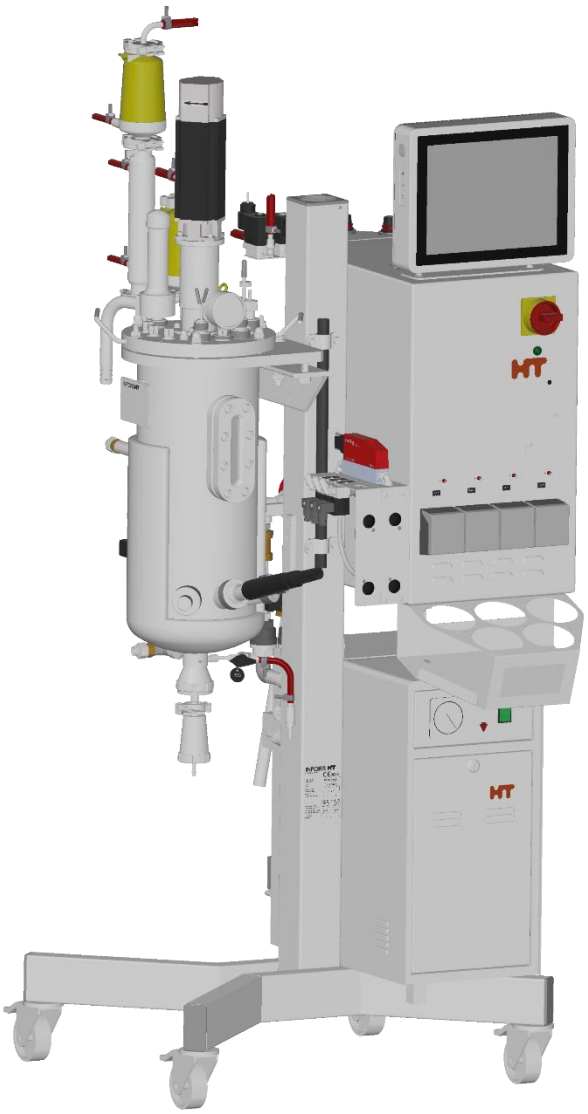
Operating Manual

Techfors-S

In Situ Sterilisable Pilot Bioreactor / Vessel Volume: 15 L
Serial No: S-000129020



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1 General Information

1.1 About this Manual

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

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

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

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

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

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

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

1.2 Explanation of Special Notices

1.2.1 Warning Notices

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

DANGER

The signal word “DANGER” indicates a dangerous situation that will lead to severe or even fatal injuries if not avoided.

WARNING

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

CAUTION

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

1.2.2 Other Notices

ATTENTION

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

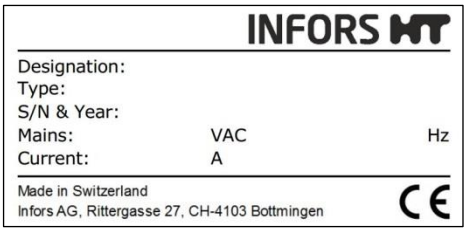
INFORMATION

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

1.3 Equipment Identification

1.3.1 Identification Plate

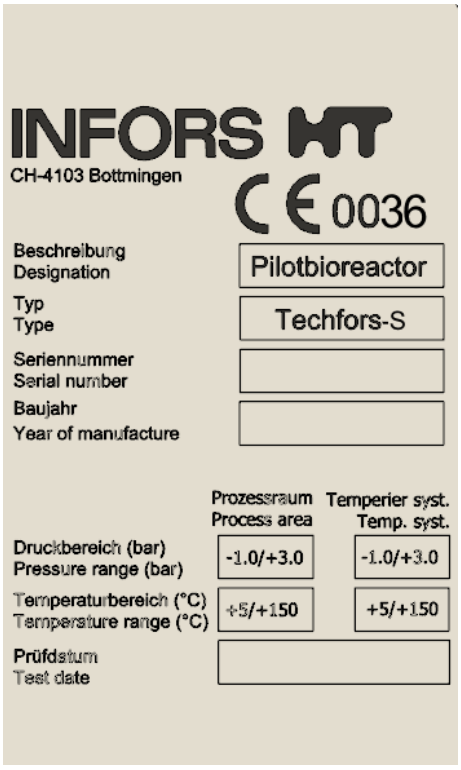
The identification plate is designed to allow clear identification of the equipment. It contains the following information:



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

1.3.2 Plant Identification Plate

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

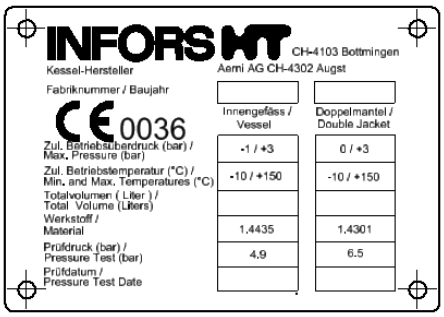


- Manufacturer name with address
- Designation of plant
- Equipment type (Name)
- Serial number
- Year of manufacture
- CE marking
- Process range (bar) in process area and temperature control system
- Temperature range (°C) in process area and temperature control system
- Test date

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

1.3.3 Vessel Identification Plate

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



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

It also contains different values for vessel and vessel jacket:

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

1.4 Declaration of Conformity

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

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

The Declaration of Conformity according to EC Machinery Directive 2006/42/EC, annex II 1 A is included in the general documentation supplied with the equipment.

1.5 Customer Service and Services

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

Due to their familiarity with the potential applications of the equipment, the Customer Service team is able to provide information on

whether the equipment can be used for a specific application or modified to handle the planned process.

Experience of working with the equipment will be published semi-regularly on the manufacturer's website in the form of "application notes".

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

2 Safety and Responsibility

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

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

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

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

2.1 Intended Use, Incorrect Use and Misuse

The in situ sterilisable pilot bioreactor Techfors-S from INFORS HT is designed especially for cultivation of microorganisms for research and development in a biotechnology laboratory.

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

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

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

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

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

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

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

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

2.2 Qualified Personnel

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

2.2.1 Provider

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

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

2.2.2 User

General

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

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

Qualified personnel

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

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

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

2.2.3 Operator

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

Qualified technicians

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

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

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

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

Technicians in training

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

2.3 Unauthorised Persons

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

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

2.4 Responsibility of the Provider

The equipment is used for industrial and scientific purposes. As such, the provider of the equipment 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 equipment remains in safe and proper working condition throughout its entire term of use.
- The provider must ensure that all safety equipment is fully functional and is not disabled.
- The provider must ensure that the equipment is only worked on by qualified users, and that said users receive sufficient training.
- The provider must ensure that the protective equipment required for working with the equipment is provided and worn.
- The provider must ensure that this operating manual remains in the immediate vicinity of the equipment throughout its entire term of use.

2.5 General Hazards

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

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

2.5.1 Electrical Current

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

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

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

2.5.2 Unauthorised Spare Parts and Accessories

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

2.6 Particular Hazards

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

Since the use of the equipment for such applications is deliberate, it is the responsibility of the operators and the provider to ensure that all personnel are protected from potential damage to health. The provider is responsible for ensuring that the appropriate protective equipment for such applications is provided, and that the necessary infrastructure is in place.

2.6.1 Hot Surfaces

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

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

2.6.2 Dangerous Gases

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

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

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

2.6.3 Flammable or Explosive Substances

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

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

2.6.4 Corrosive or Toxic Substances

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

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

2.6.5 Bioactive Substances or Pathogenic Organisms

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

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

2.6.6 Overpressure or Vacuum

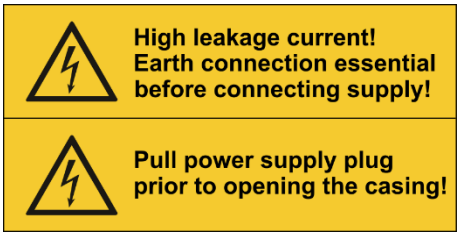
The operating pressure range specified on the vessel identification plate must be adhered to.
When carrying out manipulations on the vessel, it has to be considered that the vessel may be under pressure or vacuum.
The correct inlet pressures and the correct pressure settings of the pressure reducing valves must be ensured at all times.

2.6.7 Steam

The escape of steam can lead to severe scalding and burns!
All steam-carrying components must be checked for signs of damage and for correct position before use.

2.7 Warning Symbols on the Equipment

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



Position

- Instrumentation cabinet

- Motor

- Peristaltic pump housings

WARNING

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

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

2.8 Declaration of Decontamination

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

The following must be observed if this is the case:

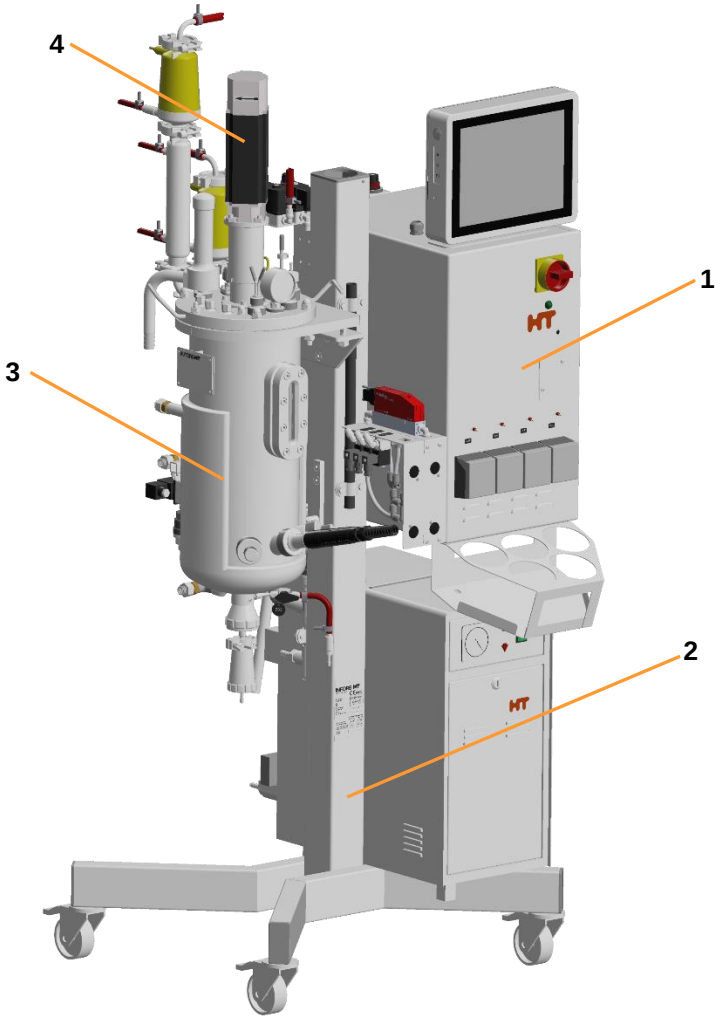
- The equipment, the component part or accessory must be entirely decontaminated before sending to the manufacturer
- The provider is therefore required to completely and truthfully fill out a declaration of decontamination, and have it signed by the person responsible.
- **The declaration of decontamination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

Important notice

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

3 Setup and Function

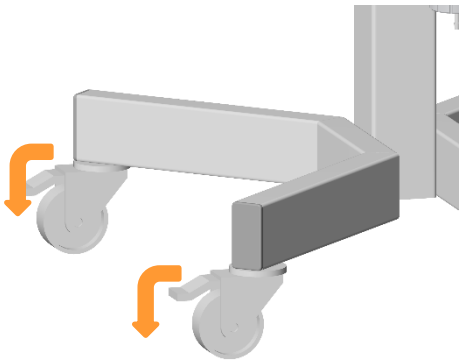
3.1 Equipment - Overview



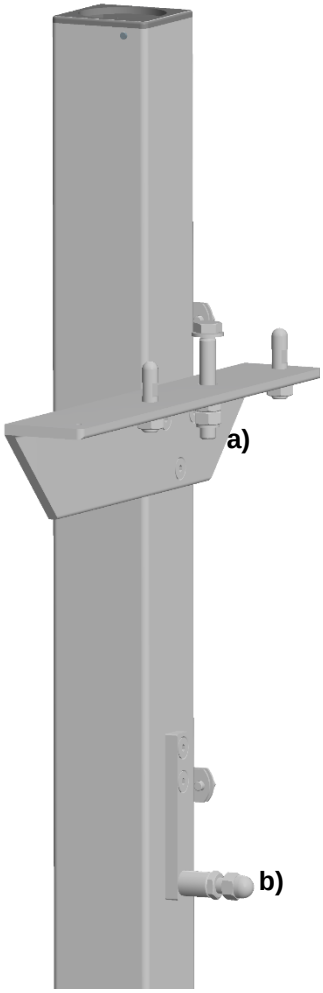
1	Instrumentation cabinet	3	Vessel
2	Central column	4	Motor

The equipment comprises the central column with support, the instrumentation cabinet with operating panel, the culture vessel, temperature control system, stirrer drive and the gassing and exit gas system. Measurement and control of pH, pO2 and antifoam is integrated by default, too.

Setup and Function

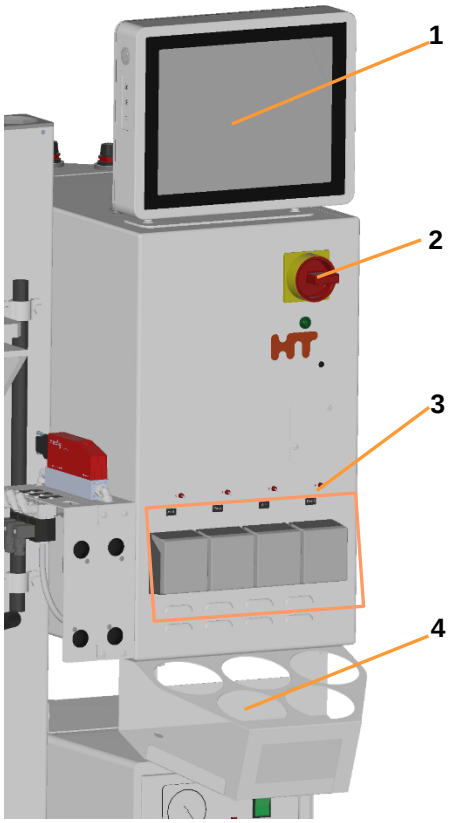


The central column with support is provided with four trolley wheels with brake. The brakes must be locked.



A support bar is fitted to the central column, to secure the vessel during transportation. The hexagon screw (a) in the middle of the two threaded bolts which fixate the vessel flange is used as transport lock. A spacer (b) is located on the column for the lower end of the vessel.

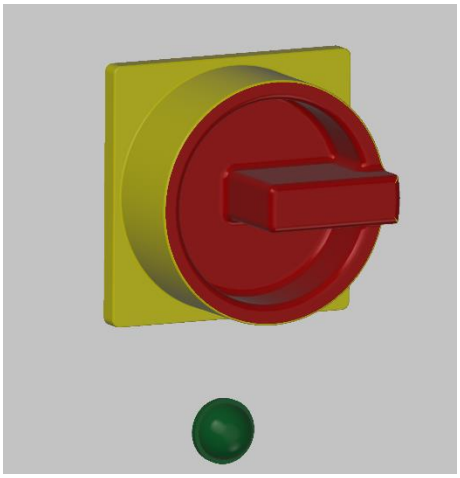
3.2 Instrumentation Cabinet



1 Touch screen operating panel
2 Main switch
3 Peristaltic pumps
4 Holder for reagent bottles

The instrumentation cabinet is attached to the right-hand side of the central column. It contains the entire measurement and control system.

3.2.1 Main Switch



The main switch can be found at the top-right of the front side of the instrumentation cabinet.

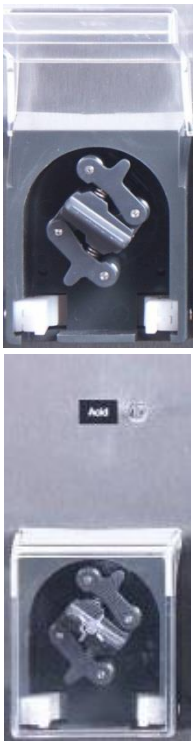
TO SWITCH ON
Turn the main switch clockwise (quarter turn) in position **I/ON** and the power indication light is illuminated.
The equipment is switched on and the bioreactor is in idle state (Phase *stopped*).

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

ATTENTION

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

3.2.2 Pumps

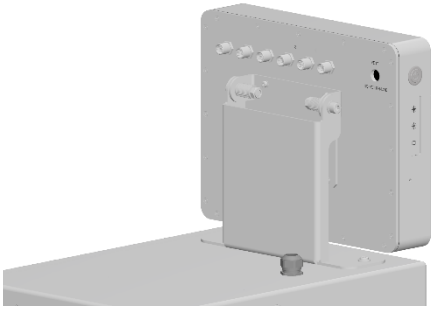


The four peristaltic pumps for addition of reagents and feed solution are located on the lower part of the instrumentation cabinet. They are driven by stepper motors and direction of rotation is clockwise in automatic running mode.
The pumps are labelled according their function: *Acid*, *Base*, *AF* (Antifoam) and *Feed1*. They have a cover made that can be folded up and down.

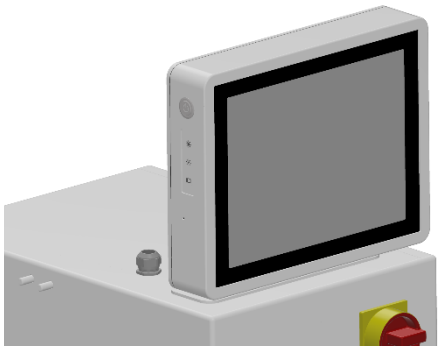
The pumps can be manually operated (forward and reverse flow) using the rocker switches above each pump head, provided that the equipment is switched on.

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

3.3 Touch Screen Operating Panel



The touch screen operating panel is attached to a bracket mounted on the top of the instrumentation cabinet. The bracket allows vertical swivelling of the panel so that it can be adjusted to the optimum viewing angle.

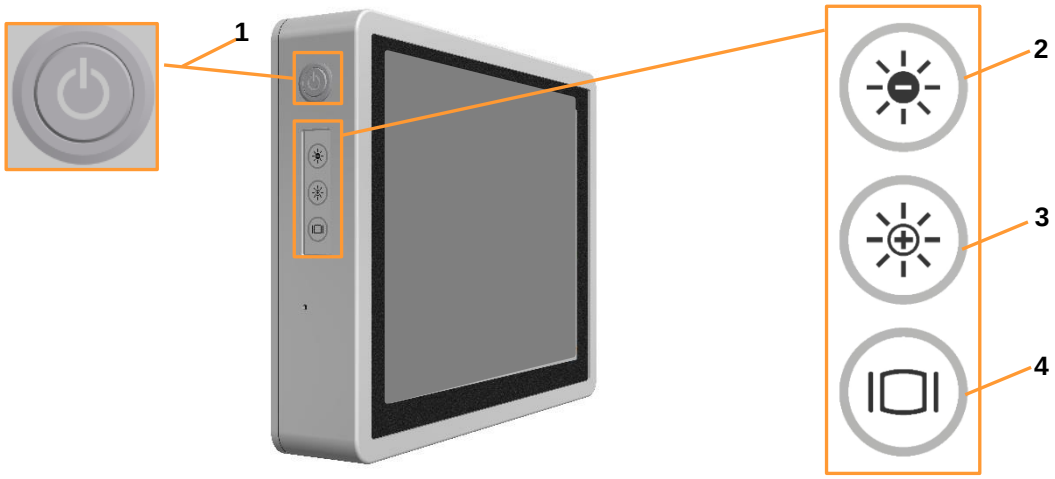


The operating panel has a 12" colour-touch screen with protection IP66.

The operator can access the desired options and functions of the bioreactor simply, quickly and intuitively by touching/pressing the various tabs, symbols and buttons on the screen.
A detailed description is given under chapter “Operation Touch Screen Software”.

3.3.1 Monitor Keys

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



1 **ON/OFF** key

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

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

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

Special details about the ON/OFF key

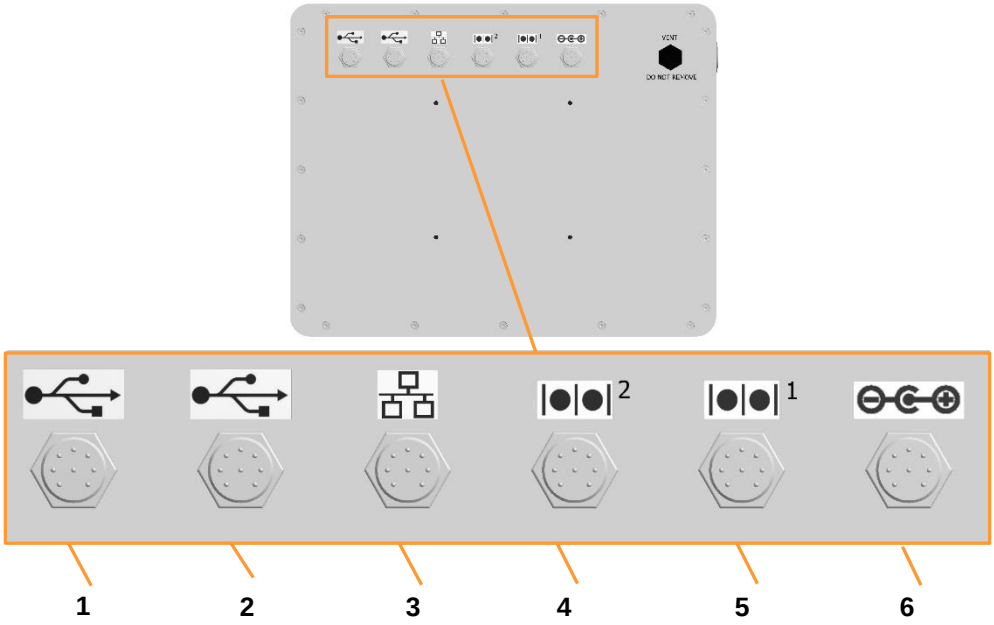
The touch screen operating panel is switched on and off at the main switch on the basic unit. Therefore separate switching on at the ON/OFF key is not necessary. The symbol on the key is illuminated when the operating panel is switched on.

INFORMATION

The **ON/OFF** key is locked when a bioreactor (fermentation) is running. A dialogue box with the appropriate message appears when pressing the **ON/OFF** key by mistake during fermentation. When pressing the **ON/OFF** key when the bioreactor (fermentation) is stopped, a dialogue box for shutting down the system appears

3.3.2 Operating Panel Connections

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



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

2 USB2.0 x 2: (Reserve)

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

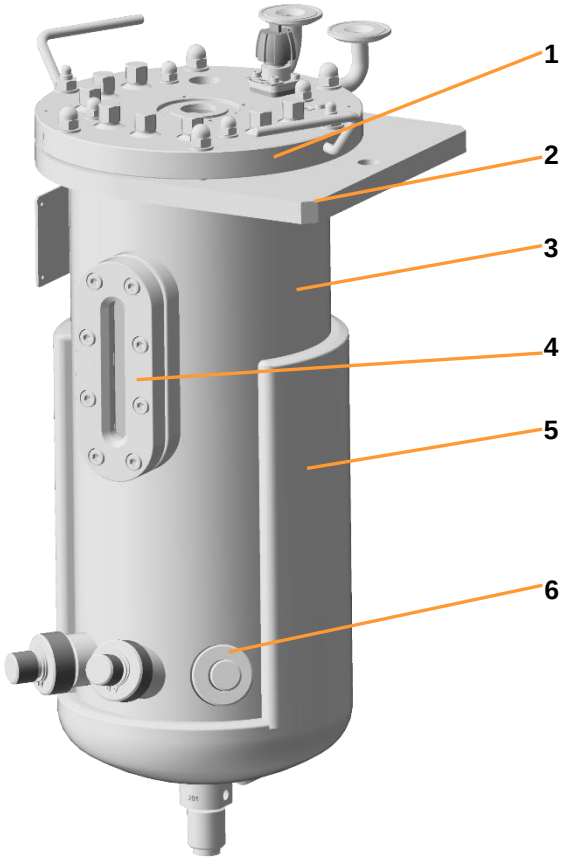
4 COM2 (Reserve)

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

6 DC: for power supply cable [1)]

[1)] Cable supplied with equipment

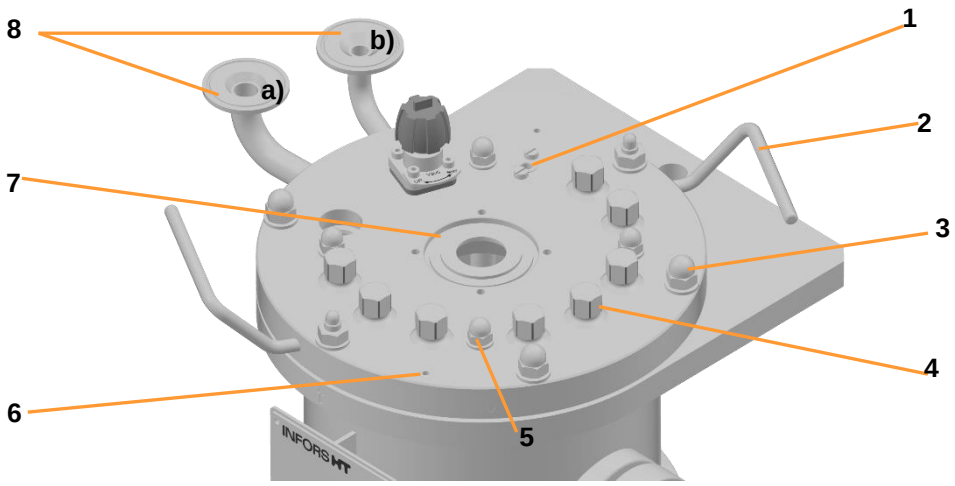
3.4 Vessel – Overview



1	Vessel top plate	4	Accessory: e.g. sight glass
2	Vessel flange	5	Vessel jacket
3	Vessel upper section	6	Standard INGOLD port

3.4.1 Vessel Top Plate

The vessel top plate has:



1 10 mm port with blind pocket for temperature sensor

2 Handle (2 pcs.)

3 Recessed hole, 6 pcs., for fixing the vessel top plate

4 19 mm port, 9 pcs., for mounting parts/accessories such as e.g.: safety valve, antifoam sensor, manometer, vessel light, inoculation needle(s), push valves, blind plugs etc.

