are only applied to the current cultivation.

2. Make required settings.

3. Press **OK**.

➡ The dialog box for user interaction appears with more or fewer user instructions depending on the device configuration.



The figure shows, as an example, the dialog box of a device with a rotameter, gas sensors for exit gas analysis, ball valves for switching between tap water/chilled water and resterilizable feed line.

4. Execute all the steps of the procedure in sequence.
5. Press **OK**.

➡ The cultivation is started.

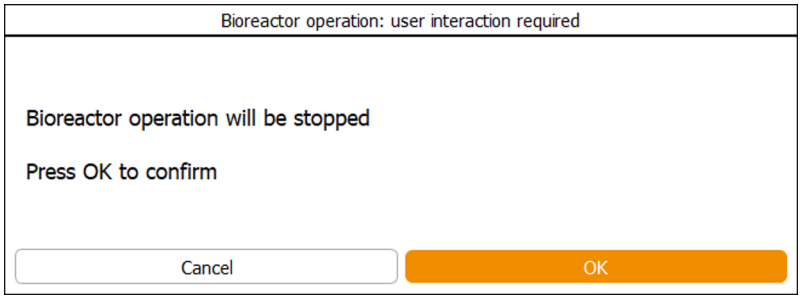
- The actual values and control outputs of the parameters are visible in the *Controller* main menu.
- A record of actual values and a display as a diagram are available in the *Trends* main menu.

8.9.7.5 Terminating the Process

To stop the cultivation, proceed as follows:

1. In the *Batch* main menu, press **Stop** next to **Start**.

➡ The dialog box for confirming the cultivation stop appears.



2. Press **OK**.

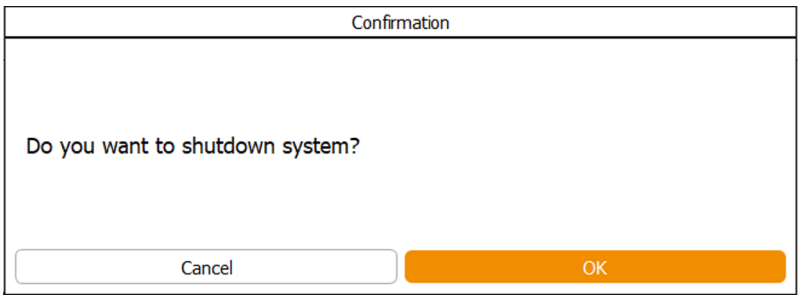
➡ The cultivation is stopped.

8.10 Shutting Down the System; Switching off the Device

To shut down the system and switch off the device, proceed as follows:

1. In the *System* main menu, press **Shutdown**.

   ➡ The *Confirmation* dialog box for confirming the shutdown appears.



2. Press **OK**.

   ➡ The system shuts down.

   As soon as the screen is dark:

3. Turn the main switch to the *0 / OFF* position.

   ➡ The device is switched off.

4. Shut off the supply lines und ensure that they are depressurized.

> **⚠ WARNING**
>
> Due to stored energy, the vessel will be pressurized even after switching off via the main switch.
>
> Prior to each manipulation of the vessel and its components, check the vessel pressure on the manometer and, if necessary, depressurise the vessel.

8.11 Emergency Shut-Off – Shut Down in Case of an Emergency

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

1. Immediately switch off the device at the main switch.
   - ➡ The device is de-energized.
   - ➡ Any cultivation that might be running will be continued when the device is switched on again.
   - ➡ If the mobile CIP unit *TechCIP* of the device manufacturer is used: the software connection to the mobile CIP unit is terminated. The system alarm *TechCIP communication error* appears there.
2. Resolve the emergency shut-off situation.

8.12 Switching On Again after Emergency Stop

CAUTION

Premature restarting when the emergency shut-off situation has not yet been rectified can be dangerous and result in material damage.

NOTICE

Any cultivation running when the emergency shut-off is triggered will continue after restarting and, if necessary, has to be aborted separately via **Stop.** All other process remain stopped in any case and have to be started again.

If additional switches for the power supply/interruption have been fitted on the operating side, the internal safety regulations for this must be observed.

After faults and the emergency shut-off situation have been rectified:

1. Ensure the emergency shut-off situation has been resolved.
2. Switch the device on via the main switch.
   - ➡ The system alarm *System restarted after a power failure* appears.
3. Start the desired process(es) again, if necessary, terminate and restart.

9 Rectifying Faults

The following chapter describes possible reasons for faults and how to resolve them. Reduce the service intervals in correspondence with the actual loads if faults become increasingly common. Contact the manufacturer or licensed dealer in case of faults that cannot be resolved by following the notices below.

9.1 Fault Tables

9.1.1 General Faults

Fault description	Cause	Remedy	Personnel
The device does not work, the green power indicator light is not lit, the screen of the operating panel remains dark.	The device is not switched on.	Switch the device on via the main switch.	Operator
	Power supply to device interrupted.	**1.** Check if the plugs are plugged in correctly. **2.** Check the mains connection.	Operator
	Circuit breaker(s) has/have tripped.	**1.** Open the instrumentation cabinet. **2.** Switch on both circuit breakers. If they are triggered again consult an INFORS HT service technician.	Technician
The green power indicator light is lit, the screen of the operating panel remains dark.	The screen of the operating panel is switched off.	Switch on the screen of the operating panel via the **ON/OFF** key on the monitor.	Operator
	The power cable is not connected to the operating panel.	Connect the power supply cable to the DC connection of the operating panel.	Operator
No communication between the device and the operating panel (alarm *no communication*)	Display cable is not connected to the operating panel.	Connect the display cable to the COM1 connection of the operating panel.	Operator
	Display cable is not connected to the control board in the instrumentation cabinet.	**1.** Open the instrumentation cabinet. **2.** Connect the display cable to the control board.	Technician

9.1.2 Faults Drive System

Fault description	Cause	Remedy	Personnel
Motor does not start.	The *Stirrer* parameter is not activated.	Activate the *Stirrer* parameter.	Operator
	Setpoint of *Stirrer* parameter = 0.	**1.** Set setpoint > 0. **2.** Check value of the *Dead Band* in the *PID* parameter option: it must have a value of 0.	Operator
	Parameter *pO_2* is activated and set to oxygen control via rotation speed stirrer (option *Cascade* in parameter *pO_2*).	Switch *Cascade* off and test the function via the *Stirrer* parameter.	Operator
The motor does not start, the *Stirrer* parameter is activated, the *Cascade* option in pO_2 is not activated.	The motor cable is not connected properly.	Connect the motor cable correctly.	Technician
	The motor has overheated or does not have sufficient mains voltage.	**1.** Turn off the device at the main switch. **2.** Wait approx. 20 seconds. **3.** Switch the device on via the main switch. **4.** If this does not work, contact an INFORS HT service technician.	Operator
Motor control erratic	Incorrect settings in the *PID* option of the *Stirrer* parameter.	Reset the PID settings to their default values.	Operator

9.1.3 Faults Temperature Control System

Fault description	Cause	Remedy	Personnel
No temperature control.	Temperature control has not been activated.	Activate the *Temperature* parameter.	Operator
	The stirrer has not been activated and/or the setpoint for the *Stirrer* parameter = 0.	Activate the *Stirrer* parameter; if necessary, set the setpoint to > 0.	Operator
No cooling or inadequate cooling.	No water supply or inadequate flow.	Check the water supply and turn on the supply tap if necessary.	Operator
	Neg. factor in the *PID* option in the *Temperature* parameter is incorrect.	Check the *Neg. factor* (negative factor) in the *PID* option: the value must be positive.	Operator
Temperature fluctuations.	Incorrect PID settings.	Check the PID settings (*PID* parameter option) and adjust as necessary (in particular *P-Term*).	Operator
Alarm *no water detected in temperature control system, refill failed.* The temperature control switches off, the circulation pump and heating are deactivated, the running process continues.	The temperature control circuit is not filled.	Fill the temperature control circuit (according to the description the in “Process Sequences” of the device’s technical documentation).	Technician
Negative temperature display.	Cable broken or other defect in the temperature sensor cable.	Replace the temperature sensor.	INFORS HT service technician or licensed dealer

9.1.4 Faults Gassing System

Fault description	Cause	Remedy	Personnel
No gassing.	The on-site gas supply has been interrupted.	**1.** Stop the cultivation. **2.** Check the on-site gas supply and switch it on, if necessary.	Operator
	If available: the rotameter is not open.	Slowly open the rotameter valve.	Operator
	The *Flow* parameter is not activated.	Activate the *Flow* parameter.	Operator
	Setpoint in *Flow* parameter(s) = 0.	Setpoint in *Flow* parameter(s) > 0.	Operator
	The *GM Flow* parameter = 0 and/or the *GasMix* parameter has not been activated.	Set the *GM Flow* parameter > 0 and activate *GasMix*.	Operator
	Inlet air escapes via unused twist valves on the filters.	Close unused twist valves on the inlet air and exit gas filter.	Operator
	The inlet air filter is blocked.	Replace the inlet air filter under sterile conditions.	Operator
The desired gas flow rate is not reached.	The inlet air filter or the exit gas filter is blocked.	Replace the filter under sterile conditions.	Operator
	Incorrect gas connection pressure.	Check the connection pressures, set it properly if necessary.	Operator
Sudden increase in evaporation losses in the vessel.	The exit gas cooler does not cool.	**1.** Check the building's water supply to the exit gas cooler, restore it if necessary. **2.** Check and ensure that valve *01.06.06* is in automatic mode and activated: set **Cooler** in main menu *Main* to *AUTO*, green font = *Exit Gas Cooler* in submenu *Valves* to *ON*.	Operator

9.1.5 Faults pH Control

Fault description	Cause	Remedy	Personnel
No display or incorrect display of pH. Digital measurement systems: error message *ERROR* instead of actual value.	Sensor cable is not connected or not properly connected.	Connect the sensor cable correctly.	Operator
	Analog measurement systems: *Temp. Compens.* (temperature compensation) function is deactivated.	Activate the function in the *Setpoint* option of the *pH* parameter.	Operator
	pH drift during long cultivation.	Recalibrate the pH with external measurements, or perform a product calibration.	Operator
	Faulty pH sensor.	**1.** Test calibration with pH 4 and pH 7 buffer. **2.** Digital measurement systems: observe the error message when calling up the calibration menu (*Show Sensor Status*). **3.** Regenerate or replace the sensor, if necessary. Consult the documentation of the sensor manufacturer!	Operator
No pH control.	The *pH* parameter is not activated.	Activate the *pH* parameter.	Operator
	Incorrect deadband setting in PID.	Check the deadband (*Dead Band* in the *PID* parameter option): switch off or enter a small value.	Operator
	No addition of reagents (acids and base).	**1.** Check the reagent bottles: refill if necessary. **2.** Check the hose connections between the reagent bottle and the vessel: connect properly if necessary. **3.** Remove/open clamps if necessary.	Operator

Fault description	Cause	Remedy	Personnel
No pH control.	No addition of reagents (acids and base).	**4.** Open the push valve(s) if necessary.	
	The (base/acid) pump does not operate properly.	**1.** Check the function of the pump using the rocker switch. **2.** Check the hose type and replace if necessary.	Operator
The pH value drifts up and down over time or acid and base are added almost continuously in turn.	The PID settings in the *pH* parameter are incorrect.	Check the PID settings (*PID* parameter option) and correct if necessary. Specifically, change the proportional factor (*Prop. Term*) or the *Deadband* setting.	Operator
	Incorrect strength of reagents: concentration is too weak or too high.	Check the strength of the reagents. Adjust if necessary: 0.1 mol to 2.0 mol.	Operator