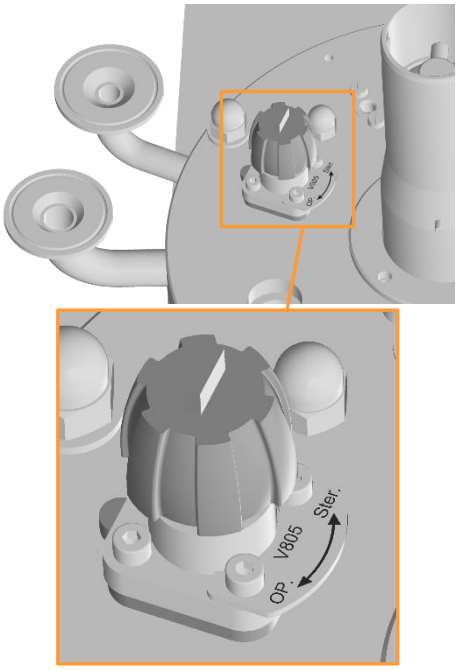
5 Recessed hole, 4 pcs., for baffles

6 4 mm hole, 2 pcs., for negative lead of the antifoam sensor

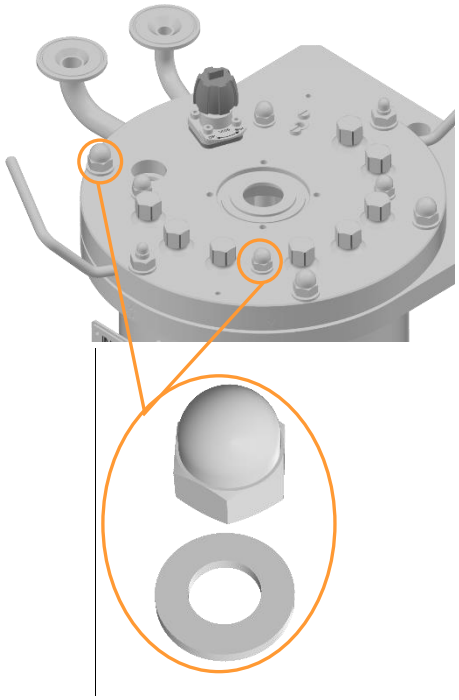
7 Middle port for drive hub for the motor

8 Tri-Clamp connection flanges for: exit gas cooler (a) and inlet air filter (b)

It is equipped with:

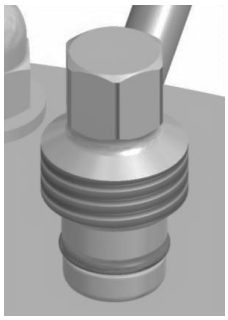


- Diaphragm valve **805** for air inlet into sparger or head room gassing (see chapter “Gassing” for details)

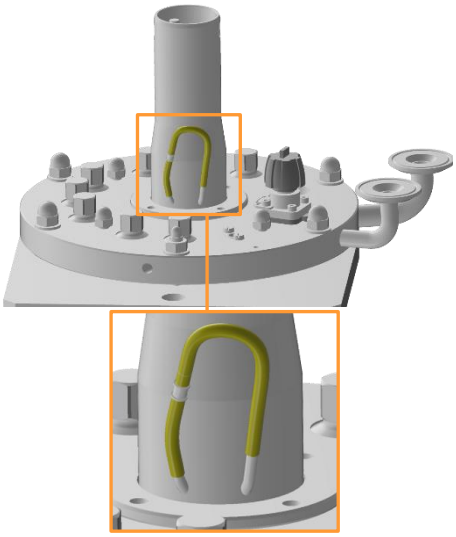


- 4 hexagon capped nuts M8 with metal washers for fixing the baffles.
- 4 hexagon capped nuts M10 with metal washers for fixing the vessel top plate.

Setup and Function

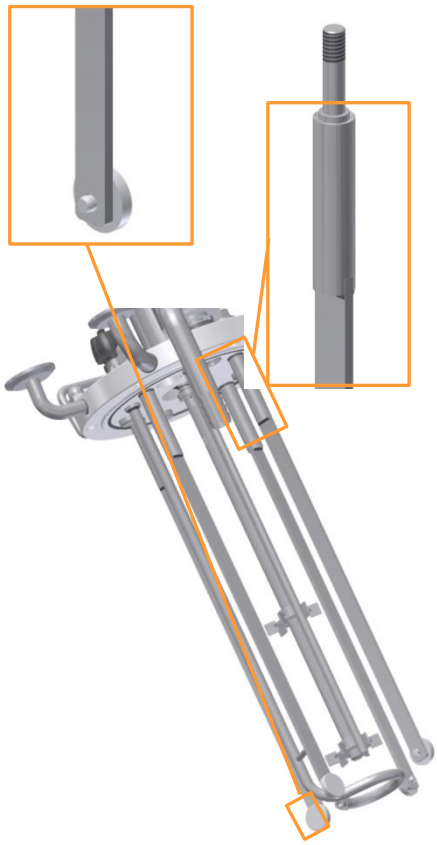


- Blanking plugs with fitted O-ring (Ø = 2,5 x 15 mm) for the 19 mm ports

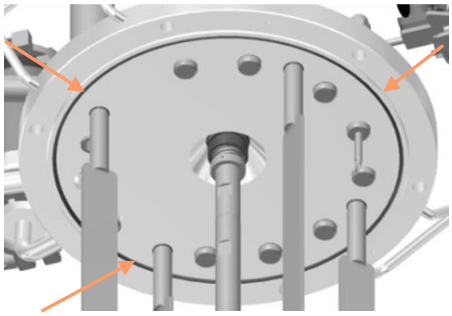


- Drive hub with connection nozzle with silicone hose for lubrication of the mechanical seal

- Drive shaft and 2 Rushton impellers (see chapter “Stirrer” for details)
- Ringsparger (see chapter “Gassing” for details).

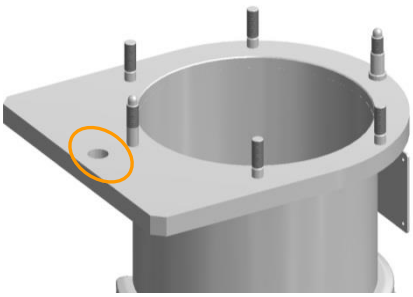


- 4 baffles with their holders and spacers on their lower end. One baffle is welded to the sparger for stabilisation (see chapter “Gassing” for details).



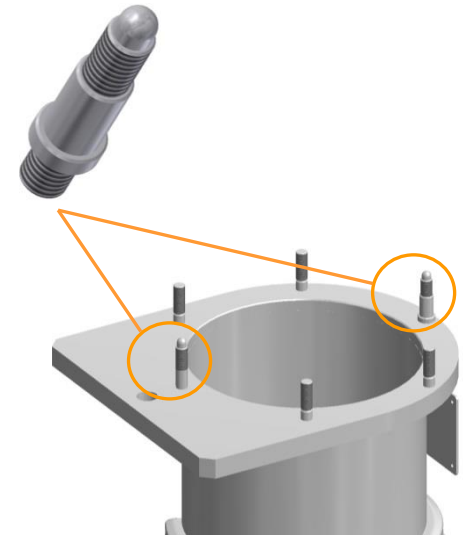
- O-ring (vessel top plate seal)

3.4.2 Vessel Flange

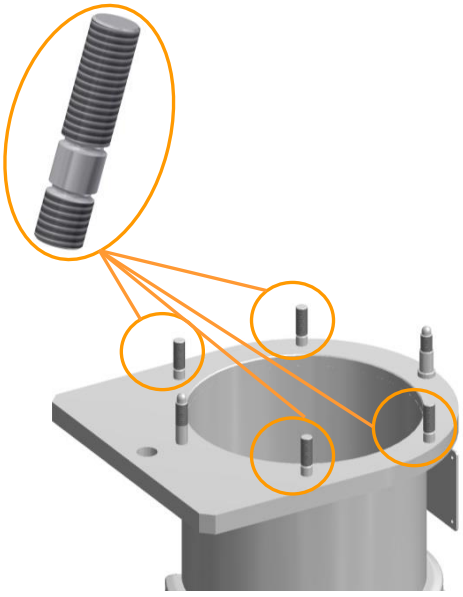


The vessel flange is extended on one side so that it can be hinged onto the support bar. A recessed hole is located in the middle of the flat extended part. It is for the screw that serves as transport lock for fixing the vessel to the central column.

Setup and Function



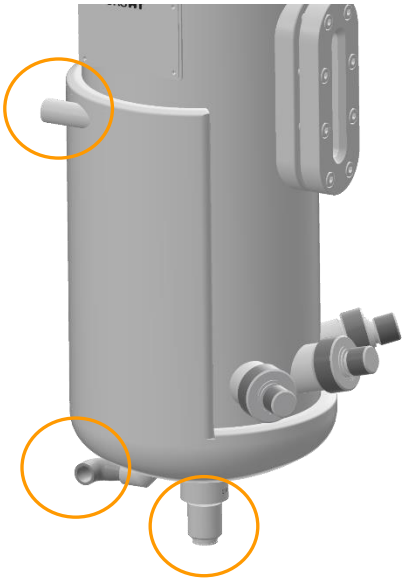
The 2 opposed round studs are for correct orientation, alignment and location of the vessel top plate.



4 further flat studs are for tightening down the vessel top plate.

3.4.3 Vessel Jacket

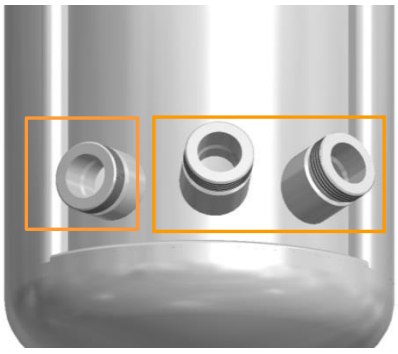
The vessel jacket encloses the dished base of the vessel. The vessel jacket has:



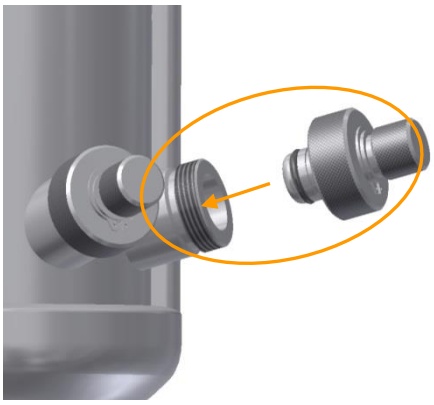
- Water outlet (upper connection)
- Water inlet (lower connection)
- A threaded nozzle for the steam sterilisable harvest/sample valve. For details see the chapter “Harvest/Sample Valve”.

3.4.4 Standard INGOLD Ports

3 standard INGOLD ports are readily accessible on the lower part of the front side of the vessel.



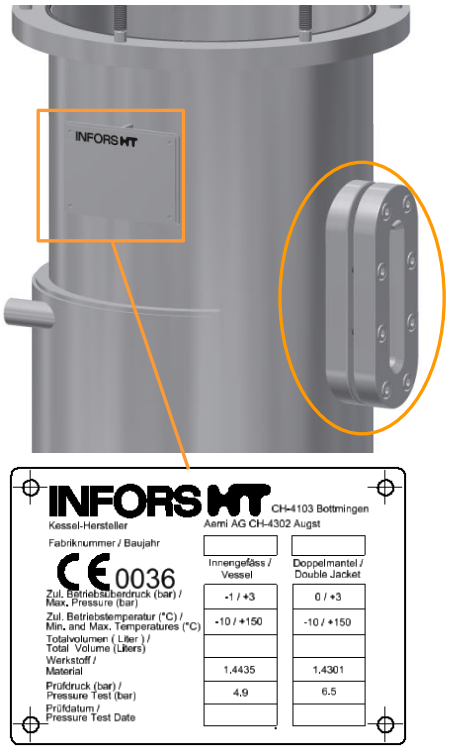
- 1 INGOLD standard port iD = 25 mm, horizontal / G1-1/4"
- 2 INGOLD standard ports, iD = 25 mm, angled (15°) / G1-1/4"



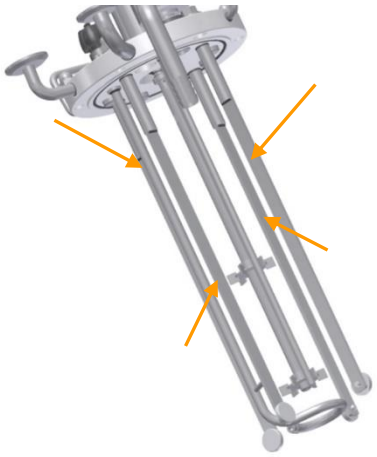
Each INGOLD standard port has a blanking plug with fixed O-ring (Ø = 3 x 20 mm).

3.4.5 Vessel Accessories

The vessel accessories consist of:



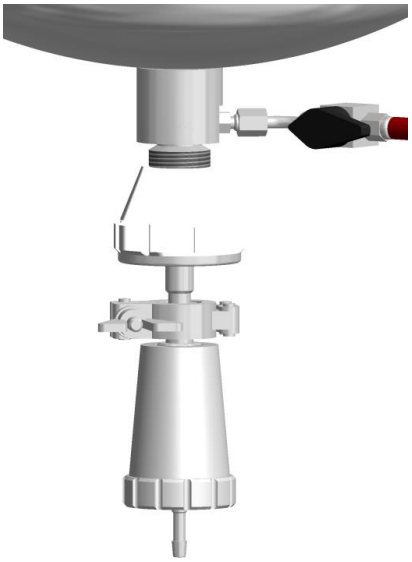
- Sparger, for details refer to chapter “Gassing”.
- Sight glass: allows a visual control of the liquid level in the vessel. The middle of the sight glass corresponds to the working volume of the vessel.
- Vessel identification plate: contains important technical vessel data and is welded to the vessel upper section. Its content is described in main chapter “General Information”, “Vessel Identification Plate”.



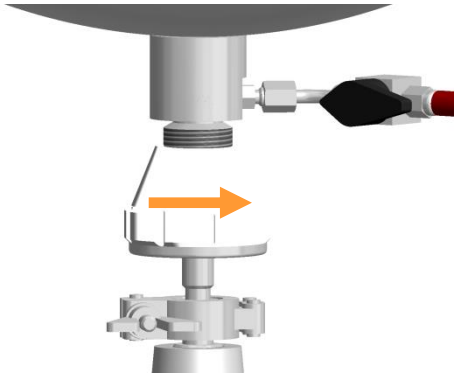
- 4 baffles with their holders and spacers on their lower end.

  The baffles are screwed into the corresponding threaded holes in the vessel top plate and fixed with a metal washer and hexagon capped nut (M8).

3.5 Harvest/Sample Valve (Bottom Valve)



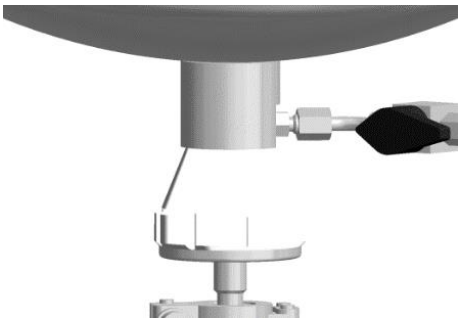
The harvest/sample valve (bottom valve) **201** is readily mounted to the threaded nozzle on the vessel's base.
This applies also to the steam trap and the clean steam line (pressure hose) with manual valve **203**.



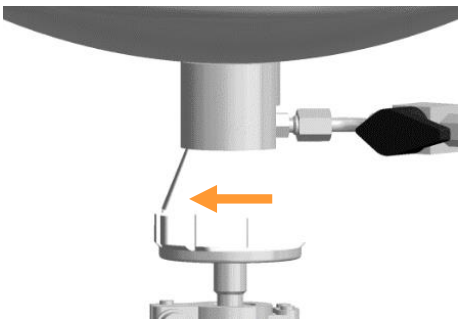
Opening and closing the harvest/sample (bottom valve)

To open:
turn it to the right

Setup and Function



The valve is open, the thread is **invisible**.



To close:
turn it to the left

The valve is closed, the thread is **visible**

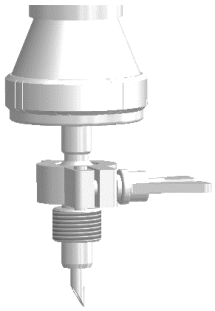
Sterilisation

The steam trap must be fitted to the closed valve for sterilisation by the means of a clamp. The flat gasket must be placed between the connection flanges before fixating the steam trap.

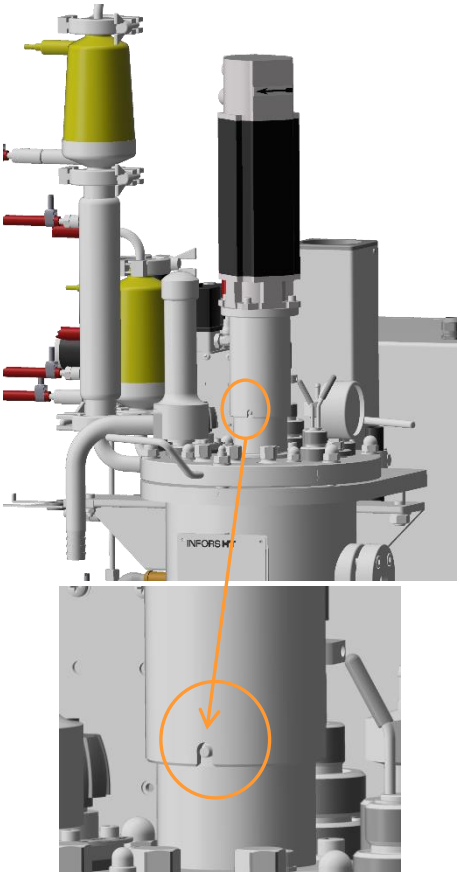
Sterilisation of the harvest/sample valve is started in the touch screen software on the operating panel. For details refer to the main chapter “Operation Touch Screen Software”.

Unscrewing the steam trap will expose the needle in order to pierce a septum e.g. in a sample bottle when sampling.

For more details about sampling refer to the chapter “Sampling” of the main chapter “Fermentation/Cultivation”.

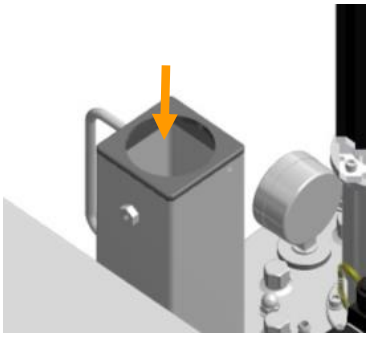


3.6 Stirrer

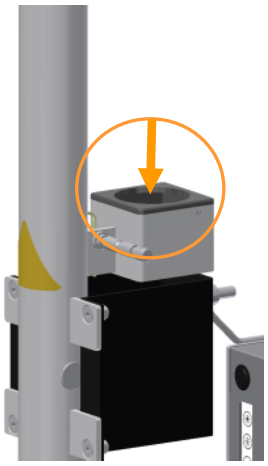


The stirrer shaft is rotated clockwise by a top drive. An air cooled servo motor is used. The range of rotation speed is from 10 up to 1500 min^{-1}.

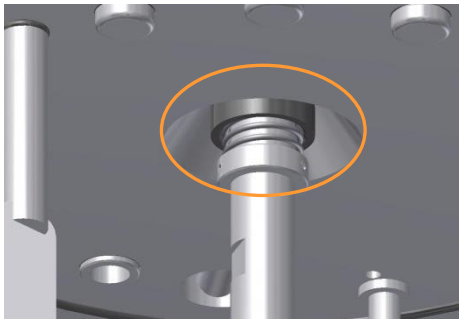
The motor is plugged onto the drive hub and thereby coupled by fitting the notch to the bolt.



After uncoupling the motor from the drive hub it can simply be inserted into the hole on the central pillar.



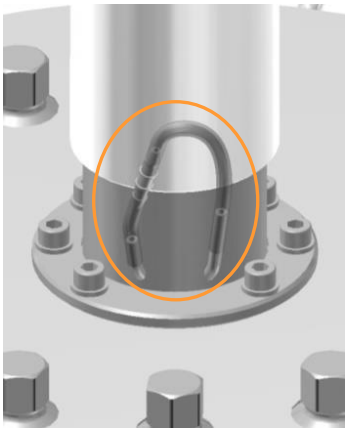
Or when in use, into the support of the lifting device for the vessel top plate.



The stirrer shaft is screwed to the drive shaft in the vessel top plate and sealed with a single mechanical seal.

ATTENTION

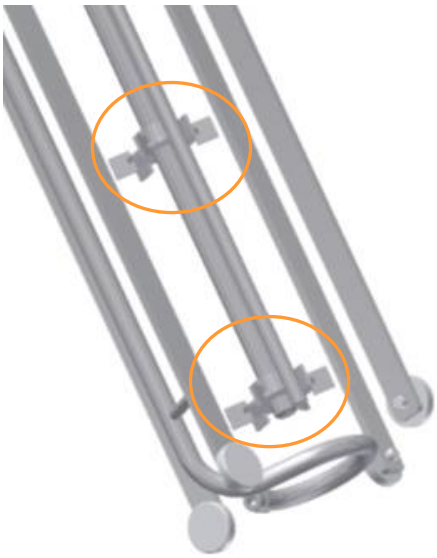
Manipulation on the mechanical seal may lead to its damage!

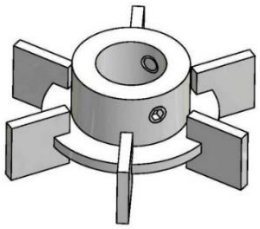


The mechanical seal must always be lubricated! Two connection nozzles with a silicone hose are located on the drive hub for this.

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

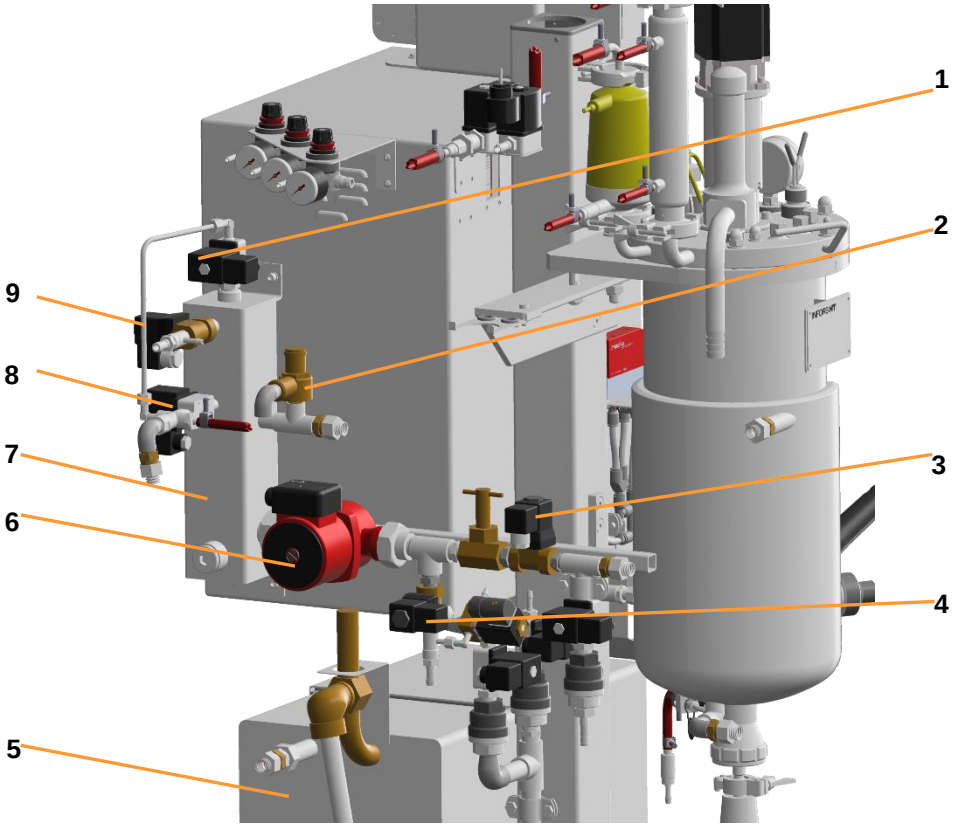
Setup and Function





Two height adjustable Rushton impellers with 6 blades with proportions 0.3 up to 0.4 x inner diameter of the vessel are fixated to the stirrer shaft by the means of grub screw

3.7 Temperature Control & Sterilisation



1 Solenoid valve **104** (*Steam in temp. control system*)
2 Safety valve **Y70** temperature control circuit
3 Solenoid valve **106** (*Condensate temp. control system*)
4 Solenoid valve **102** (*Tap water in*)
5 Steam generator
6 Circulation pump **P01**
7 Heating element (steam via injector)
8 Solenoid valve **103** (*Steam in vessel jacket*)
9 Solenoid valve **101** (*Tap water out*)

The temperature control circuit consists of a heating element with integrated steam injector for heating, an integrated circulation pump which provides water circulation into the vessel jacket.

A CE approved safety valve protects the temperature control circuit against too great of an overpressure (>3 bar).

Temperature control

The cooling is produced by using tap/utility water that leads directly into the vessel jacket respectively into the temperature control circuit.

Setup and Function

Heating is achieved by direct steam injection into the heating element. The tempering itself is automatic and controlled by solenoid valves in the temperature control circuit.

Circuit: vessel jacket – heating element - circulation pump - vessel jacket.

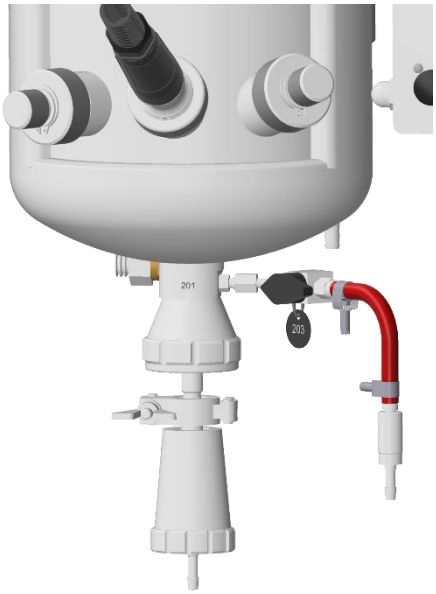
Temperature measurement

Temperature in the vessel is measured using a platinum resistance sensor (Pt100) which is inserted into the blind pocket in the vessel top plate.