9.1.6 Faults pO_2 Control

Fault description	Cause	Remedy	Personnel
No display or incorrect display of pO_2. Digital measurement systems: error message *ERROR* instead of actual value.	Sensor cable is not connected or not properly connected.	Connect the sensor cable correctly.	Operator
	Analog measurement systems: pO_2 sensor is not polarized.	Polarize the pO_2 sensor.	Operator
	Faulty pO_2 sensor.	**1.** Check calibration. **2.** Digital measurement systems: observe the error message(s) when calling up the calibration menu (*Show Sensor Status*). **3.** If necessary, replace the pO_2 sensor. Consult the documentation of the sensor manufacturer!	Operator
No pO_2 control.	The *pO_2* parameter and/or cascaded parameter is/are not activated.	Activate the parameter.	Operator
	The cascade settings are incorrect.	Check the cascade settings and change as necessary.	Operator
	No gas flow into vessel.	➥ Chapter 9.1.4 'Faults Gassing System' on page 247.	Operator
Unstable pO_2 control	Incorrect PID settings in the *pO_2* parameter.	Check the PID settings (*PID* parameter option) and correct if necessary. Specifically, the proportional factor (*Prop. Term*) and the deadband (*Dead Band*). The value in the deadband must be 0 (zero).	Operator

9.1.7 Faults Antifoam Control

Fault description	Cause	Remedy	Personnel
Foam is not detected, frequently detected or constantly detected.	The sensor cables are not connected correctly.	Connect the sensor cable correctly.	Operator
	The insulation of the antifoam sensor is damaged.	Replace insulation of the sensor.	Operator
The antifoam pump does not work.	The *Antifoam* parameter has not been activated.	Activate the parameter.	Operator
	The (*Dose time*) in the *Antifoam* parameter = 0 (zero).	Set the dose time > 0 (zero).	Operator
No or inadequate antifoam agent flow.	The reagent bottle is empty.	Fill the reagent bottle.	Operator
	Incorrect antifoam agent or incorrect concentration of antifoam agent used.	Change the antifoam agent.	Operator
	The hose line is blocked or clamped.	**1.** Check the hose line between the reagent bottle and the vessel: if necessary, connect them correctly. **2.** If necessary, open/ remove the hose clamp.	Operator
	If in use: a push valve is closed.	Open the push valve.	Operator
	The antifoam pump does not work.	**1.** Check the function of the pump using the rocker switch. **2.** Check hose type and replace if necessary.	Operator

9.1.8 Faults Feed and Pump

Fault description	Cause	Remedy	Personnel
No or inadequate flow of liquid via the feed pump.	The *Feed* parameter is not active.	Activate the *Feed* parameter.	Operator
	Setpoint of the *Feed* parameter = 0 (zero).	Set the setpoint > 0 (zero).	Operator
	The reagent bottle is empty.	Fill the reagent bottle.	Operator
	The hose line is blocked or clamped.	**1.** Check the hose line between the reagent bottle and the vessel: if necessary, connect them correctly. **2.** If necessary, open/ remove the hose clamp.	Operator
	If in use: the valve(s) of the resterilizable feed line is/are closed.	Open valves *13.16.01* (vessel feed line) and *13.16.04* (reagent feed line).	Operator
	If in use: a push valve is closed.	Open the push valve.	Operator
	The pump does not work.	**1.** Check the function of the pump using the rocker switch. **2.** Check hose type and replace if necessary.	Operator

9.1.9 Interferences Turbidity Measurement

Fault description	Cause	Remedy	Personnel
Displayed measured value is not plausible/ unusual.	Sensor cable is twisted or kinked or not properly connected.	1. Check the connection of the sensor cable, connect it properly, if necessary. 2. Check and ensure that the cable is not kinked or twisted. twisted.	Operator
	Sensor is not calibrated.	Calibrate the zero point.	Operator
	Window fouling on the sapphire windows.	Carefully clean the sensor.	Operator
	Faulty sensor cable.	Replace the sensor cable.	INFORS HT service technician or licensed dealer
	Faulty sensor.	Replace the sensor.	Operator

If the temperature of the sensor rises above 65 °C during operation in the medium, an automatic switch-off takes place.

After the medium has cooled down, the measurement continues automatically.

9.1.10 Behavior in Case of a Power Interruption

If the power supply to the device is interrupted during the running cultivation (e.g. by flicking the main switch or in case of a power failure), all parameter setpoints are stored. After restoring the power supply, the interrupted cultivation is automatically continued with the last stored setpoints. All other processes remain stopped.

The system alarm *Restart after power failure* indicates that there has been a power interruption. However, the alarm provides no information on the duration of the event.

9.2 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.

If the device, component or accessory has to be returned to the manufacturer for repair, a legally compliant declaration of decontamination is required for the safety of all parties involved and to comply with legal requirements (➥ Chapter 1.8 ‘Declaration of Decontamination’ on page 22).

10 Cleaning and Maintenance

The following chapters contain general descriptions regarding the cleaning of the vessel and its accessories, and how these can be stored.

In addition, the chapter contains a maintenance plan and corresponding descriptions for the procedures to be performed by the operator.

10.1 Cleaning Agent and Disinfectant

Purpose of use	Allowed products/tools
Vessel, slightly soiled	Water
Cleaning agent for denaturation of proteins	0.1 N NaOH
Cleaning agent for smaller parts	Ultrasonic bath
Cleaning agent for surfaces	Water
Disinfectant for surfaces	Ethanol, 70 %

⚠ CAUTION

Using spray bottles with ethanol can result in explosive mists being created!

All cleaning operations with ethanol must be carried out in an environment that is separate from the device, well ventilated and meets internal safety regulations.

10.2 Cleaning the Bioreactor

Overview of the Activities

The following checklist lists all the activities that must be carried out as part of routine cleaning (e.g. after cultivation).