Sterilisation vessel and filters

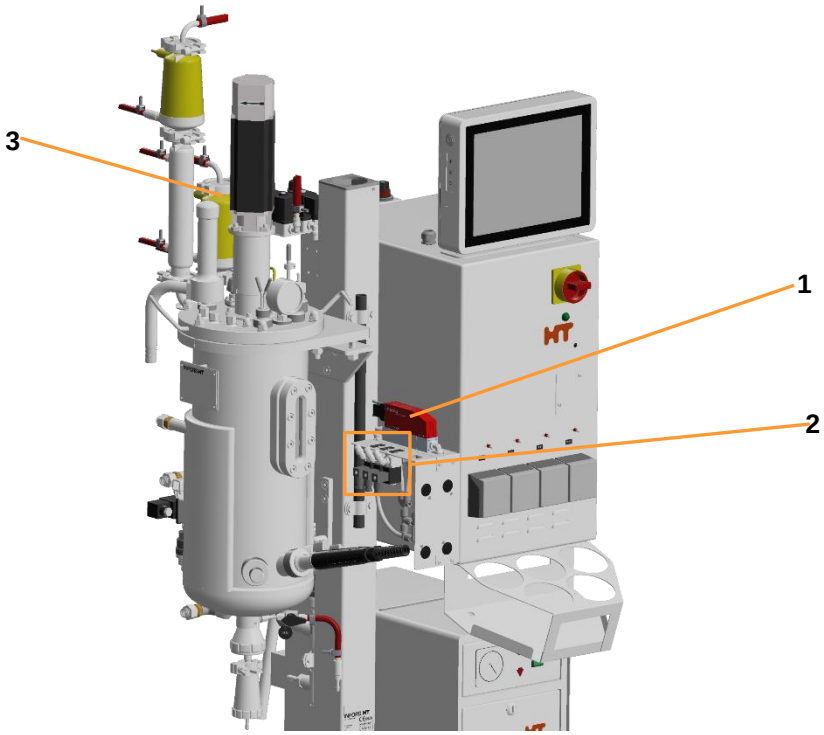
Heating up and holding the sterilisation temperature is fully automatic by steam produced by the integrated steam generator. Steam is directed into the vessel jacket, where the medium is heated and sterilised. Steam raised by the vessel content sterilises the inlet air and exit gas filter.

Sterilisation harvest/sample valve (bottom valve)



The harvest/sample valve is separately steam sterilised with steam from the integrated steam generator, too.

3.8 Gassing



1 Mass flow controller **FIC801**

2 Solenoid valves **810** (Air), **820** (O_2), **830** (N_2)

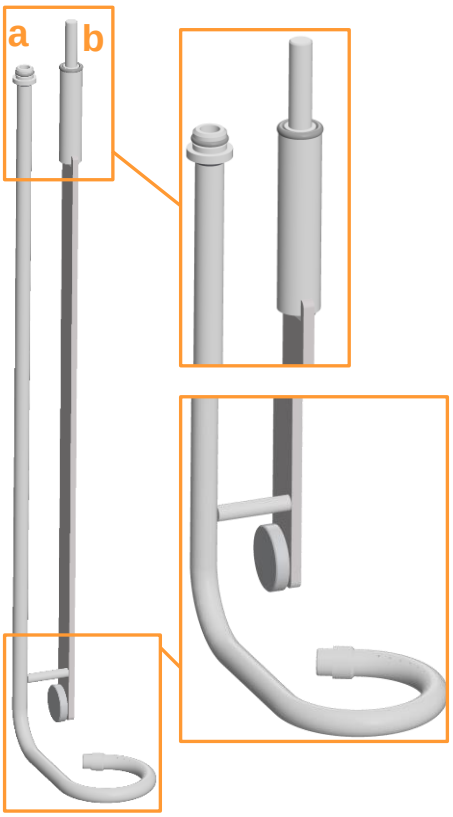
3 Inlet air filter **F01**

A steam sterilisable diaphragm filter of the type Novasip is used as inlet gas filter.

A mixture of Air, O_2 and N_2 is used for sparger gassing. Gas flow control takes place via one electronic mass flow controller. The gas mixture takes place before entry into the culture vessel via three solenoid valves. The gas flow rate of the three gases is set in the *Flow* parameter. Settings for controlling the oxygen concentration in the gas are made in the *Gasmix* parameter of the touch screen software.

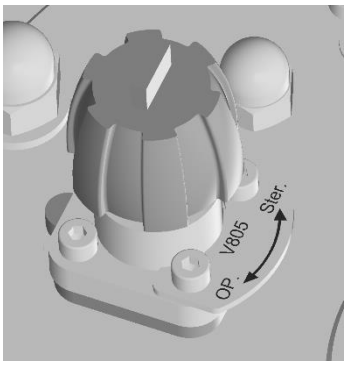
For details refer to main chapter “Operation Touch Screen Software”, chapter “Parameters”.

Setup and Function



A ring sparger (a) is used for gas entry into the culture medium in the vessel. The sparger is welded to one of the four baffles (b) for better stability.
The sparger is fitted with an O-ring and simply inserted into the corresponding port in the vessel top plate, where the manual diaphragm valve 805 is fitted, see following section.

The baffle is screwed into the corresponding threaded hole in the vessel top plate and fixed with a metal washer and hexagon capped nut (M8) like the three other baffles.

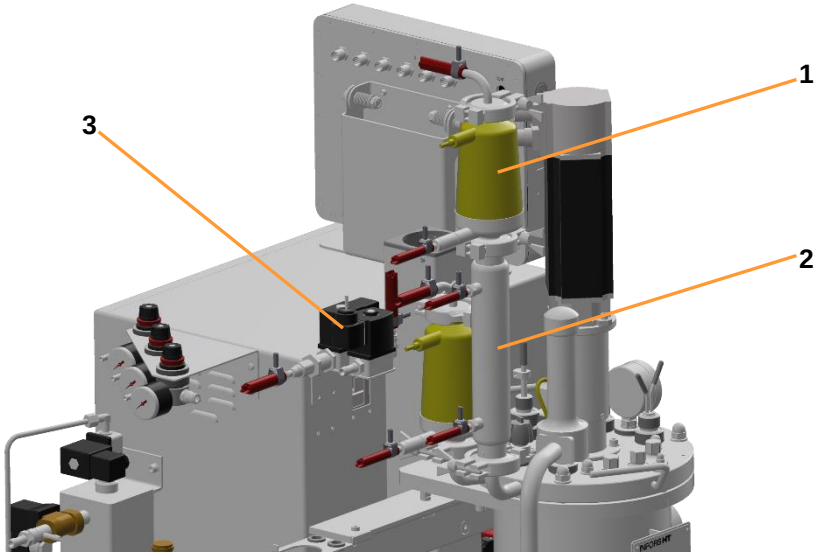


Manual Diaphragm Valve 805

The diaphragm valve **805** on the vessel top plate diverts the air into the sparger or the head space. The valve must be operated manually.

- Position ***Ster***: during sterilisation the valve must be in position *Ster.* to lead air into the head room.
- Position ***OP***: once the sterilisation process is finished and the pre-set temperature of fermentation is reached the valve must be switched back to *OP*.

3.9 Exit Gas



1 Exit gas filter **F03**
2 Exit gas cooler
3 Solenoid valve **901**

The exit gas leaves the vessel via the exit gas cooler, the exit gas filter and solenoid valve 901 into the atmosphere.

Like for inlet gas, the same steam sterilisable membrane filter of the type Novasip is used as exit gas filter.

A steam sterilisable membrane filter filters of the type Novasip are used here.

Before the exit gas filter is the thermodynamic exit gas cooler, which reduces liquid losses due to evaporation

Effectiveness of the exit gas cooler is based on the forced flow of the exit gas stream via a tube with internal baffles. These baffles greatly increase the surface area for condensation. The baffle tube is easily dismantled and cleaned.

3.10 pH Control

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

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

Measuring System

The measuring system for pH is equipped and configured for analogue sensors from the manufacturer METTLER TOLEDO.

Sensor

- Traditional pH sensor (potential measurement against reference)
- Type: 405-DPAS-SC-K8S/120
- Manufacturer: METTLER TOLEDO

Details on technical data, use and maintenance of the pH sensors can be found in the separate documentation of the sensor manufacturer. Read and follow instructions stated in there.

Calibration

As a general rule: Calibration of a pH sensor always must be carried out **BEFORE** sterilisation. This is executed in the touch screen software. For details refer to the main chapter “Operation Touch Screen Software”, “Calibrating the pH Sensor”.

Mounting of the sensor and cable connection

The pH sensor is mounted into a standard INGOLD port in the vessel. For details refer to the main chapter “Preparations before Fermentation/Cultivation”, chapter “Preparing the Sensors”, “Mounting the pH Sensor and Connecting the Cable”.

3.11 pO_2 Control

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

Increasing the pO_2

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

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

  These approaches can also be combined.

pO_2 reduction

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

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

Measuring System

The measuring system for pO_2 is equipped and configured for analogue and polarographic sensors from the manufacturer METTLER TOLEDO

Sensor

- Traditional amperometric/polarographic pO2 sensor
- Type: InPro 6820/25/080
- Manufacturer: METTLER TOLEDO

Polarographic pO_2 sensors must be polarised at initial operation or after disconnection from the voltage source. Correct calibration is not possible otherwise. This means that the pO_2 sensor must be polarised before calibration.

Details on technical data, use and maintenance of the pO2 sensors can be found in the separate documentation of the sensor manufacturer. Read and follow instructions stated in there.

Measurement und calibration

Generally speaking, the following applies: Unlike measurements such as pH, which are calibrated to absolute measurement values, the oxygen measurement is always calibrated to a relative reference point. For this purpose, the calibration is set to 100 % relative oxygen saturation, usually with air at max. stirring speed and maximum gas flow rate. The actual concentration of dissolved oxygen in mmol/L may therefore vary at 100 % saturation, depending on the process.

INFORMATION

Calibration is always carried out **AFTER** sterilisation. This is carried out in the touch screen software. Depending on the specifications defined by the user, the pO_2 sensor will be calibrated either before the vessel is filled with medium or afterwards, in the prepared medium.

For details about calibration refer to the main chapter “Operation Touch Screen Software”, “Calibrating the pO2 Sensor”.

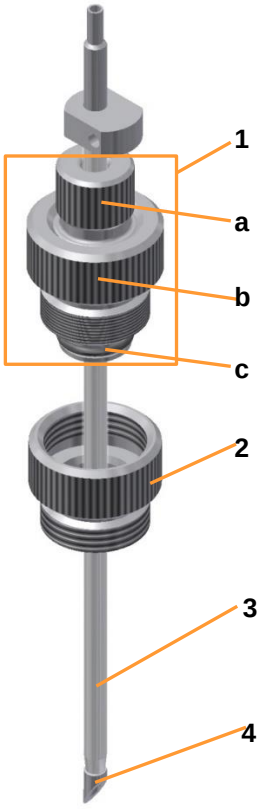
Mounting of the sensor and cable connection

The pO2 sensor is mounted into a standard INGOLD port in the vessel. For details refer to the main chapter “Preparations before Fermentation/Cultivation”, chapter “Preparing the Sensors”, Mounting the pO2 Sensor and Connecting the Cable”.

3.12 Antifoam Control

Foam hinders the exchange of gas between the medium and the gas phase in the head space. The exit gas filter can become clogged with foam, which causes a pressure build-up in the vessel. This can be prevented by using different methods. The most common method is 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 sensor also acts as a dosing needle and is prepared like an inoculation needle. When the antifoam sensor detects foam/liquid in the vessel, a signal is generated which leads to activation of the antifoam pump.



Antifoam sensor

1 Clamping adaptor with hollow screw (a), threaded housing (b) and O-ring (c)
2 Septum collar
3 Dosing needle
4 Sensor/needle tip (sharp!)

The antifoam sensor can be adjusted in its mounting depth after loosening the hollow screw in the clamping adaptor. It is provided with a septum collar and equipped with two protective caps (not visible) which are not sterilisable!

The dosing needle is equipped with a transparent insulation. A fixation of the sensor in the clamping adaptor which is too tight may damage the insulation.

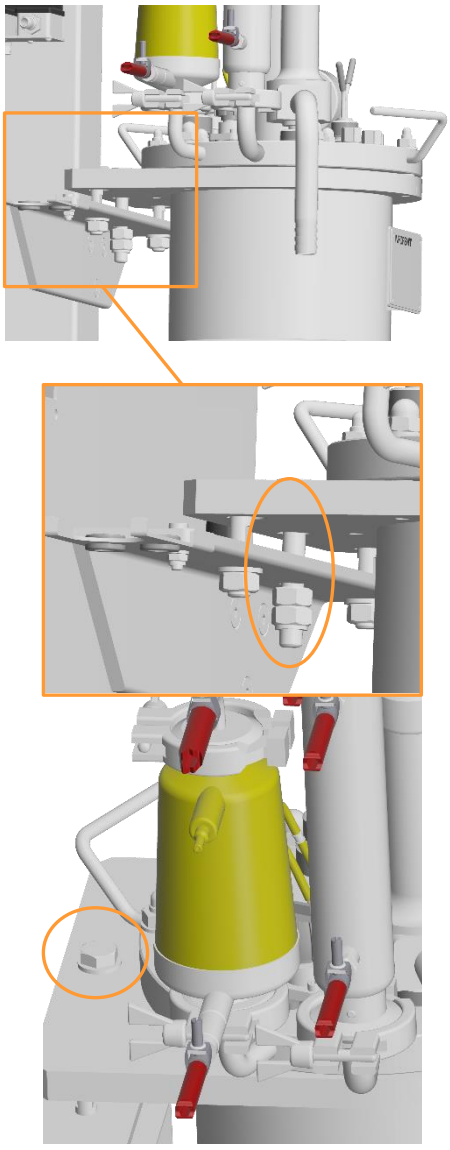
Preparation, mounting and cable connection of the antifoam sensor are described in detail in main chapter “Preparations before Fermentation/Cultivation”, chapters “Preparing the Antifoam Sensor” and “Mounting the Antifoam Sensor and Connecting the Cable”.

INFORMATION

The antifoam sensor is not in situ sterilisable and must be separately autoclaved!

3.13 Transport Lock

The transport lock locks the vessel in its position during transport. Furthermore, it also prevents the load cell from getting damaged, if present.



The vessel flange is screwed onto the support bar on the central pillar by the means of a hexagon screw M12.

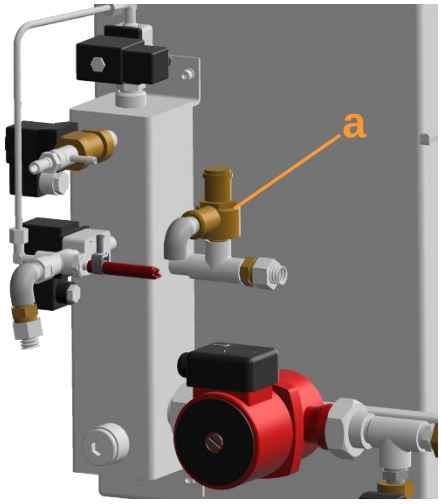
Equipment with load cell may not be operated with a mounted transport lock. Therefore it is removed during installation.
On equipment without load cell, complete removal is not necessary, the screw must only be slightly loosened.

3.14 Safety Devices

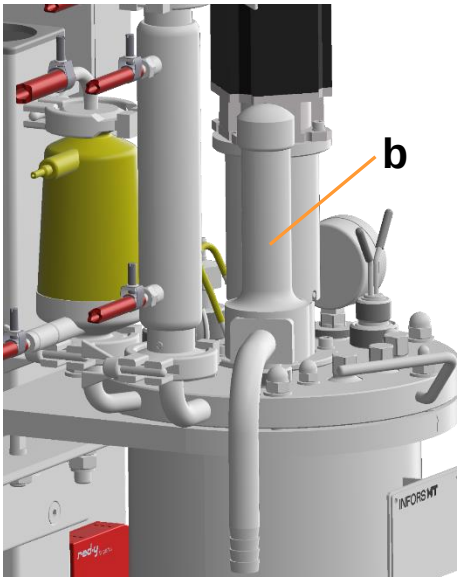
Safety Valves

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

For details about technical data, use and maintenance of the safety valves refer to the separate documentation from the safety valve's manufacturers.



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



The safety valve (b) on the vessel top plate protects the vessel (not the jacket!) against incorrect over pressure. It must always be fitted and intact when in operational mode.

Setup and Function

The valve can be opened by turning it counter clockwise. Normally it stays closed during sterilisation and fermentation/cultivation. For exceptions see the chapter “Mounting the Safety Valve to the Vessel” of the main chapter Preparations before Fermentation/Cultivation”.

4 Accessories, Consumables and Hoses

The bioreactors Techfors-S with serial number S-129020 is purchased with different standard accessories and consumables and further optional accessories. Thes standard items are listed in the tables below.

Accessories / Consumables in Starter Kit	Number
Reagent bottle, 500 mL	4
Cable tie, 2,4 x 85 mm, black	100
Hexagon socket spanner WAF 17 for blanking plugs in 19 mm ports in vessel top plate	1
Septum (inoculation diapghragm) for 19 mm ports	25
Disposable diaphragm filter, PTFE 0.2 µm, Ø = 25 mm	4
Double hose nipple 1/8'' x 1/8'', PVDF	10

Other Accessories	Number
Safety valve vessel (see “Setup & Function”, “Safety Devices”)	1
Filter, diaphragm, complete PTFE, 2 µm, for inlet air/gas and exit gas	2
Manometer for pressure indication in vessel	1
Antifoam sensor	1
Connection kit with hoses and attachments, see “Connection Kit”.	1

These standard accessories and additional accessories delivered with the equipment is described in the following chapters.

4.1 Connection Kit

The connection kit contains the following hose and hose attachment material.

Hose type	Ø mm	Application
Pump hose 5000 mm	3.2 x 6.4	Reagent bottle connection to peristaltic pumps
Pressure hose, 6 m	6.0 x 11.9	Gas connection
Pressure hose, 8 m	10.0 x 17.0	Steam connection
Pressure hose, 4 m	12.5 x 21.0	Condensate

Attachement	Ø mm	Application
Hose clamp, 8 pieces	12.0	Hose connection inlet air/gas
Hose clamp, 6 pieces	19.0	Hose connection water inlet & outlet and steam inlet
Hose clamp, 1 piece	12 – 22	Hose connection condensate

4.2 Manometer (Pressure Indication Vessel)

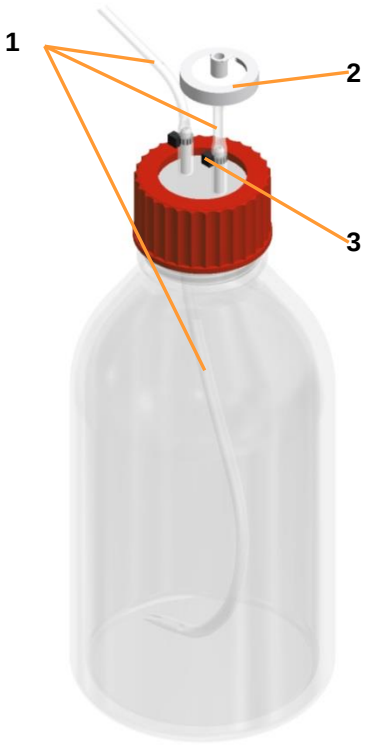
The manometer indicates the pressure inside the vessel. It is connected to one of the 19 mm ports on the top plate and has a range from 0 – 4 bar.

1 Pressure indication

2 O-ring D=2.5x15 EPDM

How to mount the manometer is described in the main chapter “Preparations before Fermentation/Cultivation”, chapter “Mounting the Manometer”.

4.3 Reagent Bottle



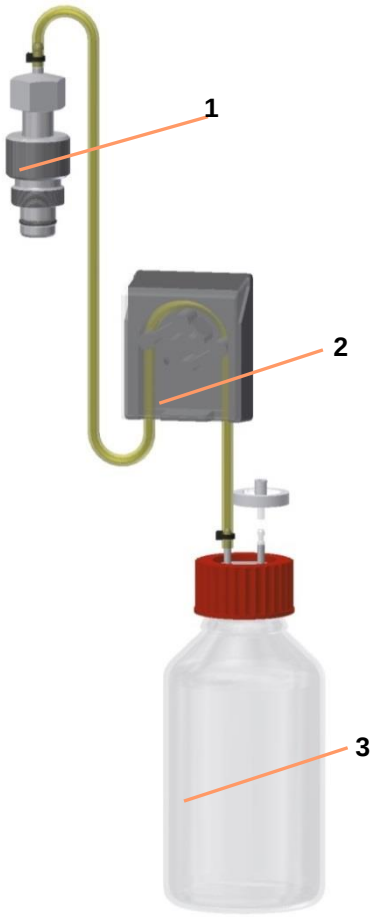
Reagent bottles are made of borosilicate glass and are supplied readily equipped with a filter and silicone hose.

1 Silicone hose: length = 0.25 m (connected to reagent bottle)
2 Filter
3 Cable tie (2 pieces)

Appropriate pump hoses are included in the starter kit.

For details about preparation of a reagent bottle see the main chapter “Preparations before Fermentation/Cultivation”, chapter “Preparing Inoculation Needles and Reagent Bottles”.

4.4 Push Valve



The sterilisable push valve allows the aseptic connection of a laboratory bottle filled with e.g. feed solution or corrective reagent to a bioreactor.

1 Push valve with fitted O-ring
2 Peristaltic pump
3 Reagent bottle

Preparation and use of the sterilisable push valve basically implies the following three steps:

1) Separate sterilisation in the autoclave:

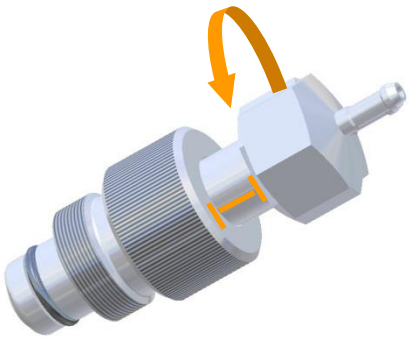
   The whole push valve (closed!) is sterilised along with the laboratory bottle, equipped with hose line and filter, in the autoclave.

2) In situ Sterilisation with the vessel:

   The exposed part of the push valve (closed!) is in situ sterilised with the vessel.

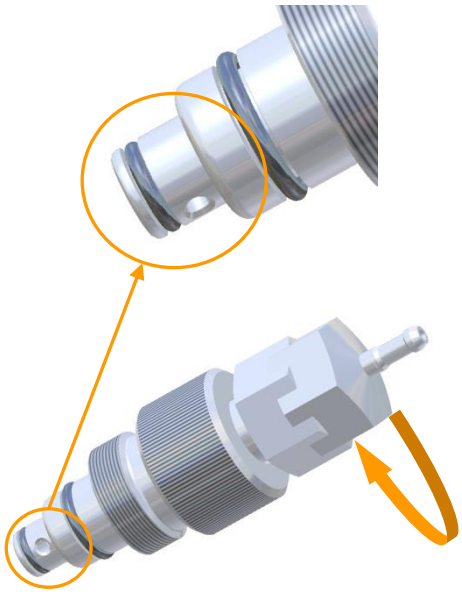
3) Fermentation/cultivation with open push valve:

   The push valve is opened for fermentation.



To CLOSE the push valve

Turn the top section of the rotating piston counter clockwise.
The bottom section of the rotating piston is retracted. The upper section sticks out from the valve body.



To OPEN the push valve

Turn the top section of the rotating piston clockwise.
The bottom section of the rotating piston is pushed downwards and the gap between top section of the rotating piston and the valve body decreases.

4.5 Sensor Insertion Housing

The insertion housing of the type *INFIT* from the manufacturer METTLER TOLEDO serves as sensor adapter for the INGOLD standard ports. It also protects the sensor connector from humidity and mechanical damage.
How to mount the sensor(s) is/are described in the main chapter Preparations before Fermentation/Cultivation".

For details about technical data and use refer to the separate documentation from the manufacturer METTLER TOLEDO.

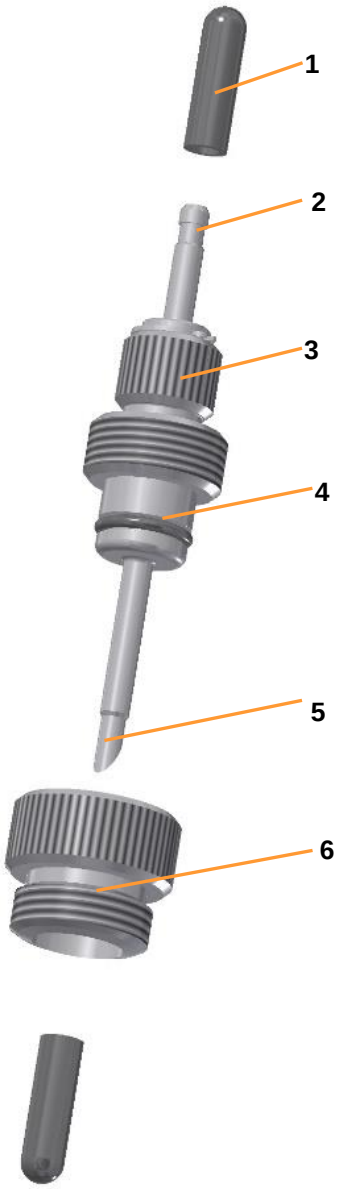
4.6 Inoculation Needles

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

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

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

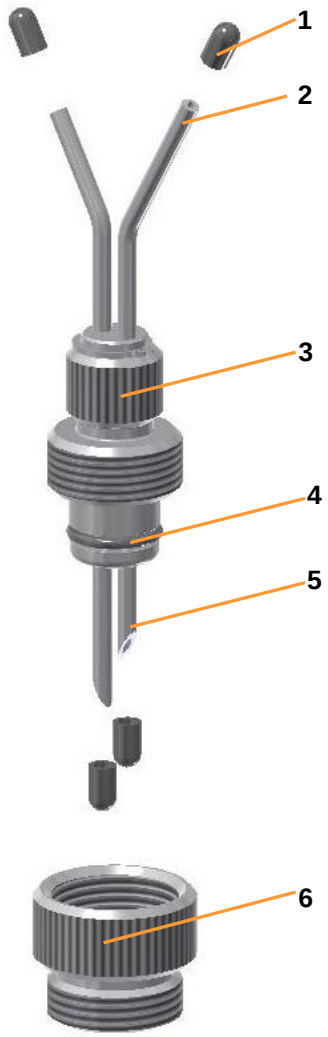
4.6.1 Inoculation Needle, Single



1 Protective cap (2 pces)
2 Hose connection (OD = 6.0 mm)
3 Hollow screw
4 O-Ring D = 2.5 x 15 mm, EPDM
5 Needle (ID = 4.0 mm)
6 Septum collar

For details about preparation of an inoculation needle along with a reagent bottle see the main chapter “Preparations before Fermentation/Cultivation”, chapter “Preparing Inoculation Needles and Reagent Bottles”.

4.6.2 Inoculation Needle, Double



1 Protective cap (4 pces)
2 Hose connection (2 pces., OD = 4.0 mm)
3 Hollow screw
4 O-Ring D =2.5x15 EPDM
5 Needle (2 pces., ID = 2.0 mm)
6 Septum collar

For details about preparation of an inoculation needle along with a reagent bottle see the main chapter “Preparations before Fermentation/Cultivation”, chapter “Preparing Inoculation Needles and Reagent Bottles”.

5 Transport and Storage

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

5.1 Transport

WARNING

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

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

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

5.2 Storage

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

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

6 Installation and Initial Operation

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

First the temperature control circuit must be filled after installation of the equipment. It is not necessary to empty the circuit, unless maintenance work on the circuit has to be done or local decisions necessitate a change. I.e. the filling has usually to be done once.

Following this, the motor cable is connected and a short test run for the basic functions of the bioreactor is executed then.

This work is not described in this operating manual because it must not be carried out by the operator. Therefore, this chapter only contains the connection conditions to be complied with and the services to be provided on site by the provider.

⚠ WARNING

Installation and initial operation requires qualified and experienced personnel. Faulty installation may lead to perilous situations or severe loss of property.

Installation and initial operation after an installation are to be carried out by the manufacturer's associates only.

6.1 General Location Requirements for Installation

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

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

6.2 Minimum Distances

To operate and maintain the equipment it must be installed with a minimum spacing of 150 mm from walls, ceilings or other equipment.

Furthermore it must be considered, that the lifting and removing procedure of the vessel top plate including its built-in components (drive hub, sparger, stirrer shaft etc.) must be possible in an easy and convenient way. Therefore the distance between equipment and ceiling should be calculated accordingly.

6.3 Power Supply

The in-house electric power supply of the equipment (bioreactor and steam generator) must meet the following conditions:

Bioreactor

- 230 V (± 5 %)
- 50 Hz
- 1 phase L1 + N (neutral) + PE (earth)

Steam generator

- 400 V (± 5 %)
- 50 Hz
- 3 phases L1 + L2 + L3 + N (neutral) + PE (earth)

Bioreactor & steam generator

- Electric power supply must be constant.
- The power supply of both, the bioreactor and the steam generator, must be individually made safe by the use of an FI-switch (or RCD – Residual Current Device) of the kind RCCB, Type B on the installation site.

⚠ WARNING

High leakage current!

Earth connection essential before connecting supply!

Detailed information about technical data, operation and maintenance of the steam generator can be found in the separate documentation from its manufacturer. Read the manual BEFORE initial

operation of the equipment and strictly follow instructions stated in there.

6.4 Cooling Water, Drain & Condensate

The in-house cooling water supply of the equipment must meet the following conditions on site:

- Constant cooling water supply at a pressure of 2.0 ± 0.5 bar
- Water quality “very soft” or “soft” ($CaCO_3$ concentration 0 mmol L^{-1} to 1.5 mmol L^{-1}) is appropriate.

ATTENTION

Cooling liquid containing alcohol may damage components of the temperature control system!

Always consult the manufacturer or the responsible dealer regarding allowed cooling liquids, if the use of alcoholic cooling liquid is foreseen.

Drainage

The in-house drainage of the water (condensate, water outlet temperature control circuit and total emptying of the steam generator) must meet the following conditions:

- The drain must be heat resistant and must not have backpressure.
- The drain must not be close-by the user.

CAUTION

Hot water and/or steam can drain out from the water and condensate outlet.

- The contaminated condensate must be drained off safely and disposed off environmentally correct.

WARNING

Health risk and danger to the environment due to contaminated condensate!

Hoses

- Only use pressure-resistant and intact hoses.
- Only use hoses with appropriate diameter, use adaptors as necessary
- Secure hoses with appropriate clamps.

6.5 Gas Supply

The in-house supply of the process gas (air = compressed air, O_2 and N_2) for the equipment must meet the following conditions:

- Constant gas supply at a pressure of ≥ 2.5 bar
- Gas is dry, clean and free of oil and dust (recommended pre-filter 10 µm)
- Recommended compressed-air quality as per DIN ISO 8573-1: Class 1,2,3,4

WARNING

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

ATTENTION

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

Hoses

- Only use pressure-resistant and intact hoses.
- Only use hoses with appropriate diameters, use adaptors as necessary
- Secure the hoses with appropriate clamps

6.6 Exit Gas

On site, it must be ensured that:

- the exit gas is safely led away by means of a suitable, gas-tight hose.
- the exit gas line/hose is higher than the exit gas filter.

- the working environment and/or the laboratory/laboratory-like facility is equipped with a sufficient ventilation system, depending on the application.

6.7 Steam Supply

Steam supply of the equipment is be provided by an integrated steam generator.

Conditions water for steam generator

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

Detailed information about connection conditions as well as technical data, operation and maintenance of the steam generator can be found in the separate documentation from its manufacturer. Read the manual before initial operation of the equipment and strictly follow instructions stated in there.

Conditions steam (vessel, inlet air and exit gas filter)

- Constant steam supply at a pressure of 2 ± 0.2 bar
- Required quantity of steam: approx. ≈ 8 kg/h

Conditions clean steam (periphery: harvest/sample valve)

- Constant clean steam supply at a pressure of 2 ± 0.2 bar
- Required quantity of steam: approx. ≈ 1 kg/h
- Quality: Steam that is used for sterilisation of the harvest/sample valve (bottom valve) must be of clean steam quality and can pass through a 5 micron filter

Hoses

- Only use pressure-resistant and intact hoses.
- Only use hoses with appropriate diameter, use adaptors as necessary
- Secure hoses with appropriate clamps.

⚠ CAUTION

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

7 Preparations before Fermentation / Cultivation

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

- Preparing the vessel and accessories:
  - Checking gaskets (O-rings) on component parts and on the vessel
  - Mounting the component parts

ATTENTION

Mounting/removing mounting parts including blanking plugs with tools may damage them and lead to inseparable screw connections!

– Only mount/remove mounting parts by hand.

– Use the hexagon socket spanner purchased with the equipment for mounting (hand-tight) and loosening the 19 mm blanking plugs.

  - Filling the vessel
  - Preparing sensors and other accessories
- In situ Sterilisation – General Information

INFORMATION

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

7.1 Securing the Position of the Equipment

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

CAUTION

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

Always lock the brakes of the trolley wheels on the base frame!

7.2 Uncoupling the Motor

Before you begin, ensure the bioreactor is stopped, the system is shut down and the equipment is switched off at the main switch and the motor has cooled down.

⚠ CAUTION

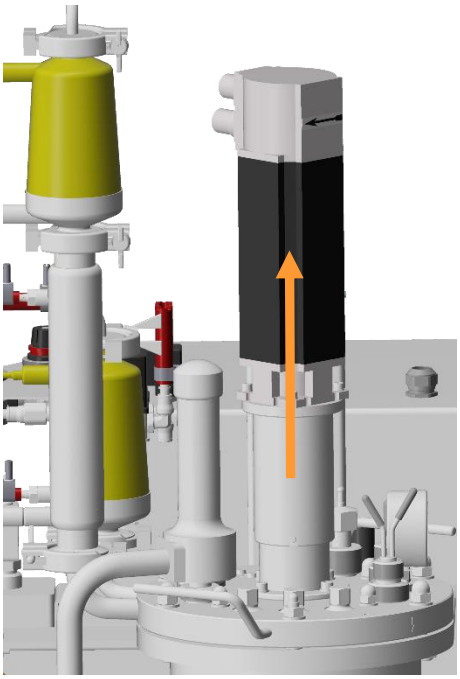
Risk of minor burns, if touching the motor during operation or cooling phase.

⚠ CAUTION

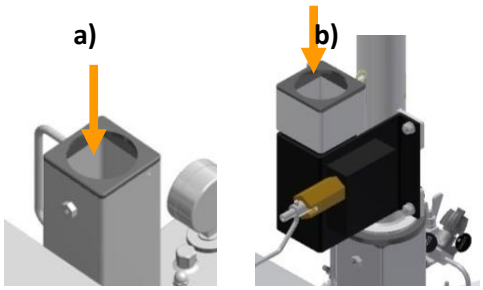
The motor is heavy! Work in a team of two when uncoupling and coupling the motor.

To remove the motor from the drive hub, proceed as follows:

Procedure



1. Lift the motor, lightly shake it to loosen it from the drive hub as necessary.



2. Plug the motor into:

a) the hole on the central pillar.

Or if present:

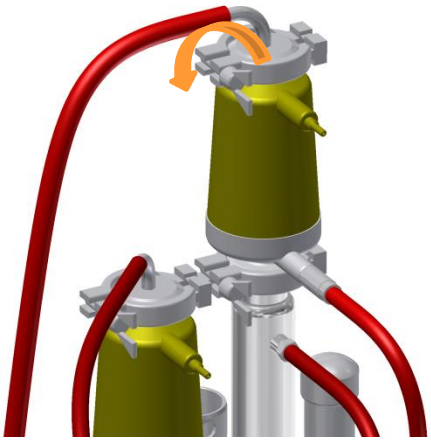
b) into the support of the (optional) vessel top plate lifting device.

7.3 Removing the Exit Gas Cooler and the Filters

The inlet air filter and the exit gas cooler with filter (as one assembly) must be removed before removing the vessel top plate. Both are fixed by the means of clamps to the connection flanges of the vessel top plate. The exit gas filter and the inlet air/exit gas lines are fixed with clamps, too.

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

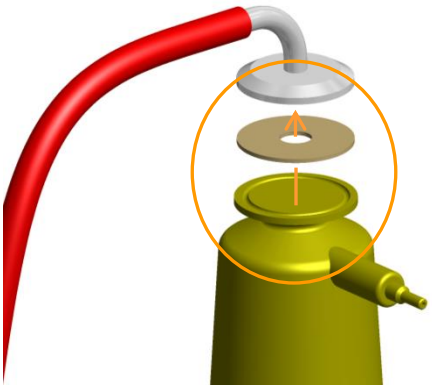
Procedure



1. Unscrew the wing nut of the clamp between exit gas filter and exit gas hose.

2. Open the clamp and remove it.

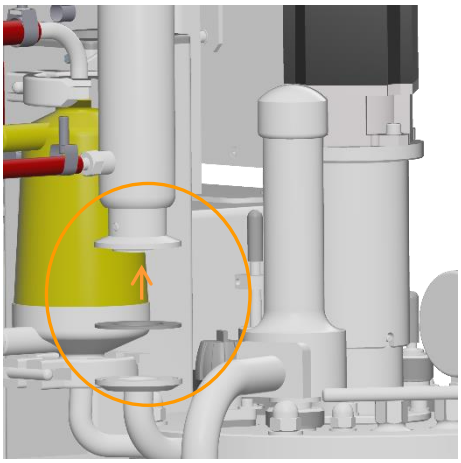
Preparations before Fermentation / Cultivation



3. Remove the exit gas line from the exit gas filter.

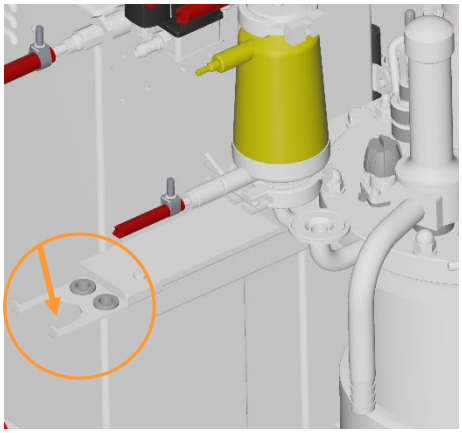
Ensure that the flat gasket does not get lost.

4. Open and remove the clamp between the exit gas cooler and the connection flange on the vessel top plate in the same way as described above.



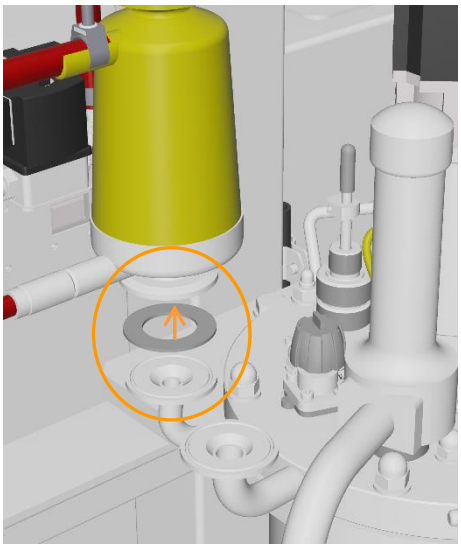
5. Remove the exit gas cooler.

Ensure that the flat gasket between the flanges does not get lost.



6. Turn the exit gas cooler upside down and hinge it onto the holding device of the vessel holder.

7. Open and remove the clamp between the inlet air filter and connection flange on the vessel top plate in the same way as described for the exit gas cooler.



8. Remove the inlet air filter.

   Ensure that the flat gasket does not get lost.

   The inlet air filter does not need a special holder due to its light weight. It can hang loose within the connecting hoses.

9. Disconnect all additional hoses and cable connections (sensors etc.) between equipment and vessel top plate.

7.4 Removing the Vessel Top Plate

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

Before you begin, ensure the following:

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

ATTENTION

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

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

CAUTION

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

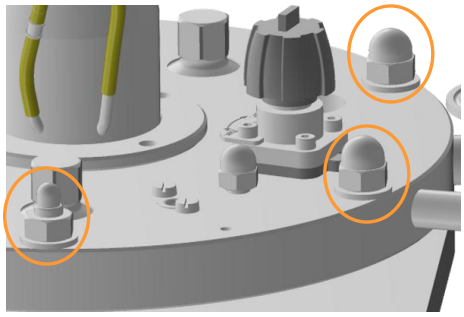
Preparations before Fermentation / Cultivation

INFORMATION

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

Proceed as follows:

Proceudre

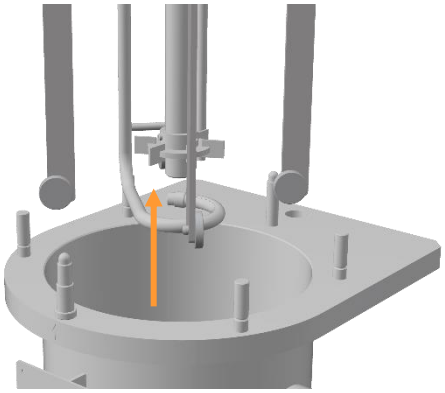


1. Loosen the capped nuts (M10) of the vessel fixing using the hexagon socket spanner provided with the equipment or with a wrench AF17.

2. Remove the capped nuts and the metal washers.
3. Disconnect any cable or hose connections between vessel top plate and basic unit or instrumentation cabinet.

Manual procedure (2 people)

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



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

ATTENTION

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

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

ATTENTION

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

7.5 Checking Impellers, Baffles and Top Plate Seal

The impellers, baffles and the top plate seal (O-ring) should be checked for tightness and correct position before refitting the vessel top plate.

Stirrer shaft & impellers

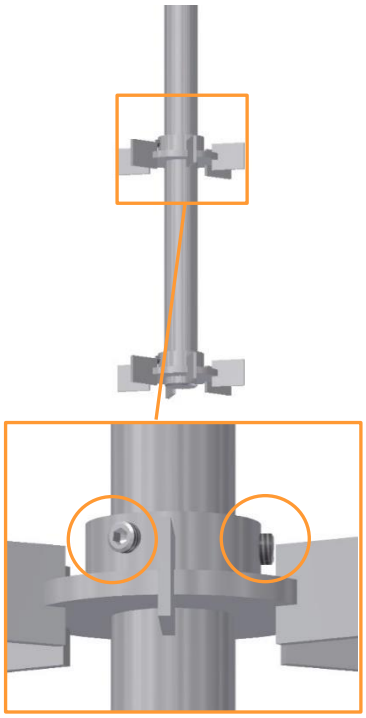
Note the following:

ATTENTION

Manipulation on the mechanical seal may lead to its damage!

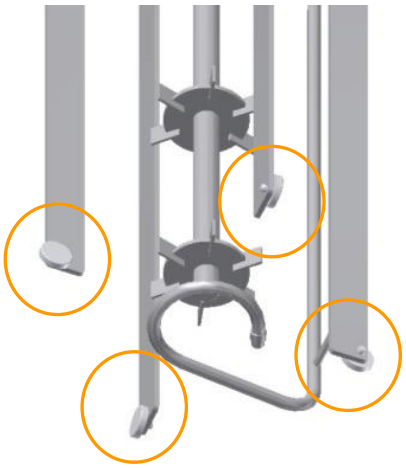
Proceed as follows:

Procedure



1. Ensure the impellers are adjusted to the desired height on the stirrer shaft and are tight.

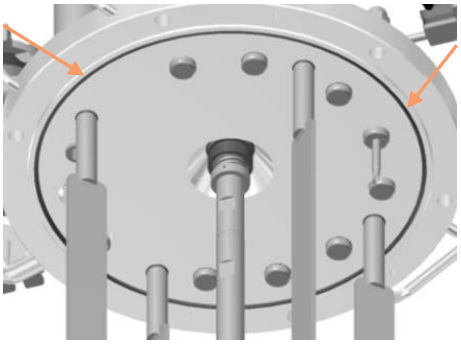
   If necessary: loosen the grub screws (M5x6, 2 pieces per impeller) on the impellers and adjust them in their position. Tighten the grub screws.



Baffles

2. Ensure that all spacers are fitted onto the baffles and fit tightly.

3. Ensure that the metal washers are fitted and the capped nuts (M8) are tightened which fixate the 4 baffles



Top Plate Seal (O-ring)

4. Ensure the intact O-ring (top plate seal) is placed firmly in the groove of the vessel top plate.

7.6 Filling the Vessel & Refitting the Vessel Top Plate

The easiest way to fill the vessel is when the top plate is still removed. If doing so, then all vessel mounting parts such as e.g. sensors which are mounted to lateral INGOLD ports must be prepared and mounted beforehand.

The vessel can be filled either with heat resistant culture medium or with water depending on the kind of used medium and on the user's specifications. Refer to chapter "In situ Sterilisation – General Information" for more details.

Liquid could also be filled in after refitting the top plate, using one of the different ports in the top plate.

When ready, the heavy vessel top plate can be refitted now. It can either manually be lifted or with an appropriate lifting device. In both cases two people are needed.

Preparations before Fermentation / Cultivation

INFORMATION

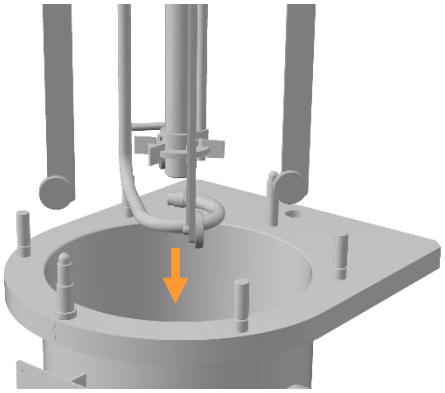
The use of the optional lifting device of the manufacturer of the equipment is recommended due to the weight of the vessel top plate. Assembly, Operation and Maintenance of the lifting device are described in detail in the separate user manual.

- Respect the same safety precautions as mentioned in chapter “Removing the Vessel Top Plate”.
- Use the help of a second person to lift the vessel top plate manually.

Manual procedure (2 people)

To refit the vessel top plate, proceed as follows:

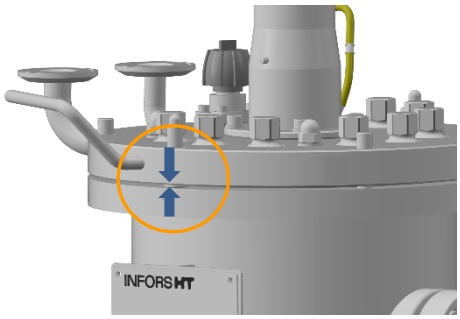
Procedure



1. Lift the vessel top plate on both handles.
2. Align the vessel top plate with the centre of the vessel and slowly lower it.

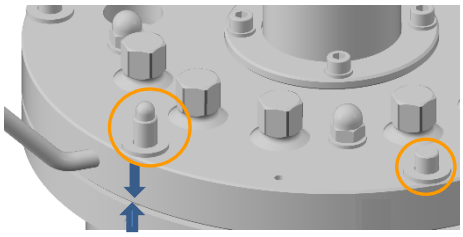
   Ensure that the baffles, the sparger and the stirrer do not knock against the inside of the vessel.

3. The recessed holes in the vessel top plate must be in line with the flat studs on the vessel flange.



4. Fit the vessel top plate.

   Two engraved marks on the vessel top plate and on the flange of the vessel designate the orientation of the vessel top plate.

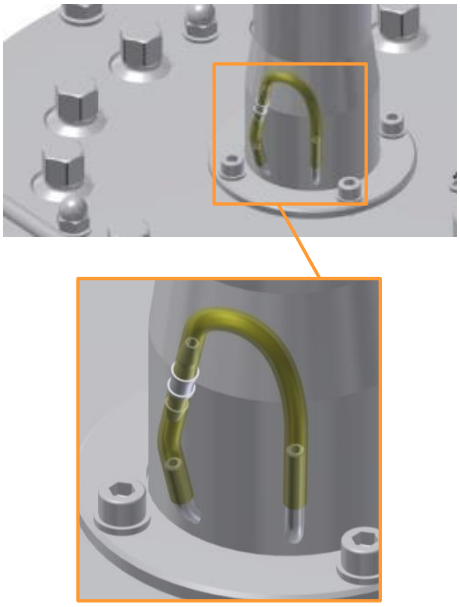


5. Place the metal washers onto the flat studs.

6. Fit the capped nuts (M10) onto the flat studs and tighten them cross-wise with a wrench AF17.

7.7 Checking Lubrication of the Mechanical Seal

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



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

! ATTENTION

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

7.8 Coupling the Motor

⚠ CAUTION

Risk of minor burns, if touching the motor during operation or cooling phase.

⚠ CAUTION

The motor is heavy! Work in a team of two when uncoupling and coupling the motor.

To couple, the motor, proceed as follows:

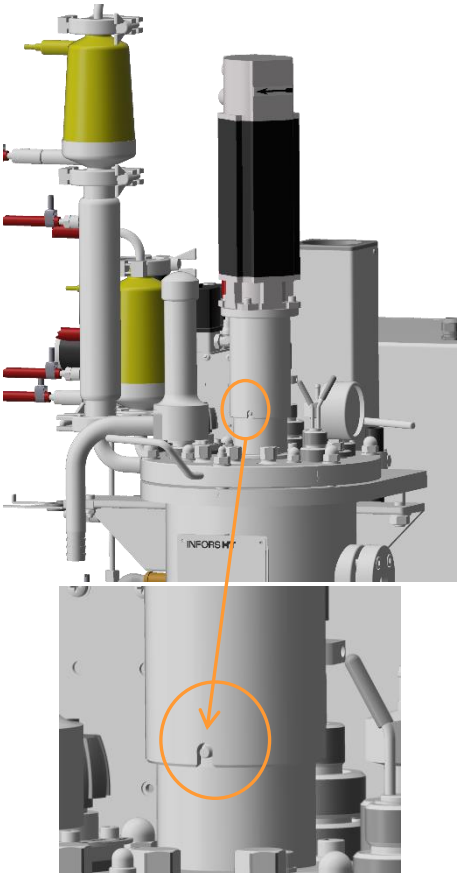
Procedure

1. Lift the motor out of:

a) the hole of the central pillar.

OR, if applicable:

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



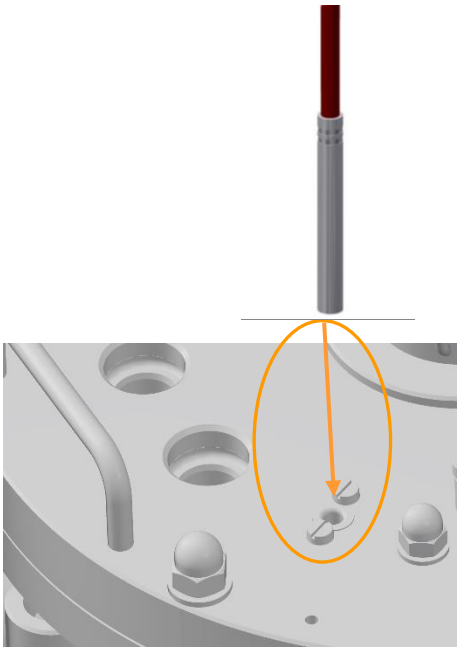
2. Plug the motor onto the drive hub of the vessel top plate.

Bring the slot of the motor coupling into line with the centre pin on the drive hub. Any other position is not usable.

7.9 Preparing the Sensors

Initial operation, maintenance and use of the sensors are described in detail in the sensor manufacturer's documentations. These instructions are strictly to be followed!

7.9.1 Mounting / Connecting the Temperature Sensor



The temperature sensor has no connector. It must simply be inserted into the blind pocket in the vessel top plate.
Ensure the temperature sensor is inserted as far as it will go (feel contact metal to metal).

7.9.2 Calibrating the pH-Sensor

A reliable pH measurement always needs a 2-point calibration with a high and low reference buffer. Calibration must be performed before each fermentation/cultivation process. This is described in detail in main chapter "Operation Touch Screen Software", chapter "Calibrating the pH Sensor – Procedure".

7.9.3 Mounting the pH Sensor and Connecting the Cable

Only mount a calibrated pH sensor into the INGOLD vessel port. For details about calibration refer to the main chapter "Operation Touch Screen Software", chapter "Calibrating the pH Sensor – Procedure".

For details about technical data, use and maintenance of the sensor see the separate documentation from the manufacturer METTLER TOLEDO.

Preparations before Fermentation / Cultivation

Mounting

To mount the pH sensor, proceed as follows:

Procedure

1. Carefully insert the (calibrated!) pH sensor into the sensor insertion housing provided with the sensor as far as it will go and screw it tight.

The picture on the left shows the sensor insertion housing with the inserted pH sensor.

2. Loosen and remove the blanking plug from the INGOLD port.

3. Carefully screw the sensor into the INGOLD port.

Ensure it is fitted in line with the port and sits neatly.

Connecting the sensor cable

To connect the sensor cable, proceed as follows:

Procedure

1. Loosen and remove the anti-kink cable gland from the protective sleeve.

2. Slip the protective sleeve over the sensor cable.

INFORMATION

Pictures of the sensor cable aid general understanding and can differ from the actual equipment as supplied.

3. Attach the sensor cable to the sensor.

ATTENTION

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

4. Turn the ring on the cable connector and screw tightly.

5. Pull forward the protective sleeve and screw tightly.

6. Slip the slotted cable grommet over the sensor cable (delivered with the sensor insertion housing of the type *In-Fit*).

7. Plug the slotted cable grommet into the protective sleeve.

7.9.4 Mounting the pO2 Sensor

The pO_2 sensor must be mounted into one of the INGOLD standard ports before sterilisation.

It is polarised and calibrated after sterilisation.

For details about technical data, use and maintenance of the sensor see the separate documentation from the manufacturer METTLER TOLEDO.

To mount the pO_2 sensor, proceed as follows:

Procedure

1. Carefully remove the green protective cap from the sensor.
2. Loosen and remove the blanking plug from the INGOLD port.
3. Carefully screw the pO_2 sensor into the INGOLD port.

   Ensure it is fitted in line with the port and sits neatly.

7.9.5 Connecting the Sensor Cable

To connect the cable to the pO_2 sensor, proceed as follows:

Procedure

1. Align the orange mark on the connector of the sensor cable with the orange mark on the sensor.

! ATTENTION

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

2. Plug the cable connector onto the sensor.
3. Turn the bajonet cap of the sensor cable clockwise und push gently towards the sensor.

   Ensure the cable is not twisted or buckled.