No.	Activity	Additional Information	☑
1.1	Clean the vessel.	➦ Chapter 2.4.6, page 40	☐
1.2	Clean the vessel top plate.	➦ Chapter 2.4.7, page 41	☐
1.3	Clean the exit gas cooler.	➦ Chapter 2.10.3, page 68	☐
1.4	Clean reagent bottles, hoses and accessories.	➦ Chapter 10.2, page 256	☐
1.5	Clean the sensors.	➦ Chapter 10.2, page 257	☐
1.6	Clean the surfaces of the instrumentation cabinet and operating panel.	➦ Chapter 10.2, page 257	☐

Cleaning the Reagent Bottles, Hoses and Accessories

1. If necessary, empty the reagent bottle and dispose of the contents in accordance with internal safety guidelines.
2. Use water to thoroughly rinse reagent bottles and hoses as well as all built-in-parts and accessories, such as inoculation needles, push valves etc.
3. Check the silicone hoses and pump hoses for damage and replace if necessary.

Depending on the operator's specifications, new hoses might be used for every cultivation.

4. Check the reagent bottles and their components for damage and replace if necessary.
5. Check the O-rings on the built-in-parts and accessories as well as the lid seals of the reagent bottles for damage, and replace them if necessary.
6. Store reagent bottles, hoses, built-in-parts and accessories dry and on a clean underlay.

Cleaning the Sensors

Cleaning and maintenance of the individual sensors are described in the corresponding, separate documentation of the respective sensor manufacturer. Read these manuals and follow the instructions therein.

Sensors from 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 must be stored clean and dry.

Cleaning the Surfaces of the Instrumentation Cabinet and Operating Panel

NOTICE

When cleaning, observe protection classes IP43 (instrumentation cabinet) and IP66 (operating panel)!

1. Wipe the surfaces of the instrumentation cabinet including the operating panel with a slightly damp, soft cloth. If necessary, clean with a suitable (non-aggressive!) disinfectant.
2. Wipe the screen of the operating panel with a cloth that is suitable for PC screens.

10.3 Maintenance Plan

WARNING

Failure to observe the maintenance plan bears a significant risk.

Users are responsible for compliance with the maintenance plan; failure to comply with it will result in exclusion of liability (see GTC).

The following sections describe the maintenance work that is required for optimal and fault-free operation.

If increased wear is detected during regular checks, the required maintenance intervals must be shorted in accordance with the actual signs of wear. Contact the manufacturer if you have questions about maintenance work and intervals.

Interval	Maintenance work	Personnel
Prior to each use	Check the hoses and hose connections.	Operator
	Check that O-rings and flat gaskets are leak-proof, replace if necessary.	Operator

Cleaning and Maintenance

Interval	Maintenance work	Personnel
Prior to each use	Check the reagent bottles and all other glass items for damage, and replace if necessary.	Operator
	Lubricate the mechanical seal (for details, see ➦ Chapter 2.7.3 'Lubricating the Mechanical Seal' on page 54).	Operator
	Check the air filters with a filter test device (if available).	Operator
After each use	Sterilize the vessel, vessel top plate, all built-in-parts as well as reagent bottles and hoses and then clean them.	Operator
	Preventatively replace silicone hoses (depending on their use).	Operator
After 20 to 50 sterilizations (recommended)	Replace the air filters. Reduce the maintenance interval if necessary.	Operator
Every 6 months	Replace all pumps and silicone hoses on the reagent bottles.	Operator
	Replace O-rings and flat gaskets. Reduce the maintenance interval if necessary.	Technician
	Check the functionality of the measurement sections (temperature, pH, etc.), use a simulator where appropriate.	Technician
	Check that the safety valves are operational according to the manufacturer of the safety valve's specifications.	Technician
Annually	Replace flat gasket(s), valve diaphragm(s) and gaskets of the vessel sight glass.	Technician
	Recommendation: complete device maintenance.	INFORS HT service technician or licensed dealer
As required	Wipe down the surfaces of the instrumentation cabinet and operating panel.	Operator
	Replace hoses and hose connections.	Technician
According to national requirements for safety valves.	Have safety valves tested by a competent external body in accordance with nationally applicable regulations.	Technician
After a defect or at the maintenance interval specified by the provider:	Replace the mechanical seal.	INFORS HT service technician or licensed dealer

For detailed information on care and maintenance of built-in-parts and accessories from other manufacturers, please refer to the documentation of the respective manufacturers and follow the instructions contained therein. This applies in particular to the safety valves.

11 Disassembly and Disposal

The device must be disassembled and disposed of in an environmentally-friendly manner if it is not in use anymore.

If the device is to be returned to the manufacturer for disassembly and disposal, a legally compliant declaration of decontamination is required for the safety of all parties involved and to comply with legal requirements (➥ Chapter 1.8 'Declaration of Decontamination' on page 22).

11.1 Disassembly

Prior to disassembly:

- Switch off the device and secure against reactivation.
- Physically disconnect the main energy supply from the device and wait for any components to fully discharge.
- Remove and dispose of all operating and auxiliary materials as well as remaining processing materials in an environmental acceptable manner.

Clean and disassemble component parts professionally with regard to any local regulations concerning employment and environmental protection. If possible, separate materials.

11.2 Disposal

Recycle disassembled components if no agreement is made concerning reclaim or disposal.

- Scrap metals.
- Recycle plastic components.
- 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.

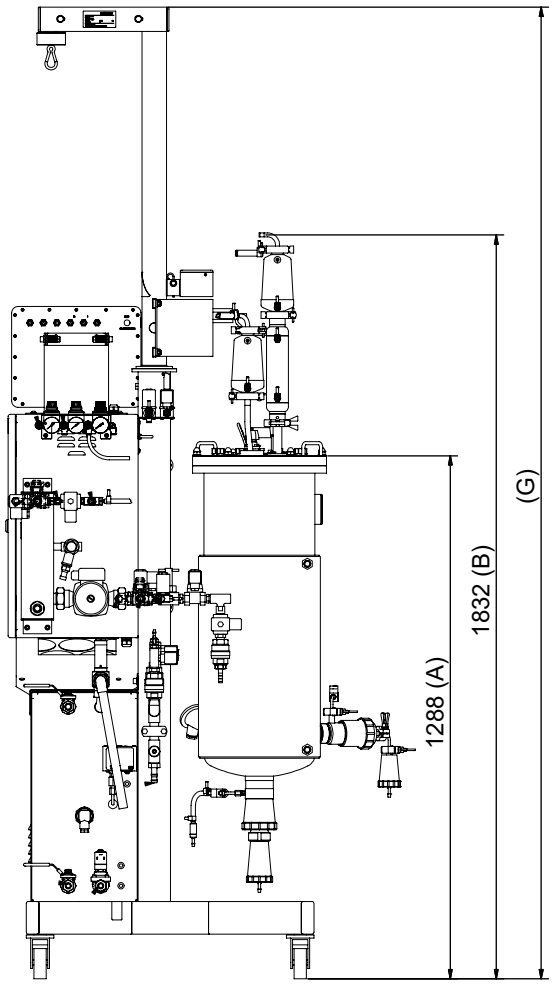
Disassembly and Disposal

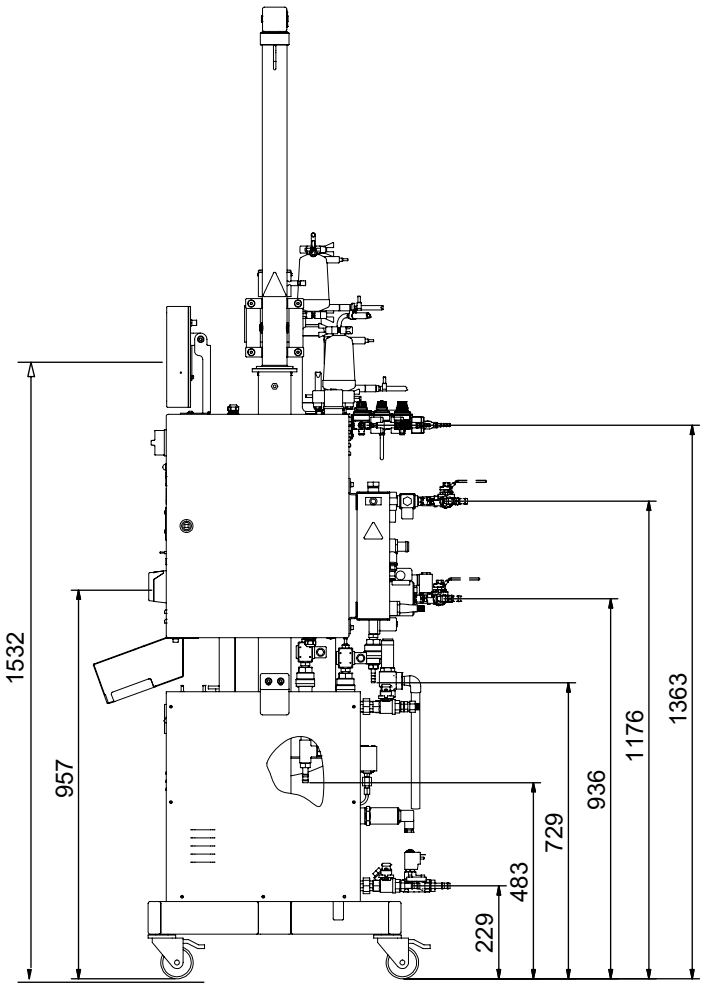
For disposal, the system units must be disassembled and dismantled into individual material groups. These materials must be disposed of according to the applicable national and local legislation. Local authorities or specialist disposal firms can provide information regarding environmentally acceptable disposal.

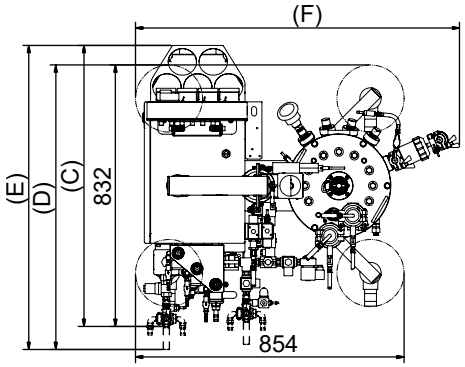
If no special arrangements have been made for return, Infors devices with the required declaration of decontamination can be sent back to the manufacturer for disposal.