7.9.6 Polarising the pO_2 Sensor (METTLER)

Polarographic pO_2 sensors must be polarised at initial operation or after disconnection from the voltage source. Correct calibration is not possible otherwise. This means that the pO_2 sensor must be polarised before calibration.

For polarisation, the sensor cable must simply be connected to the pO_2 sensor and the equipment must be switched on at the main switch.

Duration of polarisation (= polarisation time) depends on how long the pO_2 sensor has been disconnected from the voltage source (= depolarisation time)

As a general rule: if depolarisation time > 30 minutes, the minimum polarisation time is 360 minutes.

More details about polarisation can be found in the separate documentation form the manufacturer METTLER TOLEDO.

7.9.7 Calibrating the pO2 Sensor

Generally it applies that calibrating the pO_2 sensor should be performed after sterilisation because sterilisation can change the gradient of the pO_2 sensor. A 1-point calibration to 100 % is generally sufficient for an exact measurement and should be carried out again before each fermentation/cultivation.

For details about calibration refer to the main chapter “Operation Touch Screen Software”, chapter “Calibrating the pO2 Sensor – Procedure”.

7.9.8 Preparing the Antifoam Sensor

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

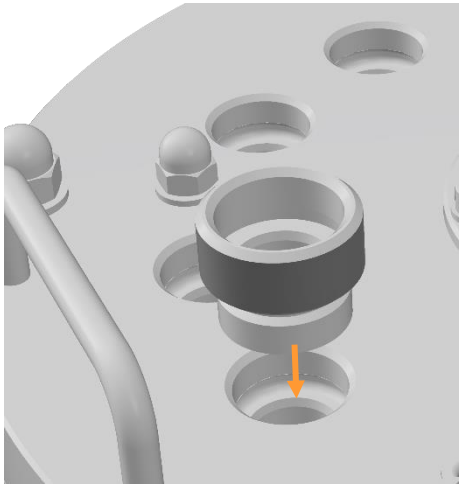
The antifoam sensor should be adjusted in its mounting depth before separate sterilisation in the autoclave. It should be mounted too low rather than too high. Pulling it up during fermentation/cultivation carries a much lower risk of contamination than pushing it down.

Preparation for autoclaving

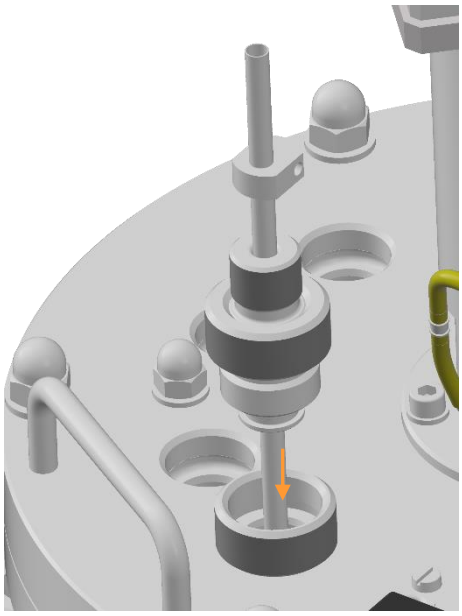
To prepare the antifoam sensor before autoclaving, proceed as follows:

Procedure

1. Loosen and remove the blanking plug from the 19 mm port in the vessel top plate using the hexagon socket spanner provided with the equipment.
2. Remove the protective caps from the antifoam sensor.
3. Remove the septum collar from the antifoam sensor.



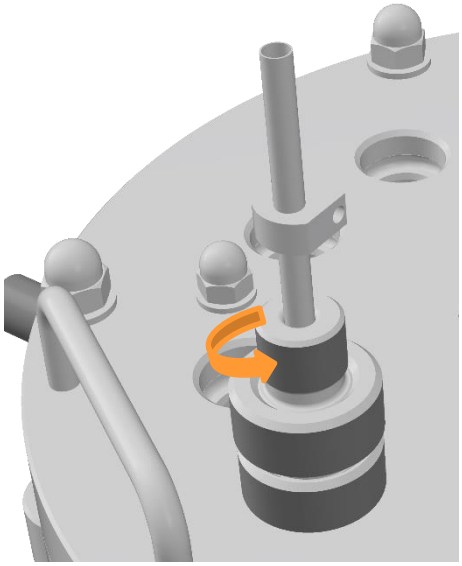
4. Screw the septum collar into the port.



5. Insert the antifoam sensor into the septum collar.

6. Tighten the antifoam sensor.

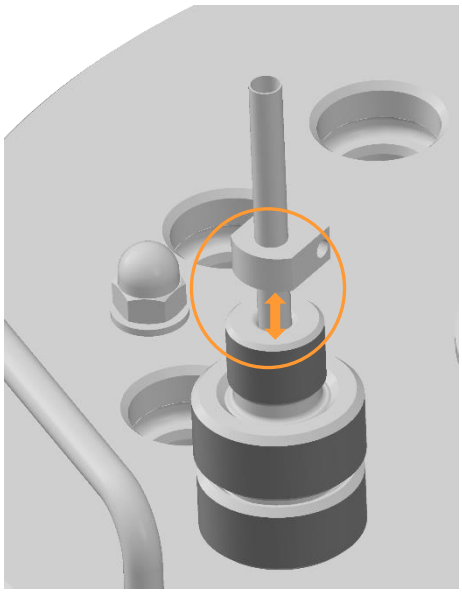
7. Loosen the clamping screw with the hand.



ATTENTION

Adjusting the mounting depth of the antifoam sensor with a tight hollow screw can damage the insulation of the sensor!

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



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

9. Tighten the hollow screw with the hand.
10. Loosen and remove the antifoam sensor from the septum collar.
11. Loosen and remove the septum collar and put aside for later use.
12. Connect the antifoam sensor with a reagent bottle filled with antifoam agent and sterilise in the autoclave.

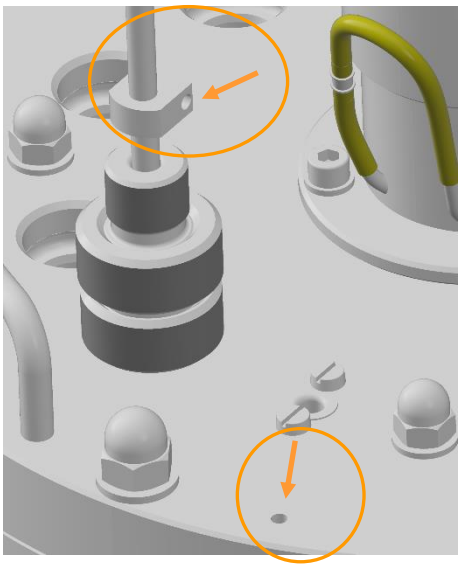
7.9.9 Mounting the Antifoam Sensor and Connecting the Cable

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

Refer to chapter “Preparing Reagent Bottles and Inoculation Needles” for details.

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

Procedure



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

7.10 Mounting the Safety Valve

The safety valve, which secures the vessel against excessive overpressure, must be mounted in operating state of the equipment (sterilisation and fermentation)!

WARNING

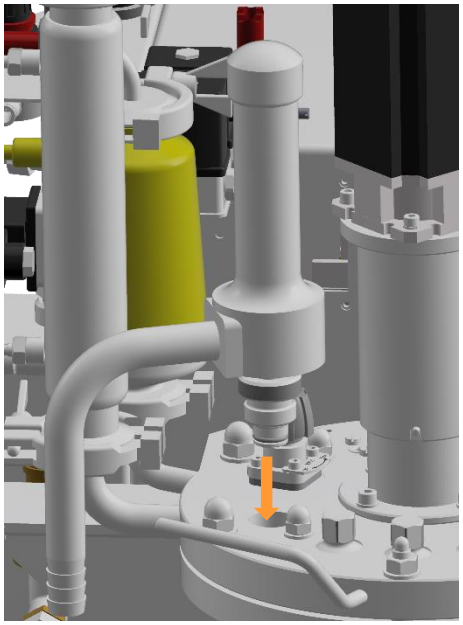
Possible overshoot of permitted pressure in the vessel cannot be relieved in a safe manner.

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

To mount it to the vessel, proceed as follows:

Preparations before Fermentation / Cultivation

Procedure



1. Insert, screw in and tighten the safety valve into the port.
2. Ensure that the safety valve is closed. Close as necessary (see the following description with figures).

To CLOSE
Turn the valve head clock-wise, the valve head is turned upside as far as it will go, the mark *CLOSED* is visible below the valve head.

To OPEN
Turn the valve head counter clockwise, the valve head is turned downside, the thread is visible and the mark *CLOSED* cannot be seen anymore.

Respect the following points:

Usually the safety valve stays closed.

To ensure that the air in the safety valve can be completely removed and replaced by steam, it is possible to manually open the safety valve during the heating phase briefly, up to 103 °C, and then close it again.

This method is not recommended because sterilisation must then be attended by the operator and manually opening/closing the hot safety valve contains a risk of injury to the user. The risk of an incomplete sterilisation due to the presence of a small amount of air is virtually impossible with the type of valve supplied.

7.11 Mounting the Manometer

The manometer **PI903** for pressure indication in the vessel must be screwed into a 19 mm port in the vessel top plate before sterilisation.

ATTENTION

The steel membrane of the manometer is very delicate and can be damaged when knocking it on solid objects or when rubbed!

Carefully mount the manometer by hand.

Proceed as follows:

Procedure

1. Ensure the manometer is equipped with an intact O-ring.
2. Loosen and remove the blanking plug from the port using the hexagon socket spanner provided.
3. Carefully insert the manometer into the port and screw it tight by hand.

   Ensure it is mounted in line with the port.

7.12 Calibrating the Pumps

If need be, pumps should be calibrated before beginning a fermentation/cultivation process. This provides an accurate value for the actual pumped volume of liquid delivered. The delivery rate is indicated in mL. Without calibration, only the number of revolutions is shown.

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

7.13 Preparing Reagent Bottles and Inoculation Needles

Reagent bottles, hoses and the inoculation needles are separately autoclaved. As a rule, bottles made of borosilicate glass are used. The seed bottle for subsequent aseptic filling close to the time of inoculation and the inoculation needle for inoculation are prepared the same way and autoclaved as described in the following.

Reagent bottles are supplied readily equipped with a filter for pressure equalisation and a long piece of silicone hose.

ATTENTION

Damaged hoses and/or clogged sterile filter may lead to undesired pressure conditions in the reagent bottles.

– Ensure each reagent bottle is equipped with an open pressure equalisation line with a clean and dry filter.

– Only use clean, intact hoses and ensure they are firmly attached.

The following section describes in detail how to prepare a reagent bottle for separate autoclaving and then how to connect it to the pump and the vessel for fermentation/cultivation.

7.13.1 Preparing and Autoclaving

Procedure

Proceed as follows:

1. Remove the lid of the reagent bottle.
2. Connect a piece of silicone hose to one of the two pipes inside the cap of the reagent bottle.

   The hose should not touch the bottom of the reagent bottle to avoid that the hose can adhere to the bottom and therefore liquid cannot be delivered anymore.

Preparations before Fermentation / Cultivation

INFORMATION

Alternatively, the hose end can be angularly cut. In this case the hose end can touch the bottom of the reagent bottle then.

3. Secure the hose with a cable tie.

4. Close the reagent bottle with the lid again.

Ensure the sealing between reagent bottle neck and lid sits and seals correctly.

Ensure the sealing between reagent bottle neck and lid sits and seals correctly.

5. Connect a long piece of silicone hose to the same pipe but on the outside of the reagent bottle lid.

The hose must be long enough to reach from the reagent bottle to the pump without tension or kinks.

6. Connect a short piece of silicone hose to the second pipe on the outside of the reagent bottle lid.

7. Connect the filter to the short piece of silicone hose.

8. Secure the hoses with cable ties.

The picture on the left shows the equipped reagent bottle.

9. Thoroughly rinse the hose with distilled water before autoclaving.
10. Clearly label the reagent bottle according to its content.
11. Depending on the application: Fill the reagent bottle with reagent up to the required amount and refit the lid.

    Or where required, fill the reagent bottles under sterile conditions after autoclaving.

ATTENTION

Usage of the highly corrosive hydrochloric acid HCl as reagent leads to damage to components made of stainless steel such as e.g. component parts or the top plate.

Use only non-corrosive acids, e.g. phosphoric acid, instead.

INFORMATION

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

12. Use hose connectors to connect a piece of pump hose to the silicone hose and then another piece of silicone hose to the pump hose end.

    The entire hose line must be long enough to reach from the reagent bottle via the pumps to the inoculation needle in the vessel top plate port without tension or kinks.
13. Connect the inoculation needle to the hose end.
14. Secure the hose end with a cable tie.
15. Lightly cap the filter on the reagent bottle and the inoculation needle with a little aluminium foil or fit the needle into the sterile housing.
16. Clamp off the reagent hose line with a hose clamp.
17. Autoclave the whole assembly together for e.g. 30 to 60 minutes at 121 °C.

7.13.2 Connecting to the Vessel and the Pump

After autoclaving and enough time to cool down, the hoses on the reagent bottles must be connected to the pumps.

The inoculation needles and the antifoam sensor are screwed into the ports in the vessel top plate AFTER in situ sterilisation, which

were equipped with septum collars and septa BEFORE the in situ vessel sterilisation.

Connecting the reagent bottle to the pump

Proceed as follows:

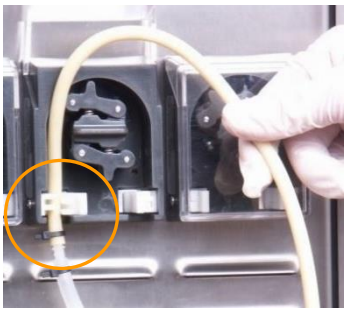
Procedure

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

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

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

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



The pump hose is fixated by the left clamp now.

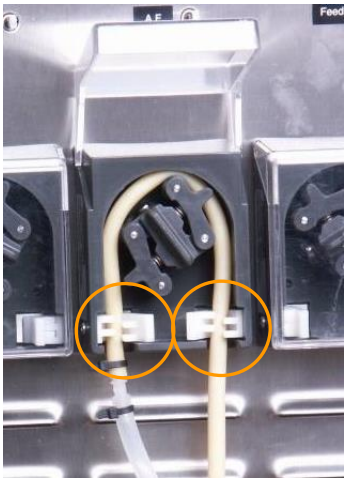
Preparations before Fermentation / Cultivation

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

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

> **⚠ CAUTION**
>
> Operating the pump electrically (only possible once the equipment is switched on) and inserting the pump hose at the same time can lead to bruising the fingers and damage to the pump hose!
>
> Always turn the pump head with the hand when inserting the pump hose.

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



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

10. Fold down the pump cover.

Preparations before Fermentation / Cultivation

Mounting the inoculation needles and the antifoam sensor

Proceed as follows:

Procedure

1. Loosen and remove the blanking plug out of the septum collar in the port using the hexagon socket spanner.
2. Remove the protective sheath, bag or aluminium foil from the inoculation needle/antifoam sensor.

INFORMATION

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

3. Instantly pierce the needle/antifoam sensor through the septum.
4. Screw the inoculation needle/antifoam sensor into the septum collar.

Filling the reagent and pump hoses

Proceed as follows:

Procedure

1. On the switched on equipment, use the rocker switch above the pump to fill the hose until it is filled up to the port in the vessel top plate.

If the reagent bottles are correctly connected:

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

7.14 Preparing Push Valves

A reagent bottle used along with a push valve must be separately autoclaved first.

After autoclaving and cooling down, the reagent bottle is connected to the pump and the push valve is mounted in closed(!) position to the vessel to plate port.

In situ sterilisation of the vessel will also sterilise the only part of the push valve to be exposed since sterilisation in the autoclave.

INFORMATION

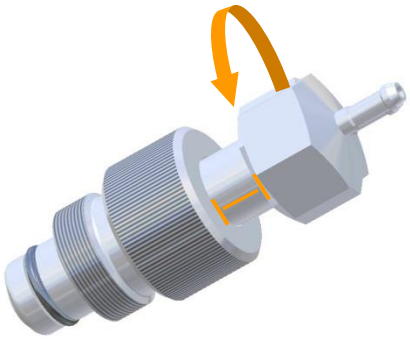
The same safety precautions as stated in chapter “Preparing Reagent Bottles and Inoculation Needles” apply and must be observed!

7.14.1 Autoclaving

To prepare a push valve along with a reagent bottle for the autoclave, proceed as follows:

Procedure

1. Prepare the reagent bottle as described in chapter “Preparing Reagent Bottles and Inoculation Needles”.
2. Connect the push valve to the hose end of the reagent bottle.



3. Ensure the push valve is in closed position, close as necessary.
4. Secure the hose end with a cable tie.
5. Lightly cap the filter on the reagent bottle and the push valve with a little aluminium foil.
6. Clamp off the reagent hose line with a hose clamp.
7. Autoclave the whole assembly together for e.g. 30 to 60 minutes at 121 °C.

7.14.2 In Situ Sterilisation

After autoclaving and cooling down, the following steps must be carried out:

- The push valve must be mounted (still closed!) into a 19 mm vessel top plate port.
- The reagent bottle must be connected to the pump.

  This is described in detail in chapter “Preparing Reagent Bottles and Inoculation Needles.

INFORMATION

The same safety precautions as stated in chapter “Preparing Reagent Bottles and Inoculation Needles” apply here, too and must be observed!

7.14.3 Fermentation/Cultivation

After the in situ vessel sterilisation, the push valve must be opened and the reagent and pump hose must be filled. Refer to chapter “Preparing Reagent Bottles and Inoculation Needles” for details.

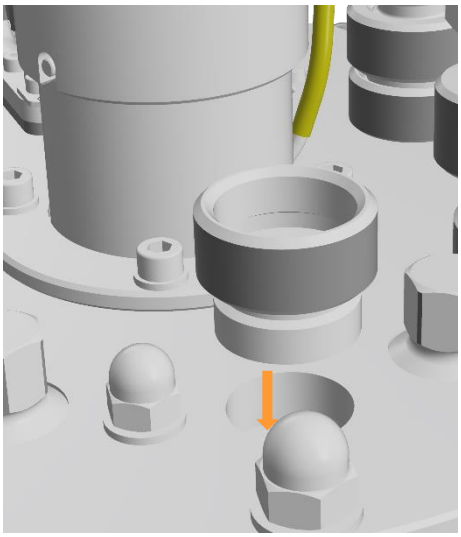
7.15 Equipping the Ports with Septa (Piercing Membranes) and Collars

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

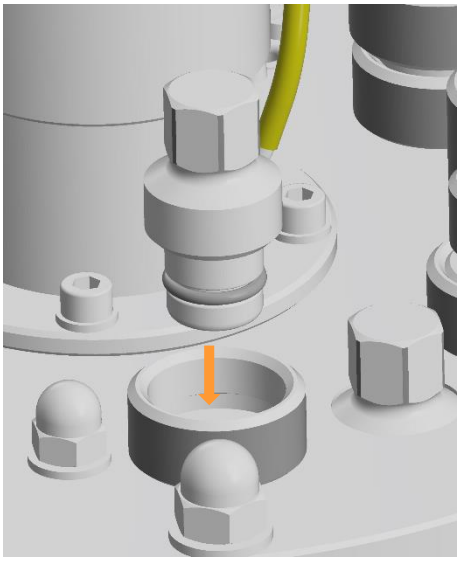
Proceed as follows:

Procedure

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



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



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

Tighten it with the hexagon socket spanner hand-tight.

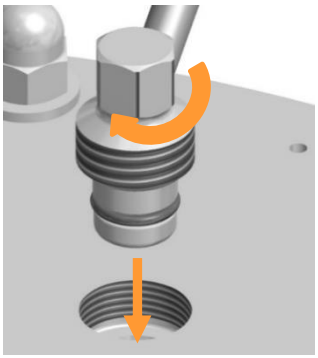
7.16 Closing Unused Ports

All unused ports in the vessel top plate and on the vessel in general must be closed with blanking plugs, i.e. blanking covers before sterilisation.

Blanking plug vessel top plate

Procedure

1. Ensure the blanking plug is equipped with an intact O-ring.

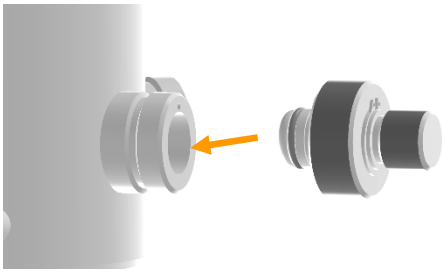


2. Screw the blanking plug into the port by hand and tighten it hand tight using the hexagon socket spanner provided with the equipment.

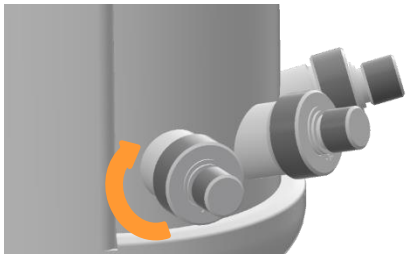
   Ensure the blanking plug is fitted in line with the port.

Blanking plugs INGOLD standard ports

Procedure



1. Insert the blanking plug equipped with an intact O-ring into the port.

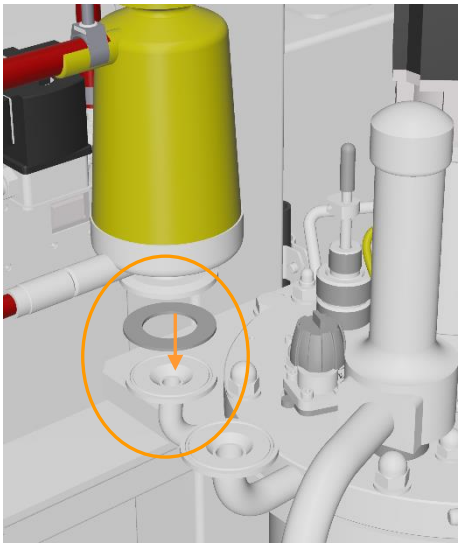


2. Screw the blanking plug hand tight.

7.17 Mounting the Exit Gas Cooler and the Filters

For mounting the inlet air filter and the exit gas cooler with its filter, proceed as follows:

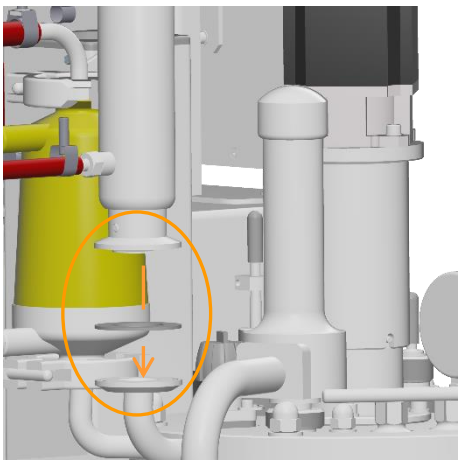
Procedure



1. Hold the flange of the inlet air filter onto the connection flange on the vessel top plate.

   Ensure that the flat gasket is placed between both flanges.

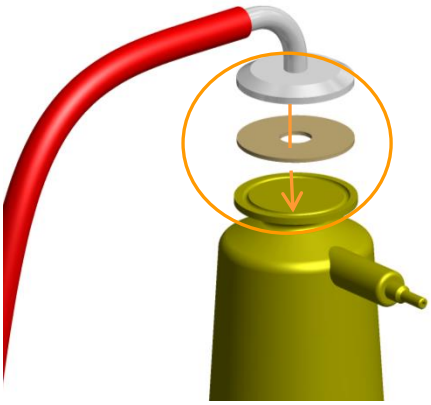
2. Place the clamp around both flanges, shut it and tighten the wing nut.
3. Remove the exit gas cooler from its holding device.



4. Hold the flange of the exit gas cooler onto the connection flange on the vessel top plate.

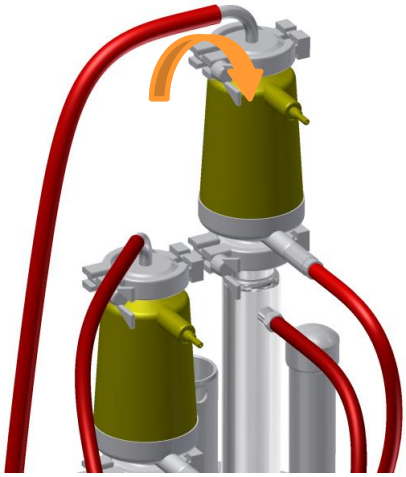
   Ensure that the flat gasket is placed between both flanges.

5. Place the clamp around both flanges, shut it and tighten the wing nut.



6. Hold the flange of the exit gas hose onto the connection flange of the exit gas filter.

   Ensure that the flat gasket is placed between both flanges.



7. Place the clamp around both flanges, shut it and tighten the wing nut.

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

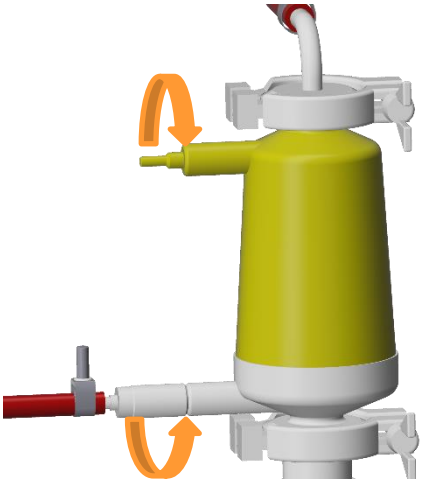
A blocked inlet air or exit gas line or clogged filters may result in poor venting/gassing of the culture or even completely interrupting it. This leads to overpressure in the vessel, which may be released in a non-sterile manner via leaky vessel connections and gaskets.

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

Therefore, check and ensure the following points:

- The air supply is correctly installed and turned on.

  The air supply must be turned on throughout the vessel sterilisation process so that no vacuum occurs during the cooling phase in the vessel sterilisation process.



- The filters for inlet air and exit gas are clean and dry. They are fitted correctly.
- Unused twist valves on both filters are closed.

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

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

7.19 In situ Sterilisation – General Information

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

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

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

Two commonly used practices are briefly described below.

Sterilising the vessel with culture medium

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

Sterilising the vessel without culture medium

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

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

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

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

INFORMATION

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

8 Fermentation / Cultivation

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

WARNING

The vessel may be under pressure during operation!

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

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

CAUTION

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

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

8.1 Preparing the Medium

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

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

INFORMATION

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

8.2 Sampling

Samples are taken from the vessel to gain material for offline analysis. The frequency and exact method of sampling can vary due to the different analyses carried out by the operator.

When the sample valve has cooled down after sterilisation, a sample can be taken.

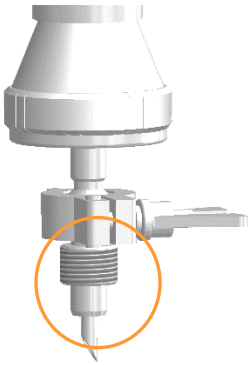
⚠ CAUTION

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

Proceed as follows:

Procedure

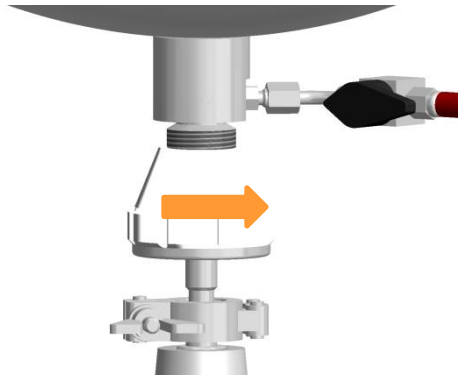
1. Unscrew the steam trap from the needle by turning the steam trap to the left.



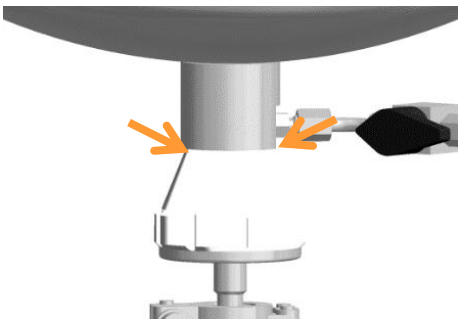
The needle is visible now.

2. Pierce the needle through the septum on the sample bottle.

Fermentation / Cultivation

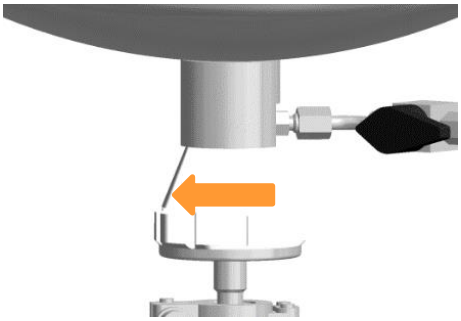


3. Open the harvest/sample valve by turning it to the right.

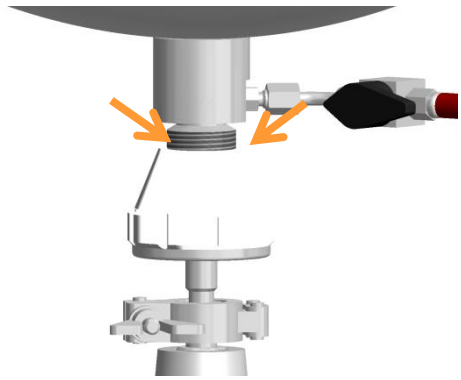


The valve is open; the thread is not visible anymore.

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



5. Close the harvest/sample valve by turning it to the left.



The sample valve is closed, the thread is visible.

6. Pull the needle out of the septum on the sample bottle.

7. Screw the steam trap on again.

The sample valve should be sterilised again now to allow enough time to cool down before taking the next sample.

8.3 Inoculation

Preparations before inoculation

Ensure the following before inoculation:

- Medium is filled in the vessel.
- Heat labile supplements are separately sterilised and added.
- Reagent bottles are connected to the vessel via the pumps and sufficiently filled with corrective reagent / feed solution for the duration of the cultivation.
- The pumps are primed.
- Correct operating temperature has been reached.
- Correct stirrer speed is set.
- Sensors are calibrated and polarised where appropriate, control is set correctly (maybe not active yet).
- Clamps are removed.

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

- Via inoculation needle and septum

  The inoculum drips into the culture. This method contains a high risk of contamination.
- Via push valve

  The inoculum drips into the culture. This method requires a sterile hose connection.

8.3.1 Inoculation with Inoculation Needle

Proceed as follows for inoculation:

Procedure

1. Fill the inoculum under sterile conditions into the prepared container.
2. Unscrew the blanking plug from the septum collar.

3. If wished, place a few drops of Ethanol (70 %) on the septum before piercing.

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

8.3.2 Inoculation with Push Valve

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

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

1) suitable for establishing a sterile hose connection

Proceed as follows for inoculation:

Procedure

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

8.4 Harvest

The culture can be harvested at the end of the fermentation/cultivation process. To prevent possible sedimentation from the culture, the stirrer can be switched on during harvest. If necessary, activate gassing for sensible cultures. However, all other parameters should be switched off, provided there are no other specifications for the user.

The simplest and safest preparations for harvest are made before the fermentation/cultivation is stopped, e.g. prepare an appropriate container or connect an appropriate hose to the harvest valve.

⚠ CAUTION

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

Basically, there are two different methods:

- Emptying using gravity (bioreactor stopped)
- Transfer of the culture medium using pressure (bioreactor is running)

8.5 Emptying the Vessel

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

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

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

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

8.6 Sterilisation after Fermentation / Cultivation

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

cultivation processes with safety-critical, pathogenic or genetically modified microorganisms.

Proceed as follows:

Procedure

1. Use the rocker switch of each peristaltic pump for completely emptying the reagent hoses.
2. Clamp off the reagent hoses and remove them from the pumps.
3. Remove inoculation needles under sterile conditions from the vessel top plate and replace the blanking plugs before vessel in situ sterilisation.

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

INFORMATION

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

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

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

INFORMATION

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

9 Operation Touch Screen Software

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

ATTENTION

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

9.1 Screen, Menu Navigation and Control Elements

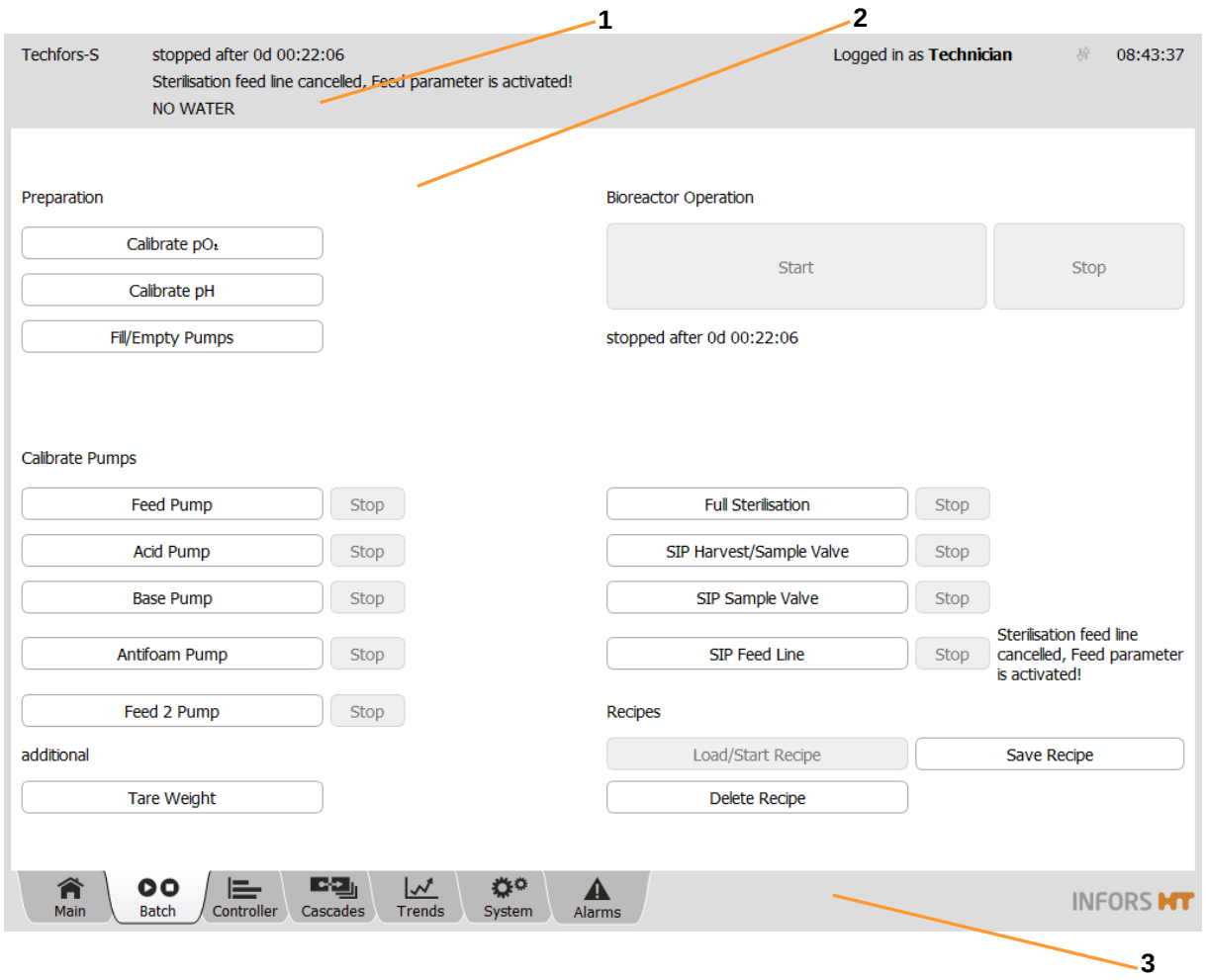
Most of the figures in this manual showing the various menus, dialogue boxes and tab pages of the touchscreen software reflect the view of a user with the user authorisation level of *Technician*.

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

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

9.1.1 Screen Areas

The screen is divided into the three sections:



1 Header

2 Main are

3 Footer

Header

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

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

Main area

shows main menus and submenus, e.g. main menu *Batch*, see figure above. Inputs are made exclusively in the main area. I.e. menus and dialogue boxes are called up by pressing buttons or input fields.

Footer

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

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

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

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

9.1.2 Control Elements

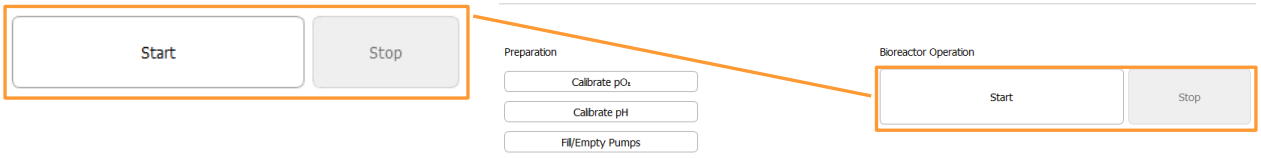
The following control elements are used in the touchscreen software:

Buttons

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

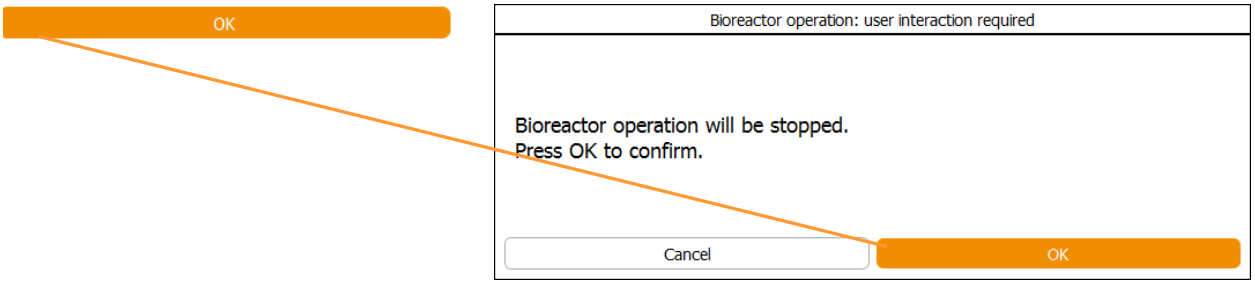
Enabled buttons are white in colour, disabled buttons are grey in colour.

Example: **Start**/**Stop** of the bioreactor (fermentation/cultivation process).



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

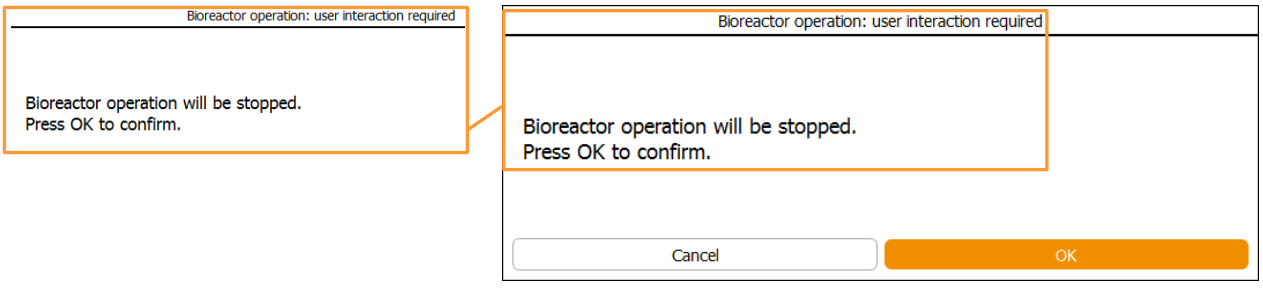
Example: Confirmation of an entry and/or starting/ending a process with **OK**.



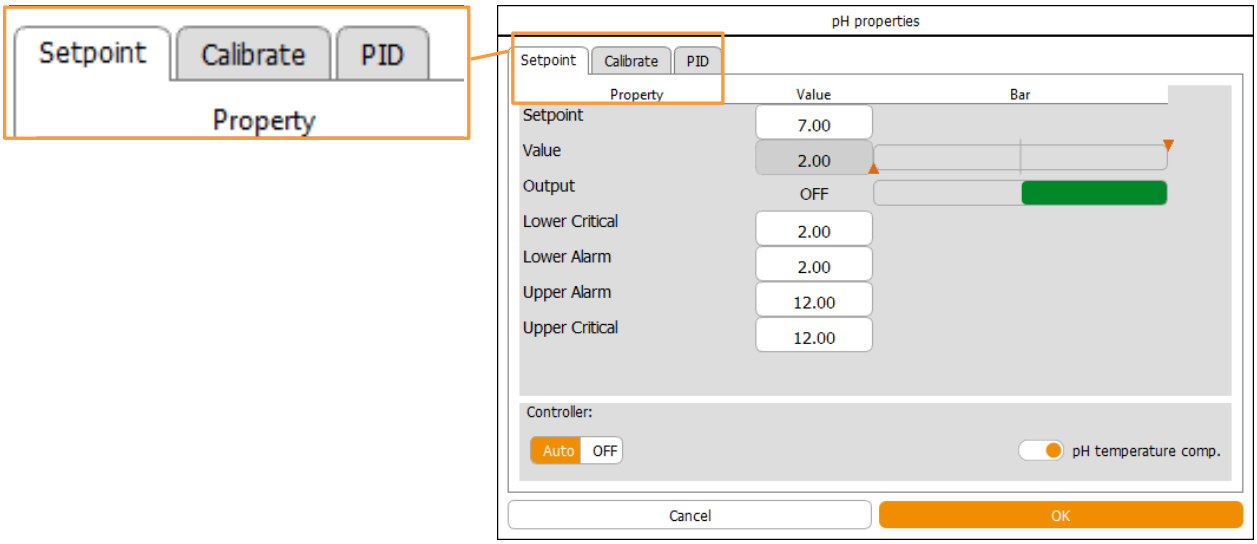
Dialogue boxes and tab pages

A dialogue box may contain further buttons, input fields or view boxes and tabs. A dialogue box may also contain instructions, notes, warnings or general information

Example: *Bioreactor operation: user interaction required* dialogue box with information and instruction.



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



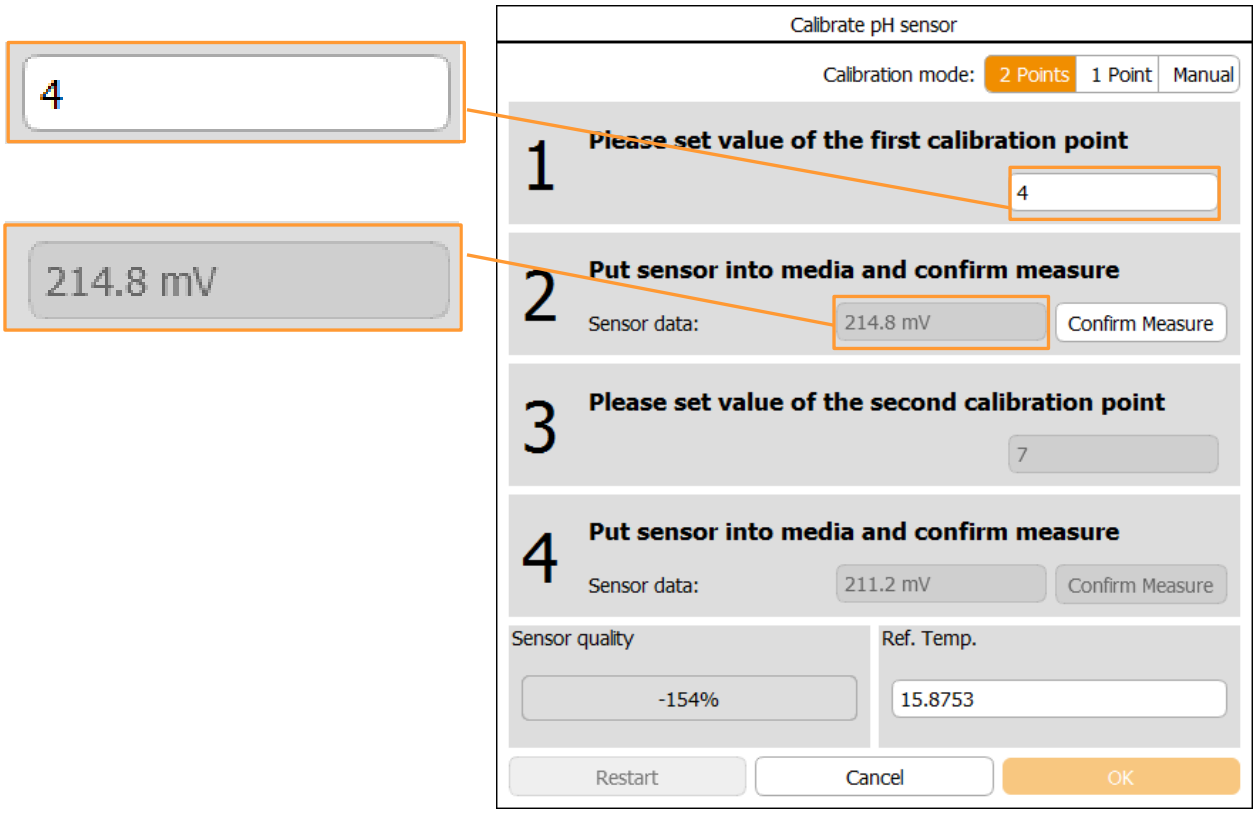
Pressing a tab leads to access of the respective option for the selected tab page. The tab for a selected tab page is displayed with a white background.

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

Input fields and view boxes

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

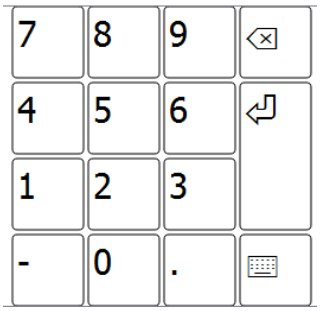
Example: *Calibrate pH sensor* dialogue box with input fields for calibration points and view boxes *Sensor data*.

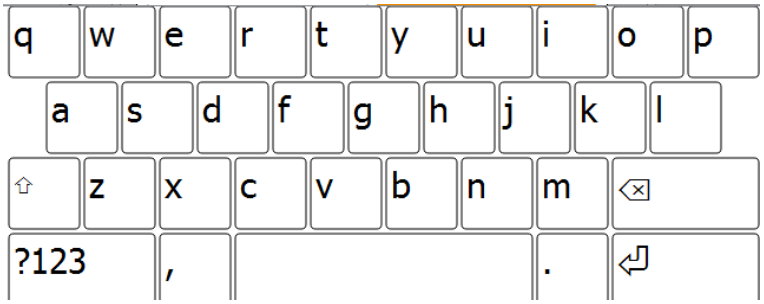


Numeric keypad and alphanumeric keyboard

Numerical values are entered using a numeric keypad (figure on the left). Alphanumerical values are entered using an alphanumeric keyboard (figure on the right).

After pressing an input field, the appropriate pad/board appears.



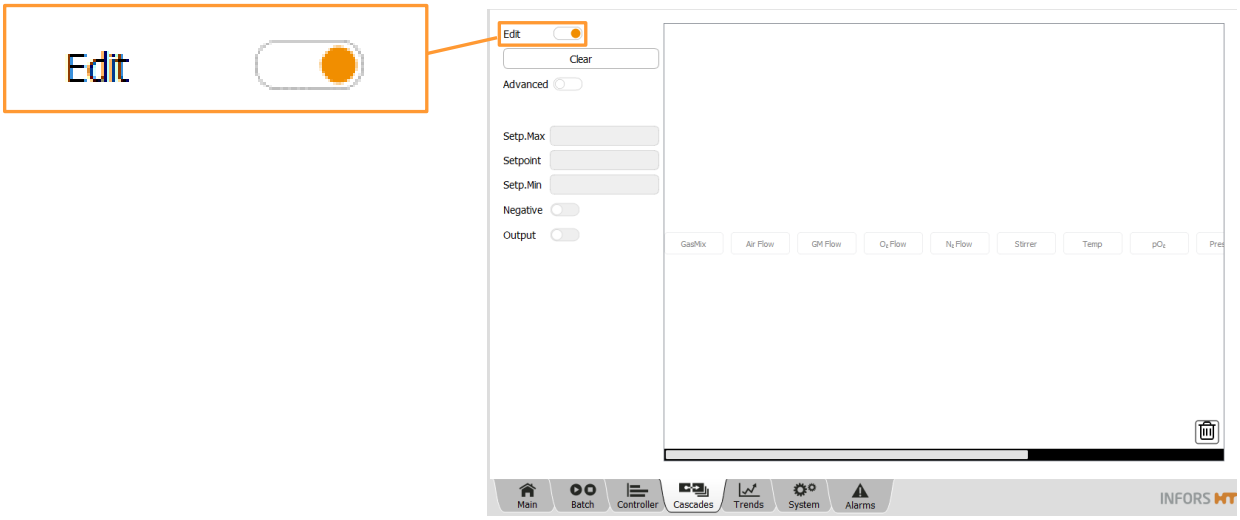


ON / OFF switch

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

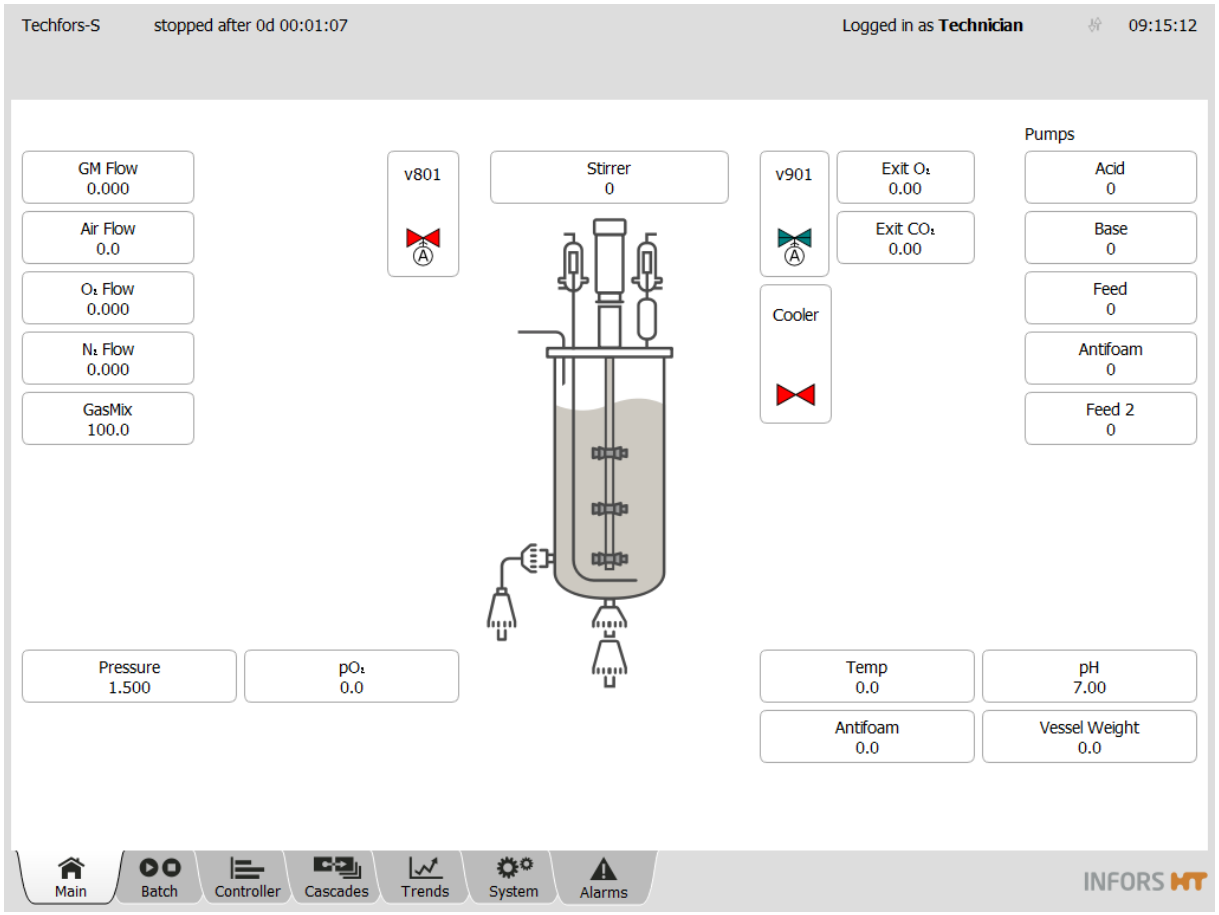
- **ON**: the switch is in orange colour
- **OFF**: the switch is in white colour

Example: **ON/OFF** switch to enable/disable *Edit* function in main menu *Cascades*

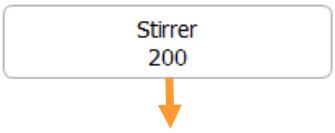


9.2 Main Menus

9.2.1 Main – Overview

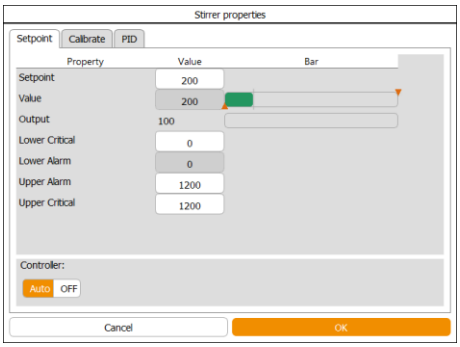


The main menu *Main* charts the bioreactor and some of its valves and offers an overview of its process parameters and pumps according to its configuration.