12 Technical Data

12.1 Dimensions





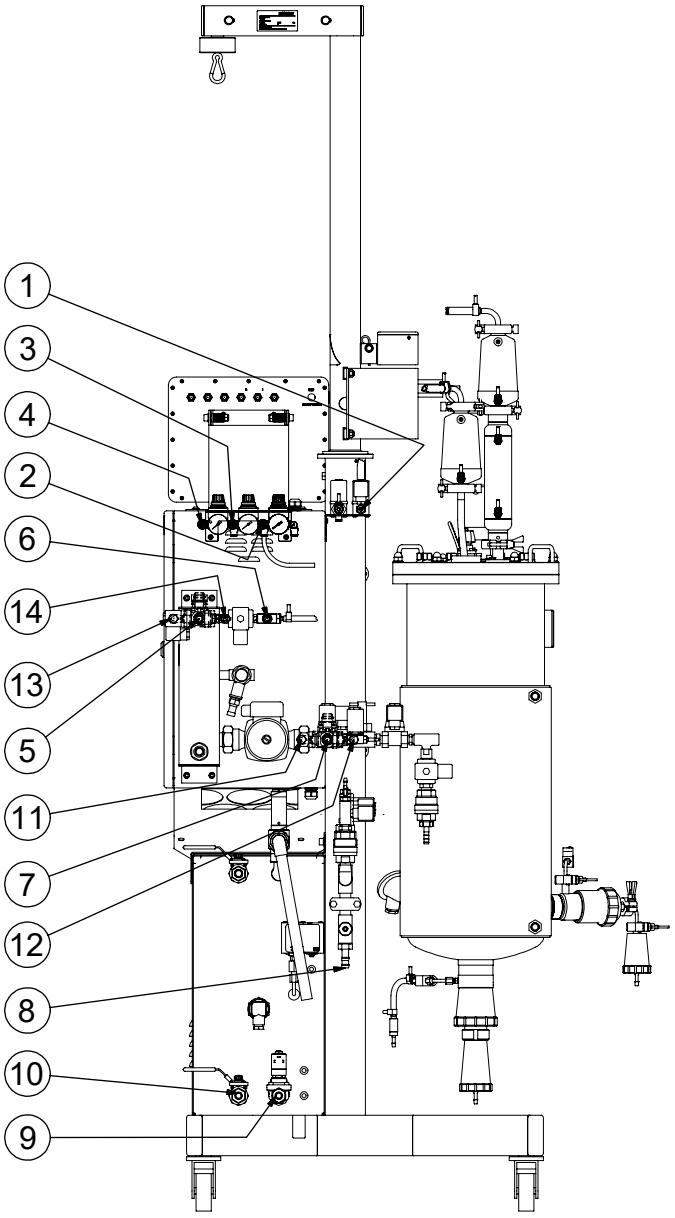


Dimensions with options	
Weight measurement	A = 1354 / B = 1870
Steam generator	C = 876
Switch between tap water/chilled water	D = 872
Switch between tap water/chilled water and steam generator	E = 934
Sample valve	F = 1017
Vessel top plate lifting device	G = 2391

All dimensions in mm

12.2 Connections and Connection Values

Overview of Connections



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)

Technical Data

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 DN13	min. 3.0 bar
10	Water out steam generator (option)	Hose nozzle DN13	Not connected
11	Tap water in (option)	Hose nozzle DN13	2.0 ± 0.5 bar
12	Chilled water in (option)	Hose nozzle DN13	2.0 ± 0.5 bar
13	Tap water out (option)	Hose nozzle DN13	(no backpressure)
14	Chilled water out (option)	Hose nozzle DN13	(no backpressure)

All Tri-Clamp connections as per DIN 32676 B (ISO1127) +A14 and DIN 32676 C (ASME-BPE 2009)

Electric Connection Values

Electric connection values for the bioreactor					
Variant	**Voltage**	**Frequency range**	**Max. rated current**	**Leakage current**	**Connector**
50 Hz	230 V (± 5 %); 1 phase, L1 + N (neutral) + PE (earth)	50 Hz	16 A	> 3.5 mA	CEE16/3
60 Hz	200 – 230 V (± 5 %); 1 phase, L1 + N (neutral) + PE (earth)	60 Hz	16 A	> 3.5 mA	NEMA L6-20P 20A

12.3 Specifications of the Basic Unit

12.3.1 Instrumentation Cabinet

Data	Value	Unit
Width	320	mm
Depth	450	mm
Height	550	mm
Protection type	IP43	
Material	1.4301	

12.3.2 Operating Panel

Data	Value
HMI	Color touch screen 12"
Protection type	IP66

12.3.3 Vessel

Vessel Sizes

Total volume (TV)	Working volume (AV)		Total volume (TV) vessel jacket
	Max.	Min. [1)]	
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

[1)] *Values apply to cultivation*

Technical Data

Dimensions

Vessel TV	Height [1)]	ID	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*

Limits

Data	Value	Unit
Temperature range vessel inside	-10 to +150	°C
Temperature range vessel jacket	-10 to +150	°C
Pressure range vessel inside	-1 to +3	bar
Pressure range vessel jacket	-1 to +3	bar
Permitted vessel load change	12860	
Permitted vessel jacket load change	85289	

Materials

Data	Value
Parts in contact with medium	AISI 316L
Parts not in contact with medium	AISI 304

Surface Roughness

Data	Value
Parts in contact with medium	Ra ≤ 0.6 µm, electropolished
Parts not in contact with medium	Ra ≤ 1.0 µm, electropolished

Ports and Ingold Nozzles

Vessel top plate port	15 L TV	30 L TV	42 L TV
Tri-Clamp ISO DN25/1, ID = 50.5 mm (exit gas)	1	1	1
Tri-Clamp ISO DN08, ID = 50.5 mm (inlet air/gas)	1	1	1
ID = 19 mm (Rd28x1/8")	8	8	9
ID = 10 mm (temperature sensor)	1	1	--

Ingold nozzles	15 L TV	30 L TV	42 L TV
ID = 25 mm, angled (15°)	2	3	4
ID = 25 mm, horizontal	1	1	1

Inside Diameter Harvest/Sample Valve

Activity	15 L TV	30 L TV	42 L TV
Harvest	8 mm	8 mm	25 mm
Sampling	8 mm	8 mm	4 mm

12.3.4 Temperature Control System

Temperature Sensor

Data	Value
15 L and 30 L TV vessel	Pt100 class B, 1/3 DIN
42 L TV vessel	Pt100 class A, 1/3 DIN

Temperature Range

Data	Value	Unit
Sterilization	110 to 125	°C
Cultivation [1)]	20 to 79	°C

[1)] *The minimum temperature depends on the ambient temperature, the cooling system used, stirrer speed and viscosity of the medium.*

Accuracy Measurement and Control (Cultivation)