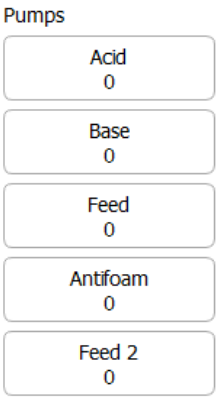


Parameters

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



Pumps



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

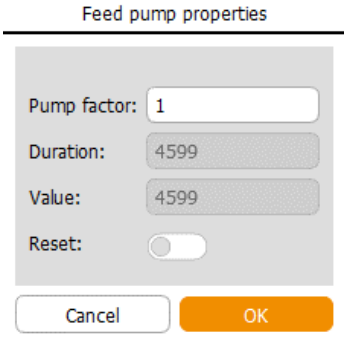
- *Acid*
- *Base*
- *Antifoam*
- *Feed*

The *Feed 2* pump is optional.

The delivered volume (in mL) of a calibrated pump is continuously shown while the bioreactor is running. This numerical value is displayed on the appropriate pump button, as the example for the Feed pump shows on the left.

INFORMATION

For pumps which are not calibrated, the number of rotations (standard pumps), respectively its total running duration (opt. Feed 2 pump) is displayed instead.

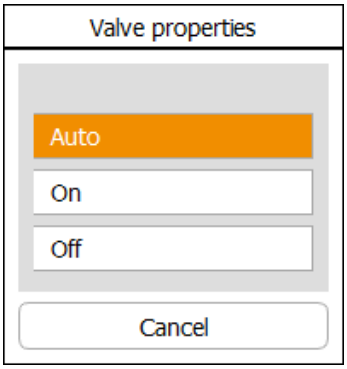


When pressing one of the pump buttons, a dialogue box appears where the number of rotations of the selected pump can be reset to zero.
The pump factor calculated during pump calibration is also visible and can be changed manually here.

Operation Touch Screen Software

Valves

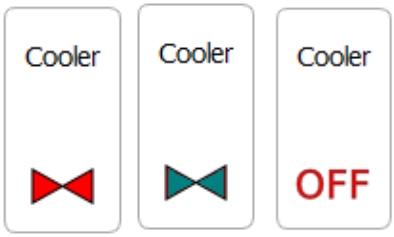
- The **red** colour signifies a closed valve.
- The **green** colour signifies an open valve.
- The letter **A** signifies, that the valve is switched to automatic mode.
- The letter **M** signifies that the valve is switched to manual mode i.e. it is “forced”.



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

ATTENTION

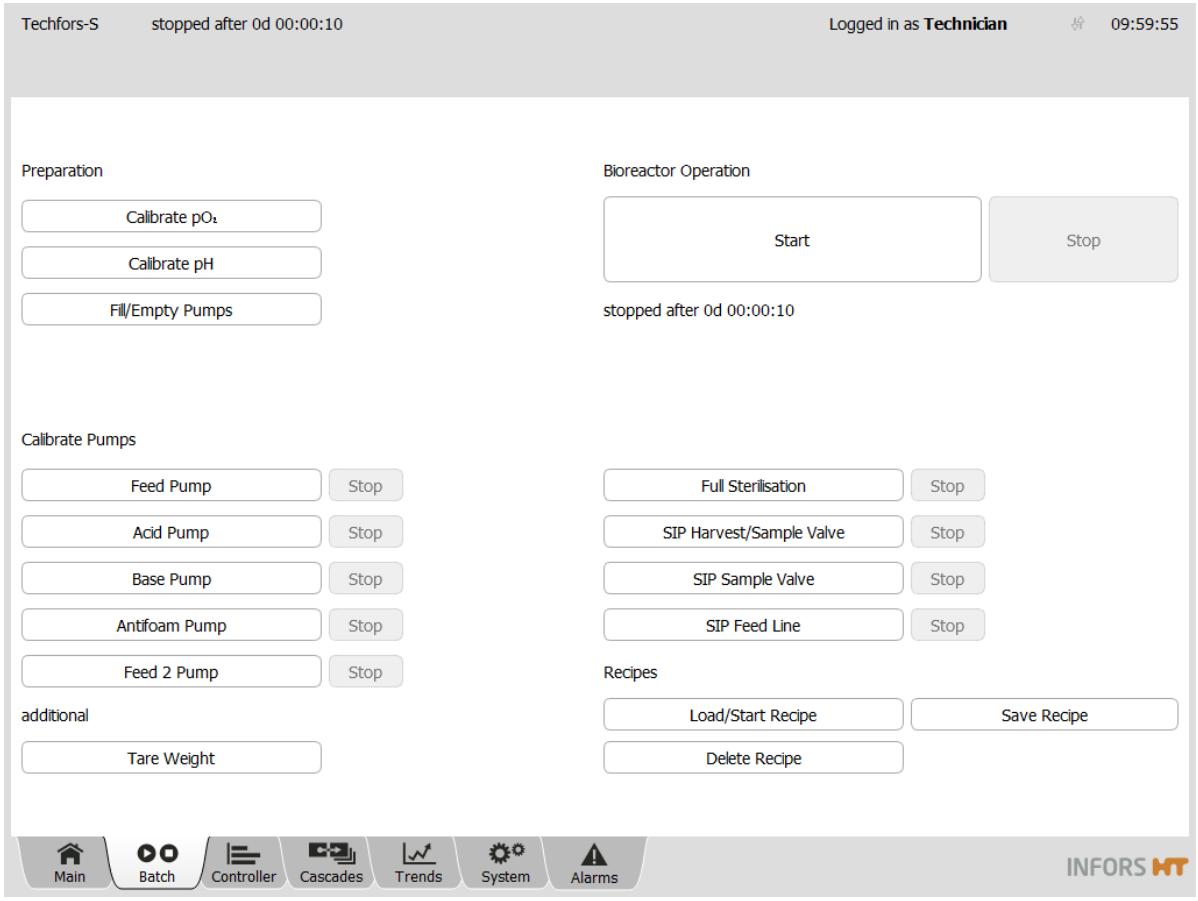
All valves are set to automatic mode (*Auto*) ex-factory. These settings may not be changed!



Exit gas cooler

The **Cooler** button (exit gas cooler) with the valve symbol signifies the valve (118) for the water supply of the exit gas cooler.
The valve automatically opens during fermentation and in the cooling phase during full sterilisation when switched to automatic mode.
If this valve is manually switched off, water supply is not possible anymore, the valve remains closed! This is indicated with the word *OFF* in red letters instead of the valve symbol on the **Cooler** button.

9.2.2 Batch – Start Menu



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

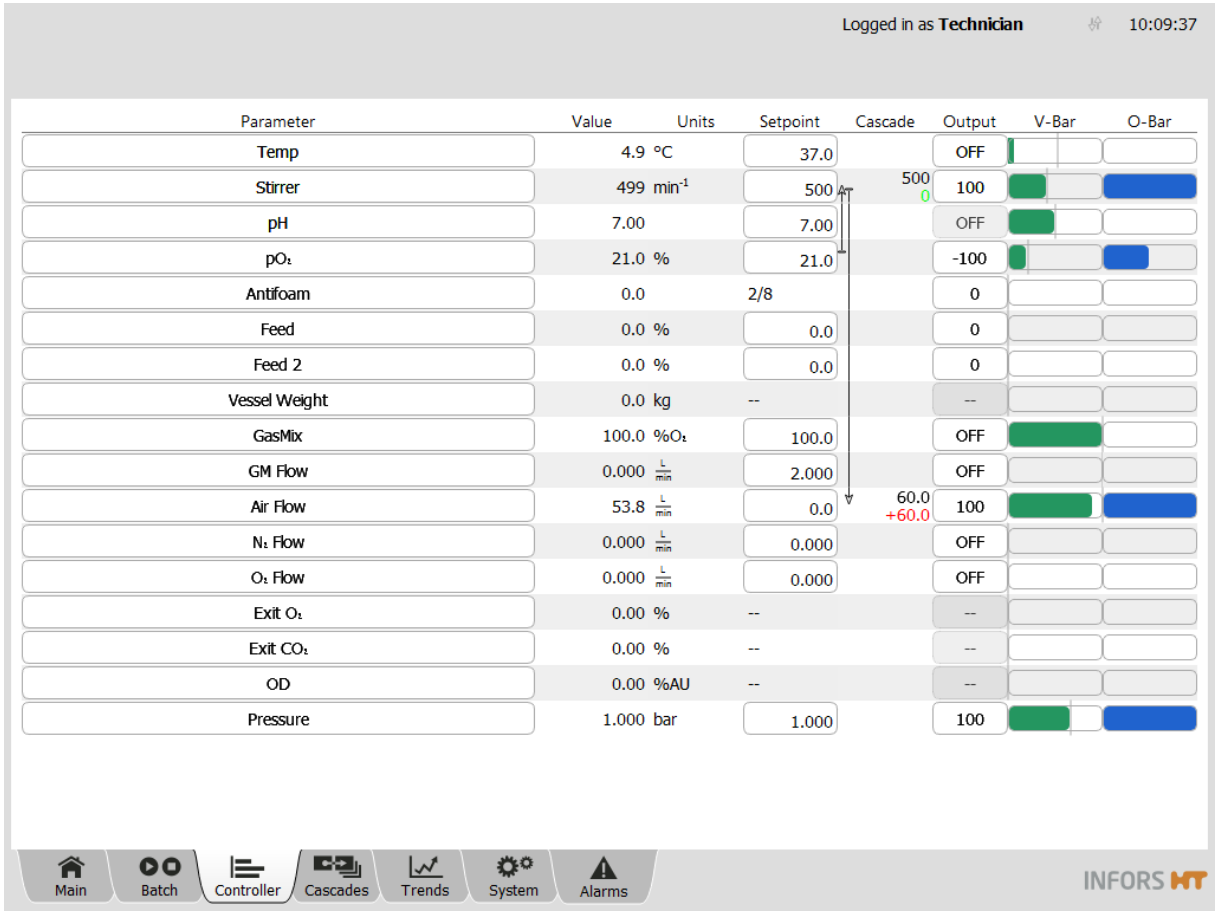
pH and pO_2 sensors and pumps are calibrated here, too. If required, pump hoses can automatically be filled and emptied.

Recipes are stored, loaded or deleted in this menu. If the optional vessel load cell is installed, the weight display is tared here.

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

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

9.2.3 Controller – Value Display



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

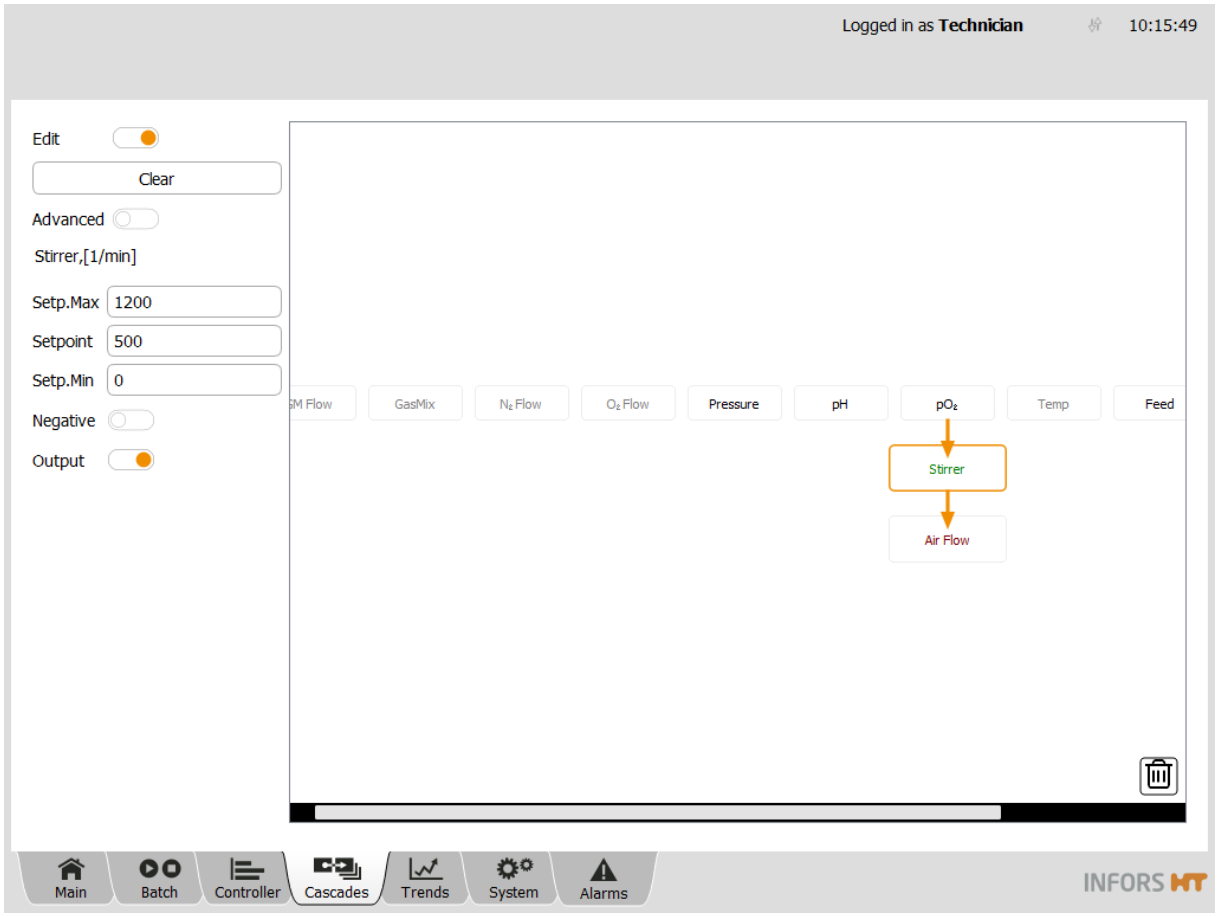
- *Parameter*: lists the available parameters. Pressing the desired parameter button leads to the parameter options, see chapter “Calling up Parameter Options”.
- *Value*: displays the actual parameter values
- *Units*: displays the units of the parameters
- *Setpoint*: to enter/change setpoint values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

INFORMATION

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

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

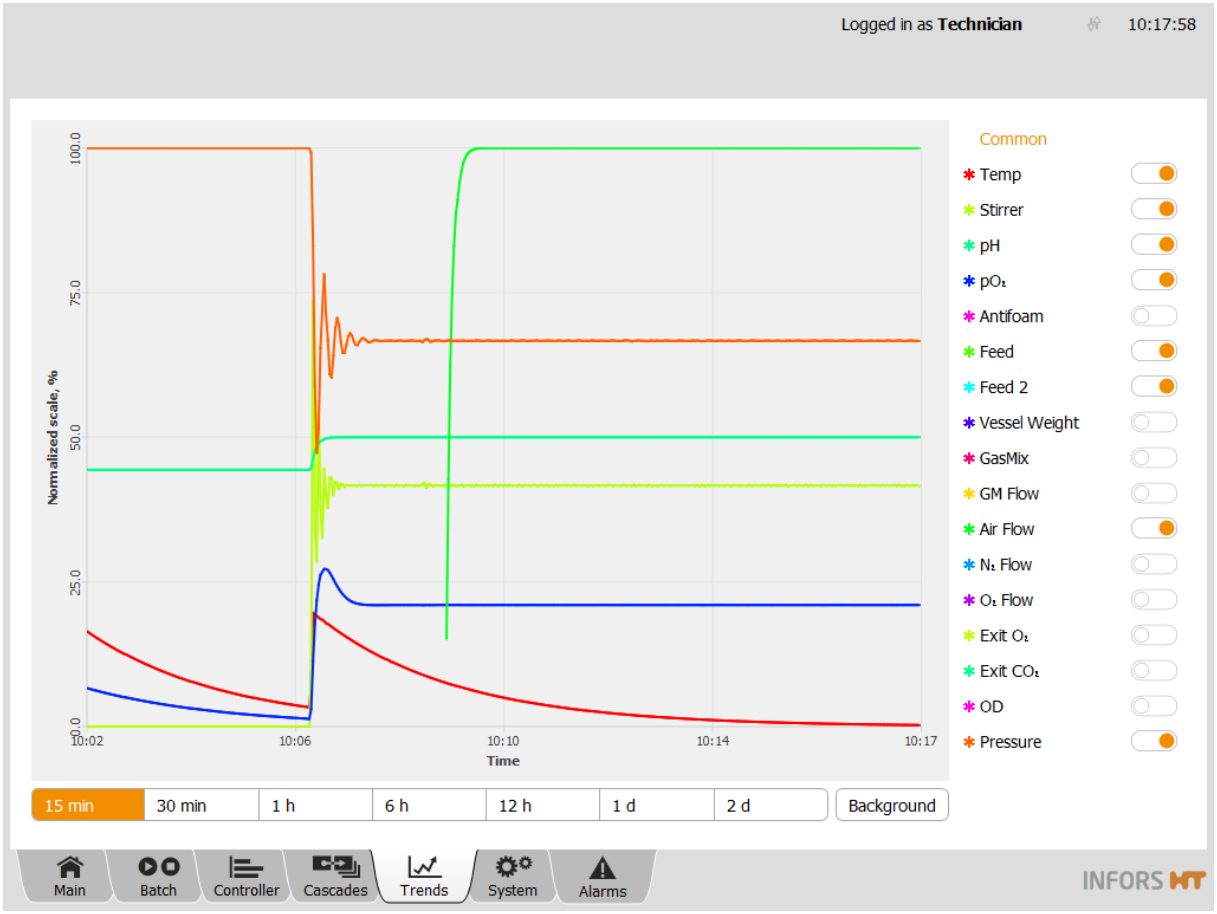
9.2.4 Cascade



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

The cascade settings are made in the left-hand section of the screen and the main section presents these schematically. The individual process parameters can be added to a cascade by dragging & dropping them.

9.2.5 Trends – Trend Lines



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

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

The parameters of the bioreactor are listed on the right-hand side of the screen. The **ON/OFF** switch next to each parameter allows to activate/deactivate the display of its trend line in the main area of the screen.

All trend lines are normalised to the value range of the respective parameter. The maximum value (= 100 % of the normalised scale) is located on the top of the diagram, the minimum value (= 0 % of the normalised scale) on the bottom. When a parameter is selected from the list, the labels on the Y axis will switch to the value range of the selected parameter. When *Common* is selected, the labels on the Y axis are reverted to the normalised scale.

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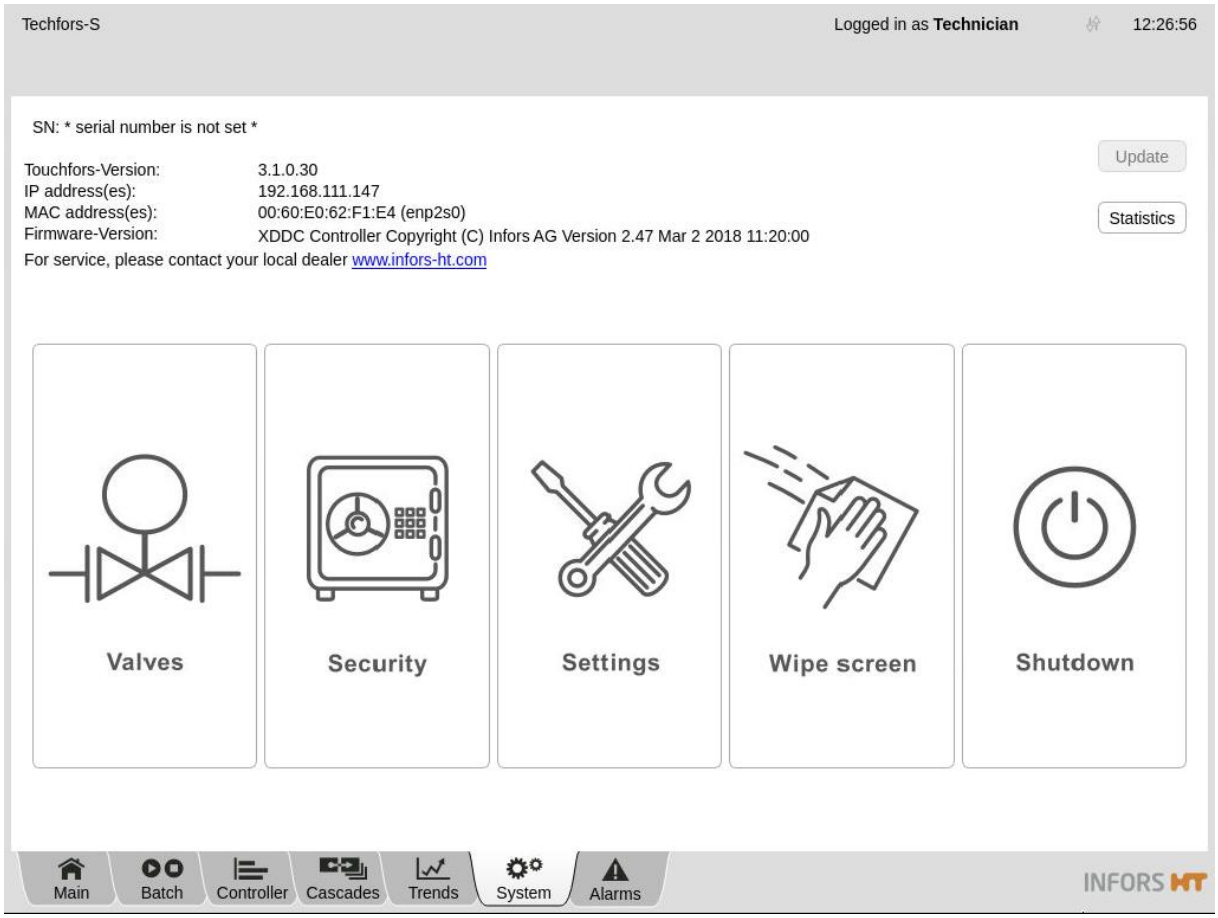
The sideways spread of the diagram can be selected via the buttons below the diagram:

- **15 min** and **30 min**: 15 and 30 minutes
- **1 h**, **6 h** and **12 h**: 1, 6 and 12 hour(s)
- **1 d** and **2 d**: 1 and 2 day(s)

The **Background** button allows to change the background colour of the diagram display (white, grey and black).

9.2.6 System – System Settings



The main menu *System* shows the following:

- Serial number
- Software version
- IP address of the system(s)
- MAC (hardware) address
- Firmware version
- Manufacturer's internet address (Domain)

Two buttons are situated in the upper right side of the screen:

- **Update**: for software updates. Refer to chapter "Update – Installing Software Updates" for details about this function.
- **Statistics**: enables viewing some statistics of the software communication with the control board, i.e. the hardware of the bioreactor. The function is only used for fault diagnosis for the technical support from the manufacturer.

The menu has 5 buttons which access the submenus with various functions:

- **VALVES**: displays the status of the digital outputs.
- **SECURITY**: for system log-in and log-off, passwords and user management
- **SETTINGS**: for the system and basic settings of the bioreactor
- **WIPE SCREEN**: to lock the screen for 20 seconds, e.g. for screen cleaning
- **SHUTDOWN**: to shut down and switch off the system

A detailed description of the submenus can be found in the appropriately titled chapters.

9.2.6.1 Statistics – Software Communication with Bioreactor Hardware

The *Statistic* function (**Statistics** button) in main menu *System* enables viewing some statistics of the software communication with the control board, i.e. the hardware of the bioreactor. This function is only used for fault diagnosis for the technical support from the manufacturer.

9.2.6.2 Update – Installing a Software Update

The Update function in main menu *System* enables to install software updates from a USB stick onto the system.

INFORMATION

It is recommended to create a backup copy on an USB stick of the existing system configuration using the Backup function in submenu Settings before installing the software update.

ATTENTION

The existing configuration is preserved in the best possible way when performing a software update. In individual cases, e.g. for customized equipment, it may be necessary to make specific adjustments after the update. Therefore, always consult the Infors service or an authorised service partner before installing an update.

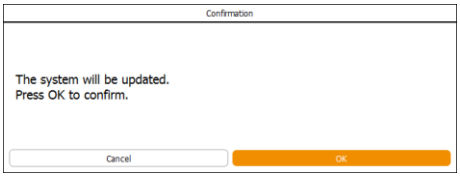
Proceed as follows:

Procedure

1. Use the special cable provided with the equipment and connect it to the appropriate connector (see figure on the left) on the rear side of the operating panel.

2. Connect the USB stick.
3. Log on to the system on user level *Administrator*.
4. Call up main menu *System*.

5. Press **Update**.



The *Confirmation* dialogue box appears with:

- Information: *The system will be updated*.
- Instruction: *Press OK to confirm*.
- **OK**: to execute the update
- **Cancel**: to cancel and close the dialogue box without changes.

6. Press **OK**.

   Progress is continuously displayed on the screen.

   Once the update is completed, the system is restarted with its standard settings and the message *Configuration files from previous version detected!* in main menu *Alarms* indicates that configuration data of a previous version were detected.

Restoring individual settings

The Restore function is used now, to restore the previous individual bioreactor setttings.

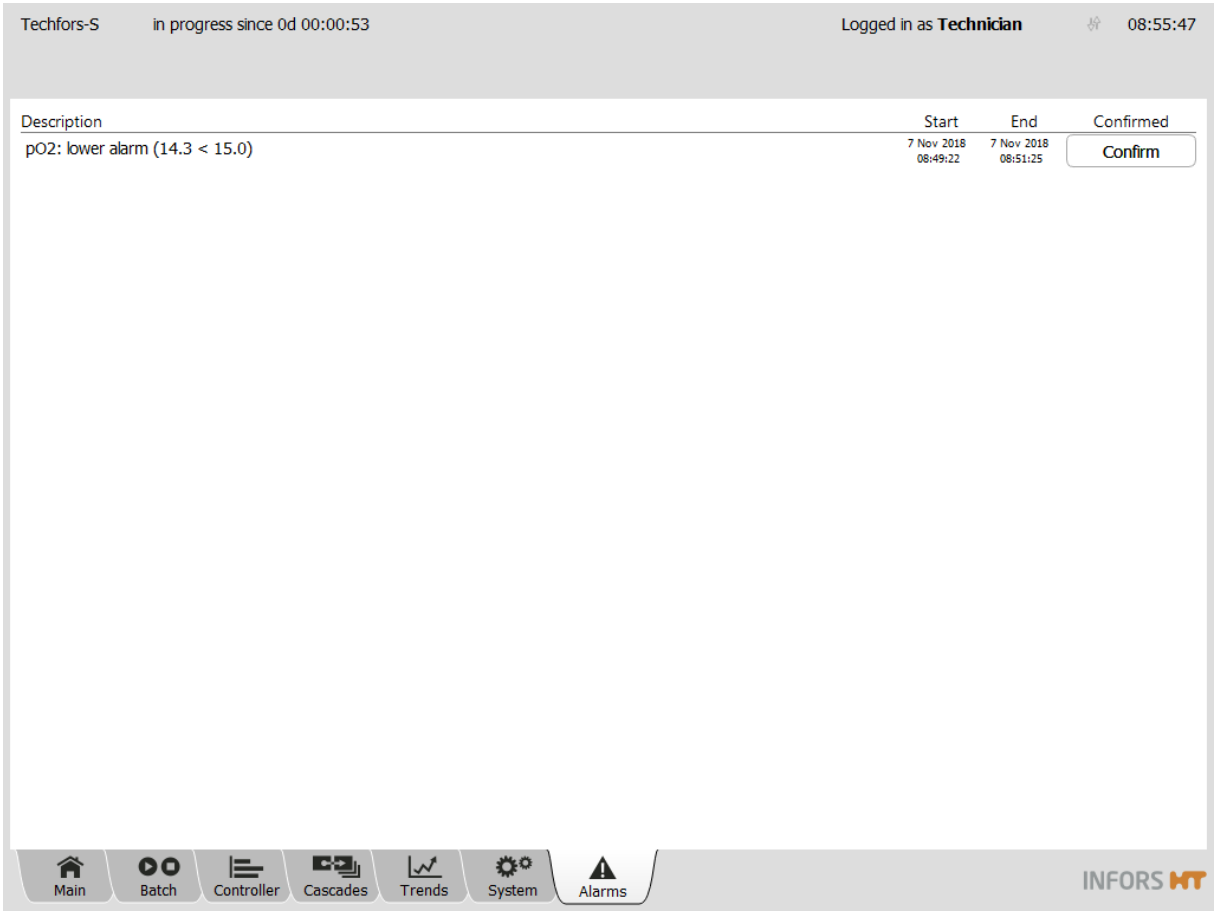
Proceed as follows:

Procedure

1. If applicable, connect other USB stick with the previously saved data via Backup function.
2. In main menu System, call up submenu *Setting*s and press **Restore**.