Data	Value	Unit
Accuracy at ≤ 60 °C	± 0.3	°C
Accuracy at > 60 °C	± 0.5	°C

12.3.5 Stirrer

Drive

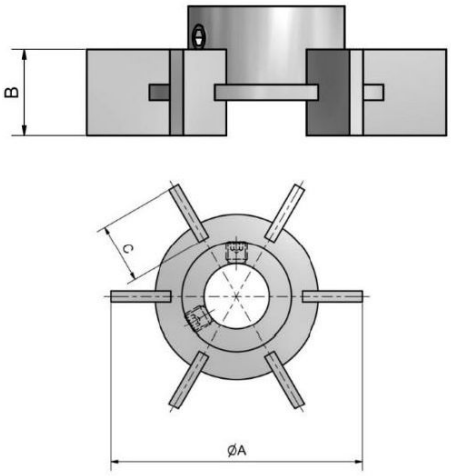
Data	Value
Type	Top, with single mechanical seal
Direction of rotation stirrer shaft	Clockwise (top view)
Motor type	AC servo motor, brushless

Rotation Speed und Accuracy

Data	Value	Unit
Rotation speed [1] 15 L TV vessel	20 to 1500	min^{-1}
Rotation speed [1] 30 and 42 L TV vessel	20 to 1200	min^{-1}
Control accuracy at 20 to 1000 min^{-1}	± 5	min^{-1}
Control accuracy at > 1000 min^{-1}	1 % setpoint	

[1] *Rotation speed ranges apply in liquid with viscosity similar to water, without gassing with 2 or 3 Rushton impellers.*

Impellers



Data	Value
Type	Rushton impeller with 6 blades
Material	AISI 316L
Surface	Ra 0.8 µm, electropolished

Dimensions and quantity of impellers				
Vessel TV	**A**	**B**	**C**	**Quantity**
15 L	66 mm	13 mm	16 mm	2
30 L	80 mm	16 mm	20 mm	3
42 L	89 mm	18 mm	23 mm	3

12.3.6 Gassing System

12.3.6.1 Components

Mass Flow Controller (MFC)

Data	Value
Type	Red-y smart, Hi-Performance

Rotameter

Data	Value
Type	Flow meter with float

Technical Data

Control Ranges of MFCs and Rotameter

Vessel size	Basic (rotameter)	Standard/High End (MFC)
15 L TV (max. WV 10 L)	2.0 to 20.0 L min^{-1}	0.20 to 20.0 L min^{-1}
30 L TV (max. WV 20 L)	4.0 to 40.0 L min^{-1}	0.40 to 40.0 L min^{-1}
42 L TV (max. WV 30 L)	6.0 to 60.0 L min^{-1}	0.60 to 60.0 L min^{-1}

Specific gas flow rate calculated for max. WV: 2 min^{-1}

The mass flow controller is calibrated by the manufacturer ex-factory at standard conditions, i.e. at 1.013 bar and 20 °C. Therefore, for every gas flow rate the standard volume flow is stated as L min^{-1}.

Filter

Data	Value
Type	Novasip, can be sterilized with steam
Model	C3PFRP1A

Data	Value	Unit
Max. pressure	6.5	bar
Max. temperature	142	°C
Retention rate	0.2	µm

Steam Trap

Data	Value
Type	Thermal steam trap
Material	Stainless steel

12.3.6.2 Gassing Variants

General

Data	Value
Gas entry	Ring sparger
Gas(es)	Air / Air + O_2 / Air + N_2 / Air + O_2 + N_2

Basic Variant

Data	Value
Gas flow control	1 rotameter
Gasmix control (if present)	1 solenoid valve per gas

Data	Value	Unit
Accuracy rotameter	± 4	% FS

Standard Variant

Data	Value
Gas flow control	1 MFC
Gasmix control (if present)	1 solenoid valve per gas

Data	Value	Unit
Accuracy measurement and control gas flow	± 2	% FS

High End Variant

Data	Value
Gas flow control and Gasmix (if present)	1 MFC per gas

Data	Value	Unit
Accuracy measurement and control gas flow	± 2	% FS

12.3.7 Exit Gas System

Exit Gas Cooler

Data	Value
Material	Stainless steel

Filter

Data	Value
Type	Novasip, can be sterilized with steam
Model	C3PFRP1A

Data	Value	Unit
Max. pressure	6.5	bar
Max. temperature	142	°C
Retention rate	0.2	µm

Steam Trap

Data	Value
Type	Thermal steam trap
Material	Stainless steel

12.3.8 pH Control

Data	Value
Control	Peristaltic pumps for acid and base
Control range	pH 2 to pH 12
Measurement accuracy	pH ± 0.1

Measurement System Analog

Data	Value
Sensor type	405-DPAS-SCK8S/ 120
Sensor measurement principle	Potential measurement against reference
Measurement range	pH 2 to pH 12

Measurement System Digital Variant HAMILTON

Data	Value
Sensor type	Easyferm Plus ARC
Sensor measurement principle	Potential measurement against reference with integrated electronics
Measurement range	pH 0 to pH 14

The pH sensors of the Easyferm Plus ARC type have been preconfigured by the INFORS HT device manufacturer. Replacement sensors must be configured before use.

Measurement System Digital Variant METTLER

Data	Value
Sensor type	InPro 3253i, ISM with M100 transmitter
Sensor measurement principle	Potential measurement against reference with integrated electronics
Measurement range	pH 0 to pH 12

12.3.9 pO_2 Control

Data	Value
Control via cascade	Parameters in cascade are dependent on device configuration

Data	Value	Unit
Control range	0 to 100	%-sat
Measurement accuracy	± 1	%

Analog Measurement System

Data	Value
Sensor type	InPro 6820/25/080
Sensor measurement principle	Amperometric/polarographic

Data	Value	Unit
Measurement range	0 to 150	%-sat

Digital Measurement System, HAMILTON Variant

Data	Value
Sensor type	Visiferm DO ARC / RS485-ECS
Sensor measurement principle	Optical

Data	Value	Unit
Measurement range	0 to 300	%-sat

Digital Measurement System, METTLER Variant

Data	Value
Sensor type	InPro6860i, ISM
Sensor measurement principle	Optical

Data	Value	Unit
Allowed temperature	0 to 60	°C
Measurement range	0 to 285	%-sat

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

12.3.10 Antifoam Control

Data	Value
Sensor	Conductive with dosing needle, mounting depth adjustable
Display	0 % (no foam) / 100 % (foam)
Control	Antifoam peristaltic pump

12.3.11 Pumps

Digital Pumps

Data	Value
Type	Peristaltic
Number	3 (*Acid*, *Base*, *Antifoam*)

Data	Value	Unit
Speed (fixed rotation speed)	150	min^{-1}
Accuracy	± 5	min^{-1}

Analog Pumps

Data	Value
Type	Peristaltic
Default number	1 (*Feed*)
Number of optional ones	2 (*Feed 2, Feed 3*)

Data	Value	Unit
Speed	0 to 150	min^{-1}
Setting range (0.1 % increments)	0 to 100	%
Accuracy	± 5	min^{-1}

Pump Hoses

Data	Value	Unit
Inner diameter	3.2	mm
Wall thickness	1.6	mm
Material	Bioprene	

12.3.12 Vessel Pressure Display (Manometer)

Data	Value
Connection	19 mm port in vessel top plate
O-ring material	EPDM

Data	Value	Unit
Measurement range	0 to 4	bar

12.3.13 Safety Valves

Vessel Safety Valve

Data	Value
Type	Clean service spring-loaded safety valve

Data	Value	Unit
Response pressure	3	barg

Temperature Control Circuit Safety Valve

Data	Value
Type	Standard safety valve, angle type, spring-loaded

Data	Value	Unit
Response pressure	3	barg

12.4 Specifications of the Options

12.4.1 Steam Generator

6 kW Variant

Data	Value	Unit
Power	6	kW
max. steam power	8	kg/h
Suitable for vessel volume	15	L

10 kW Variant

Data	Value	Unit
Power	10	kW
max. steam power	14	kg/h
Suitable for vessel volume	30 and 42	L

Electric connection values				
Type	**Voltage**	**Frequency range**	**Max. rated 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

12.4.2 Recirculating Chiller

Data	Value	Unit
Max. cooling power	1.7	kW
Tension	230	V
Frequency	50/60	Hz

12.4.3 Level Detection

Data	Value
Sensor	Conductive, mounting depth adjustable
Display	0 % (no liquid) / 100 % (liquid)

12.4.4 Pressure Control

Data	Value
Sensor type	Piezo-resistive pressure transmitter
Control	Proportional valve with electronic open-loop control

Data	Value	Unit
Measurement range	-1 to +3	bar
Measurement range	0 to 2.0	bar
Control range	0 to 1.5	bar
Measurement and control accuracy	± 0.1	bar

12.4.5 Weight Measurement Vessel – Load Cell

Data	Value
Sensors	Bending rod load cells

Data	Value	Unit
Measurement accuracy	± 100	g

12.4.6 Turbidity Measurement

Data	Value
Sensor type	ASD25-N
Optical path length	OPL01, OPL05 or OPL10
Measurement principle	Single channel light absorption

Data	Value	Unit
Absorption measurement range	0 to 4	CU
Measurement wavelength	840 to 910	nm
Constant temperature	5 to 65 [1)]	°C
Max. temperature (60 min/day)	135	°C

[1)] *The measurement system switches off automatically if the temperature of the sensor exceeds 65 °C during operation in the culture medium. Once the culture medium has cooled down, the measurement is continued automatically.*

12.4.7 Exit Gas Analysis

For Aerobic Bioprocesses

Sensor type selection	Measurement range vol. % CO_2	Measurement range vol. % O_2
BlueInOne Ferm	0 to 10	1 to 50
BlueVary with O_2 cartridge ZrO_2	0 to 10	0.1 to 50

For Aerobic and Anaerobic Bioprocesses

Sensor type selection	Measurement range vol. % CO_2	Measurement range vol. % O_2
BlueInOne Cell	0 to 10	0 to 100
BlueVary with O_2 cartridge ec	0 to 25	0 to 25
BlueVary with O_2 cartridge ec	0 to 10	0 to 100

12.4.8 pCO_2 Measurement

Data	Value
Sensor type	InPro5000i, ISM (digital)
Measurement principle	Potentiometric
Transmitter type	M400

Data	Value	Unit
Measurement range	0 to 1000	hPa

12.4.9 Redox Measurement

METTLER Analog Measurement System

Data	Value
Sensor type	Pt4805-DPAS-SC-K8S
Sensor measurement principle	Oxidation reduction potential measurement against a reference

Data	Value	Unit
Measurement range	-2000 to +2000	mV
Accuracy	± 10	%

HAMILTON Digital Measurement System

Data	Value
Sensor type	Easyferm Plus ORP ARC
Sensor measurement principle	Oxidation reduction potential measurement against a reference

Data	Value	Unit
Measurement range	-1500 to +1500	mV
Accuracy	± 10	mV

12.4.10 Permissive Measurement

Data	Value
Measurement system (sensor and transmitter)	ABER Futura

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

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

12.5 Operating Conditions

Data	Value	Unit
Ambient temperature	5 to 35	°C
Relative humidity, non-condensing	20 to 90	%
Altitude operating location	Max. 2000	m.a.s.l
Pollution degree as per EN 61010-1	2	
Min. distance from walls, ceilings and other equipment	150	mm

The distance from the ceiling has to be selected so that the vessel top plate with its built-in-parts can be comfortably lifted off the vessel.

12.6 Operating Materials

Purpose of use	Allowed products
Lubricant for mechanical seal	Medicinal glycerine 85 % Quality: PhEur

12.7 Emissions

Data	Value	Unit
Sound pressure level	< 70	dB(A)

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