3. Select the file "*ModifiedConfiguration_number_of_previous version".* Alternatively, select desired backup data from USB stick.
4. Continue as described in chapter "Restore – Restoring Saved Data or Factory Settings".

9.2.7 Alarms – Parameter Alarms, User Alarms, System Alarms



The main menu *Alarms* lists the parameter alarms for all running bioreactors by time of occurrence. The following user alarms and system alarms are shown here, too:

- *Password Expiry*
- *Difference in board configuration*
- *System restarted after power failure*.
- *Invalid modbus map for Parameter xy*

INFORMATION

This alarm can only occur if modbus settings were modified. Modbus settings can only be modified on user level Service.

- *No water detected:* no water in the temperature control system or insufficient water supply. For details refer to main chapter

"Interferences", chapter "Interferences Temperature Control System".

- *No communication*: no communication between controller board and operating panel. For details refer to main chapter "Interferences".
- *Requested specialized configuration not installed*: Error occured while restoring saved data (Restore function) or during installation of a software update (Update function).

A parameter alarm is signalled by the *Alarm* tab flashing light red and dark alternately.

The screen contains the following columns:

- *Description*: describes the alarm
- *Start*: shows the date and time when the alarm started.
- *End*: shows the date and time when the parameter alarm ended.
- *Confirmed*: indicates confirmed and not confirmed alarms.

  Not confirmed alarms are confirmed by pressing **Confirm**.

  Confirmed alarms are displayed with the date, time and user.

9.2.7.1 Parameter Alarms

A parameter alarm occurs as soon as the current value of a parameter is outside the set alarm tolerances.

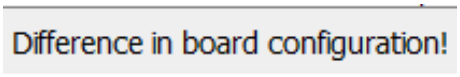
A parameter alarm is triggered as soon as a value drops below the lower alarm value or exceeds the upper alarm value.

The example in the figure on the left shows: *pO2: lower alarm (14.3 < 15)*. I.e. the current value of parameter pO2 (= 14.3 %) is below the lower alarm value (= 15 %).

INFORMATION

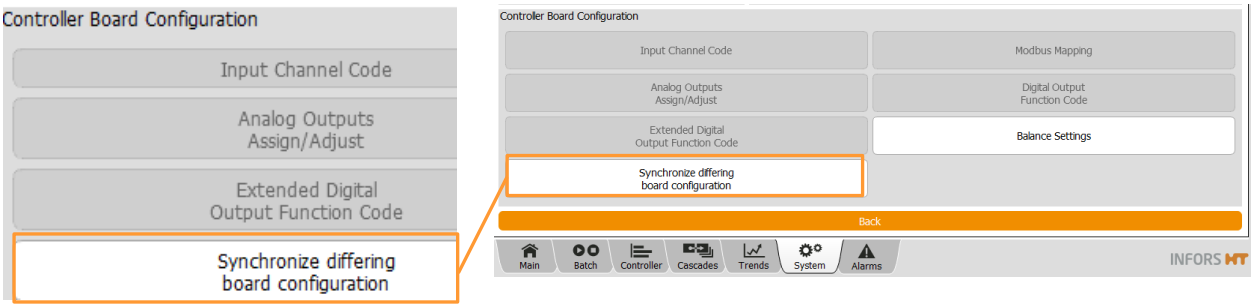
The values in brackets always refer to the current value compared with the setting of the alarm value or the critical value.

9.2.7.2 System-Alarm “Difference in board configuration”

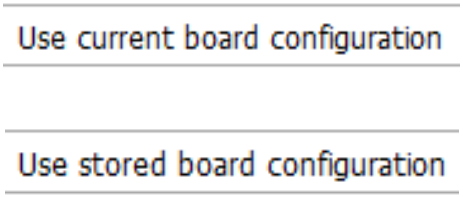


A backup of each control board configuration of the equipment is stored in the touch screen. If there are differences between the backup and the current configuration after a firmware update / exchange of the control board respectively the touch screen, the alarm *Difference in board configuration* will occur. This signifies that the configurations do not correspond with each other.

To enable to select the appropriate configuration, the **Synchronize differing board configuration** appears and is enabled in the *Controller Board Configuration* section of the main menu Settings.



After selection of this function (pressing the button), the menu appears with the two following options:



- **Use current board configuration**: to replace the backup in the touch screen with the current configuration of the control board.

  This is appropriate after exchange of a touch screen.
- **Use stored board configuration**: to overwrite the configuration of the control board with the configuration from the backup.

  This is appropriate after a firmware update, respectively replacement of a control board.

The alarm disappears as soon as the function is executed.

9.2.7.3 System Alarm “No water detected in temperature control system”

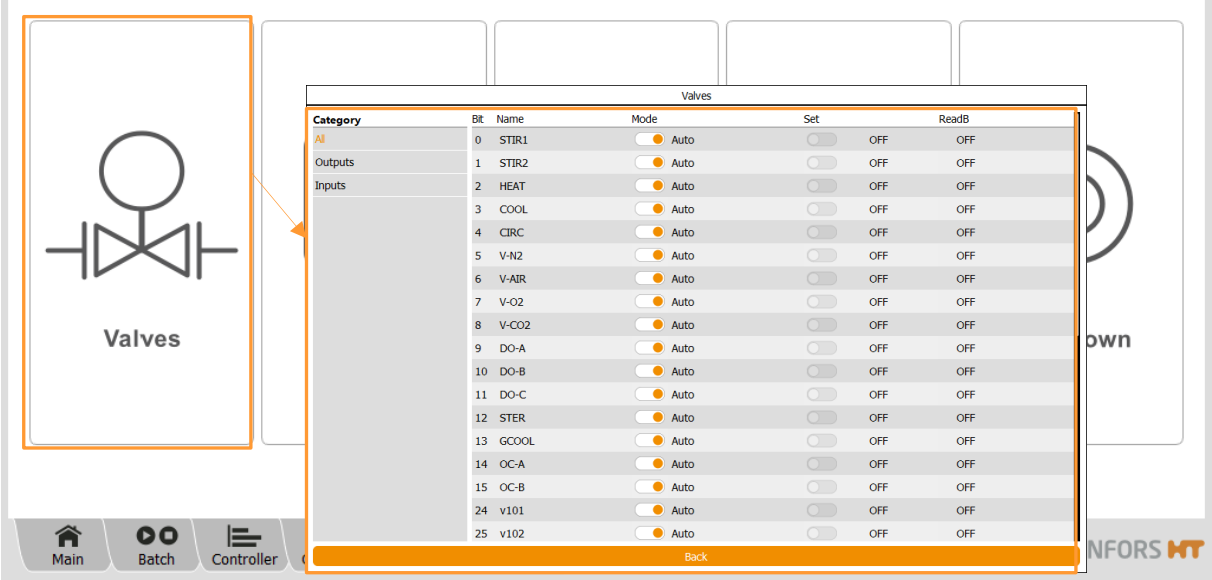
The filling of the temperature control system is usually done once after installation by qualified personnel from the manufacturer or licensed dealer.

If the water sensor does not detect liquid in the temperature control system during fermentation or full sterilisation, the system will automatically try to refill the circuit. The status message *REFILLING CIRCULATION* signifies this.

If the filling procedure has failed, the alarm *No water detected* in *temperature control system* will appear. Temperature control will be deactivated, the circulation pump and heating are switched off. The active process continues running.

9.3 Submenus

9.3.1 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!

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The menu display can be selected in column *Category*:

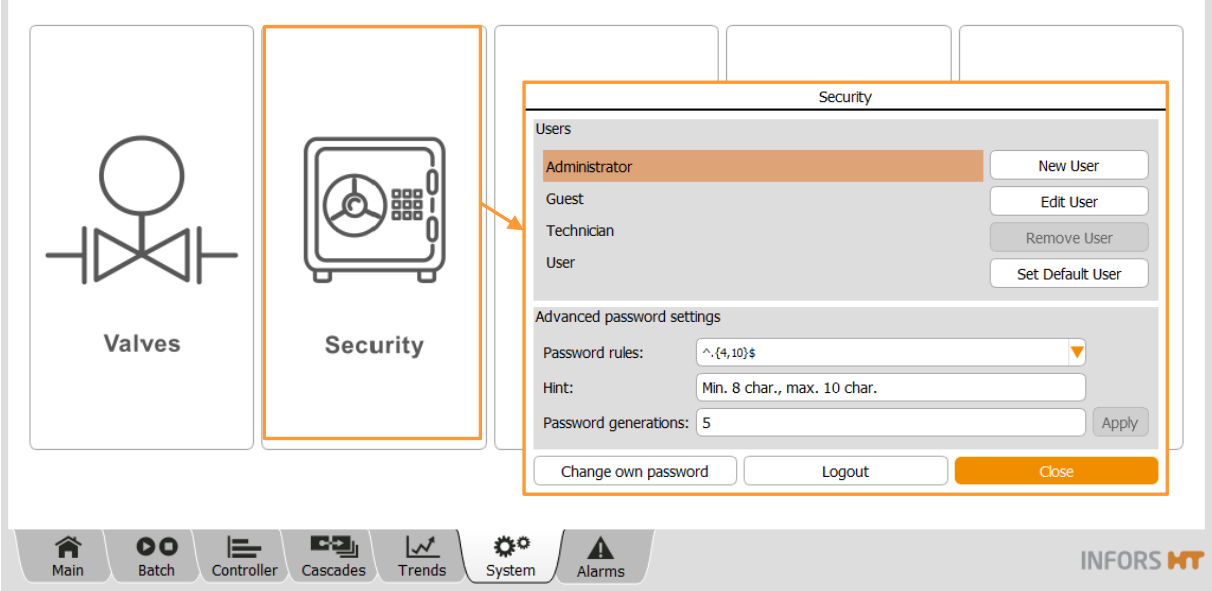
Display (*Category*)	
All	Outputs and Inputs
Outputs	Outputs only
Inputs	Inputs only

The main column contains:

Main column		
Bit / Name		Channel number and designation
Mode	*Auto*	Automatic switching
	Manual	Manual switching, outputs are forced, i.e. the automatic switching is thus disabled.
Set (Switching status of the digital output)	*OFF / ON*	Output is switched off / on
ReadB (electronic feedback channel, which confirms the change in status.	*OFF / ON*	Readback is switched off / on
If the electrical connection is faulty, it is displayed as FALSE		

Back: leads back to main menu *System.*

9.3.2 Security – User Management



The submenu *Security* is used for logging on and off the system. This is where users can also be added or deleted, passwords can be issued and access authorisations can be assigned.

More or less buttons may be enabled in this menu depending on the access authorisation of the registered user:

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

The different user levels, access authorisations and functions are described in the following chapters.

9.3.2.1 User Levels

The system has five user levels with different access authorisations. The user levels are designated and defined as *Groups*.

Service: This user group has access to all system and bioreactor settings. This user level is accessible for the manufacturer's (INFORS HT) qualified service employees only and access for all other users is blocked.

Administrators: This user group has access to basic system and bioreactor settings. New users can only be added, altered and deleted by users allocated to the user groups *Service* or *Administrators*. The default setting for the login to the system is predefined as *Administrator*.

Technicians: This user group has limited access to system and bioreactor settings. The default setting for the login to the system is predefined as *Technician*.

User: This user group only has restricted access to the system. The default setting for the login to the system is predefined as *User*.

Guests: This user group has viewing authorisations only and no access authorisations. Exception: users with this user level can select trend lines in the main *Trends* menu to display or hide them, change the background colour for the diagram display and select the time range for the diagram display. This user level serves as protection against unauthorised access to the system or unintentional changes to settings.

This user level is set automatically as long as no user is logged on to the system. This is indicated by the words *Guest mode* in the header on the screen.

The default password setting for the user groups *Administrators*, *Technicians* and *User* is the same: qwertyuiop.

INFORMATION

Passwords should be changed and managed by the authorised person (users with user level Administrators) after commissioning for the first time.

9.3.2.2 Access Authorisations of User Groups

The following tables group the various functions of the touch screen software with an indication of the access authorisations of the user groups. Optional functions, are listed, too. These functions are only present with the correspondingly ordered equipment configuration. These functions are labelled with an asterisk (*)

Key:

- V (view) = visible, function cannot be executed
  Visible means that, depending on the function, the button or the menu/dialogue can only be viewed.
- E (execute) = Visible and function can be accessed for execution
  I.e. functions are executable
- Empty field = cannot be viewed and function cannot be executed

BIOREACTOR	**User Groups**				
	Guests	User	Technician	Admin.	Service
Start / Stop Fermentation/Cultivation	V	E	E	E	E

STERILISATION	**User Groups**				
	Guests	User	Technician	Admin.	Service
Full Sterilisation	V	E	E	E	E
SIP Harvest/Sample Valve	V	E	E	E	E

RECIPES	**User Groups**				
	Guests	User	Technician	Admin.	Service
Load/Start	V	V	E	E	E
Save	V	V	E	E	E
Delete	V	V	E	E	E

PUMPS	**User Groups**				
	Guests	User	Technician	Admin.	Service
Calibrating pump(s)	V	E	E	E	E
Resetting counter (*Reset*)	V	E	E	E	E
Setting pump factor manually (*Pump factor*)	V	E	E	E	E
Filling/emptying hoses automatically (*Fill/Empty Pumps*)	V	E	E	E	E

PARAMETERS	User Groups				
	Guests	User	Technician	Admin.	Service
Setpoint	V	E	E	E	E
Setting alarm and critical values (*Upper/Lower Alarm, Upper/Lower Critical*)	V	E	E	E	E
Switching parameters on and off (*Output active ON/OFF*)	V	E	E	E	E
Calibrating pH sensor (*Calibrate pH*)	V	E	E	E	E
pH sensor: changing *Slope* and/or *Offset* (*Manual* calibration mode)		E	E	E	E
Calibrating pO2 sensor (*Calibrate pO2*)	V	E	E	E	E
Function *USE AS SETPOINT* in calibration menu pO_2		E	E	E	E
Function *USE AS SETPOINT* in all calibration menus except pO_2				E	E
Calibrate, all except pH and pO_2			V	E	E
Calibrate, manually (manual calibration mode), all except for above mentioned				E	E
PID			E	E	E
Options					E

CASCADES	User Groups				
	Guests	User	Technician	Admin.	Service
Setting a cascade	V	E	E	E	E
Setting an advanced cascade (*Advanced option*)			E	E	E

TREND LINES (Trends)	User Groups				
	Guests	User	Technician	Admin.	Service
Change display settings	E	E	E	E	E

ALARMS (Alarms)	User Groups				
	Guests	User	Technician	Admin.	Service
Confirming alarms	V	E	E	E	E

SYSTEM	User Groups				
	Guests	User	Technician	Admin.	Service
Loading software update (*Update*)	V	V	V	E	E
Viewing statistics of communication between software and bioreactor hardware (*Statistics*)	V	V	E	E	E

DIGITAL INPUTS/OUTPUTS (System / Valves)	User Groups				
	Guests	User	Technician	Admin.	Service
Manually switching digital inputs and outputs	V	V	E	E	E

Function	User Groups				
SECURITY user management (Security)	Guests	User	Technician	Admin.	Service
Logging on to the system (*Login*)	E	E	E	E	E
Logging out from the system (*Logout*)		E	E	E	E
Changing password (*Change Password*)		E	E	E	E
Adding a new user (*New User*)		V	V	E	E
Deleting a user (*Remove User*)		V	V	E	E
Changing user settings (*Edit User*)		V	V	E	E
Setting automatic user login (*Set Default User*)		V	V	E	E
List of all users				V	V

SYSTEM SETTINGS (System / Settings)	Benutzergruppen				
	Guests	User	Technician	Admin.	Service
Settings					
Network settings (*IP Settings*)	V	V	V	E	E
Changing date and time (*Change Time*)	V	V	V	E	E
Files					
Saving data (*Backup*)	V	V	V	E	E
Restoring data (*Restore*)	V	V	V	E	E
Settings in Service Menu (*Service Menu*)					E
Exporting log files (*Export Logs*)		V	E	E	E

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Controller Board Configuration					
Setting codes for input channels (*Input channel code*)			V	V	E
Assigning/changing analogue outputs (*Analog Outputs Assign/Adjust*)			V	V	E
Setting extended function codes for digital outputs (*Extended Digital Output Function Code*)			V	V	E
Synchronising different configurations of the controller board (*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
Settings for balances (*Balance Settings*)	V	V	V	E	E

TEMPORARY SCREEN LOCK (System / Wipe Screen)	**User Groups**				
	Guests	User	Technician	Admin.	Service
Activating the temporary screen lock	V	E	E	E	E

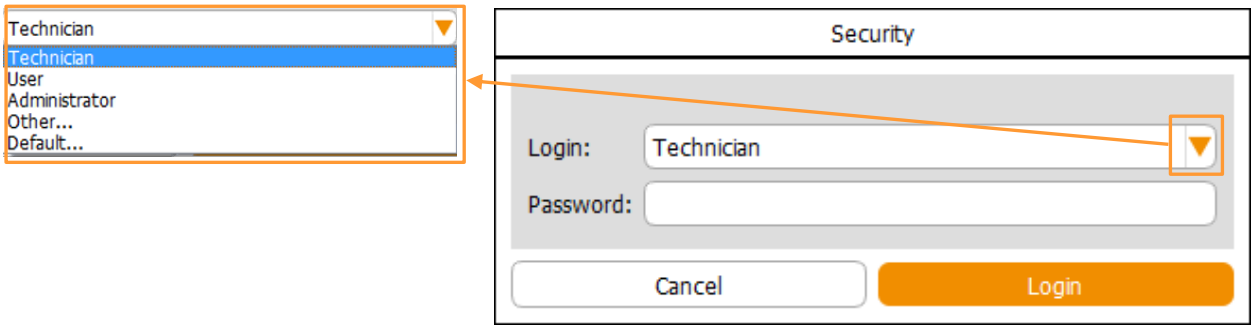
SYSTEM SHUTDOWN	**User Groups**				
	Guests	User	Technician	Admin.	Service
Shutting down and switching off the system	V	E	E	E	E

9.3.2.3 Login – Logging on to the System

To log on to the system, proceed as follows:

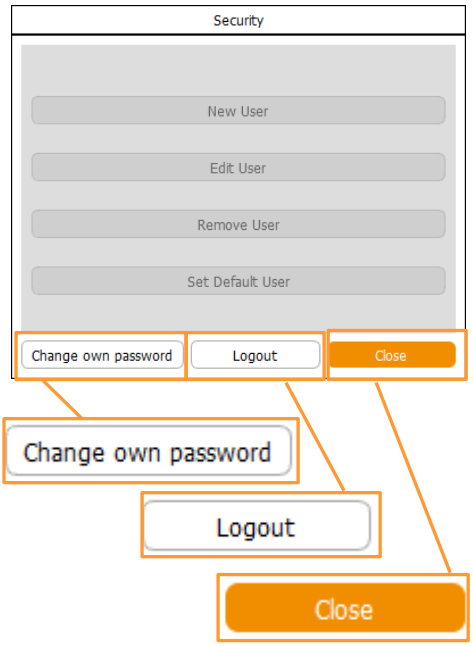
Procedure

1. Call up the main menu *System* and press **Security**.
   Submenu *Security* appears with:



- *Login*: Drop-down menu with users available by default with factory settings (see picture above to the left):
  - *User*
  - *Technician*
  - *Administrator*
  - *Other*: for use by INFORS HT service employees only
  - Default: automatic user login without entering a password if previously set using **Set Default User**
- *Password*: to enter the password.
- **Cancel**: to cancel and close the menu without changes.
- **Login**: to log on to the system (after password entry).

2. Select the desired user, e.g. *Technician.*
3. Press the input field *Password*.
   The alphanumeric keyboard appears.
4. Enter the password and confirm with the **OK** key.
   The input is saved; the alphanumeric keyboard disappears.
5. Press **Login**.



The user is logged in as *Technician*. This is shown in the header on the screen and the different functions are listed as buttons in the *Security* menu. The buttons **Change Password, Logout**, and **Close** are enabled on all user levels (except for *Guest*).

INFORMATION

On user level Administrator and above, the password rules can be configured here, too. For details refer to chapter “Password Security – Defining Password Rules”.

6. Press **Close**.

   Submenu *Security* disappears.

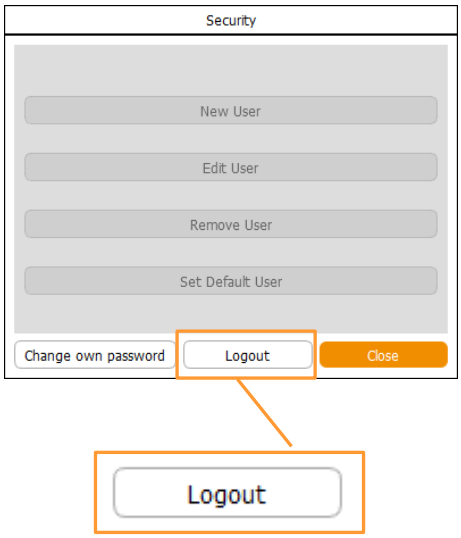
9.3.2.4 Logout – Logging off the System

To log off from the system, proceed as follows:

Procedure

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

   Submenu *Security* appears.



2. Press **Logout**.

   The user is logged off, menu *Security* appears for login.

3. Press **Cancel**.

   Menu disappears.

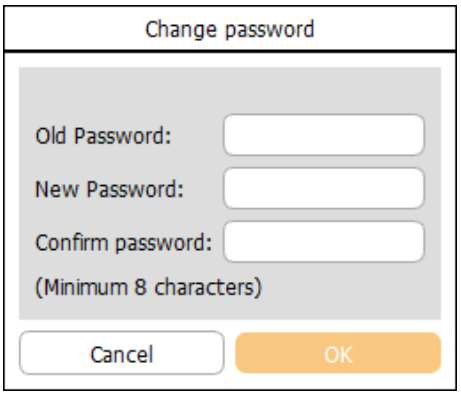
9.3.2.5 Change Password

Users of all user groups can change their own password. In order to be able to change a password, the user must be logged on to the system.

Proceed as follows:

Procedure

1. Call up submenu Security and press **Change Password**.



The *Change password* dialogue box appears with:

- *Old Password*: to enter the old password
- *New Password*: to enter the new password
- *Confirm Password (minimum 8 characters)*: to confirm then new password (here: min. 8 characters).

INFORMATION

Depending on the password rule settings, the password must meet different conditions. Password rules are configured on user level Administrator and above. For details refer to chapter “Password Security – Defining Password Rules”.

- **OK**: to confirm inputs, save changes.

  This button is not enabled until the inputs have been made.
- **Cancel**: to cancel without saving.

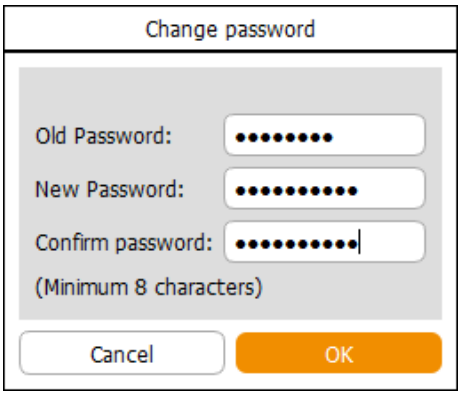
2. Press the input field *Old Password.*

The alphanumerical keyboard appears.

3. Enter the old password and confirm with the **OK** key.

Inputs appear as dots in the input field.

4. Proceed the same way with the new password in the input fields *New Password* and *Confirm Password*.



All inputs are displayed as dots in the input fields.

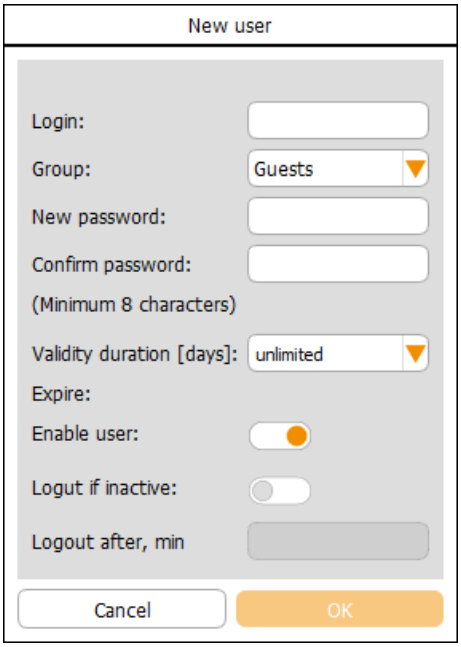
5. Press **OK**.
   The dialogue box disappears; the new password is saved.

9.3.2.6 New User – Adding a New User

To add a new user to the user list, proceed as follows:

Procedure

1. Log on to the system on user level Administrator.
2. Call up the submenu *Security* and press **New User**.



The *New User* dialogue box appears with:

- *Login*: to enter a new user (name).
- *Group*: to select the user group.
- *New Password*: to enter the password.
- *Confirm Password (minimum 8 characters)*: to confirm the password with min. 8 characters.

INFORMATION

Depending on the password rule settings, the password must meet different conditions. Password rules are configured on user level Administrator and above. For details refer to chapter “Password Security – Defining Password Rules”.

- *Validity duration [days]*: to enter the validity duration of the password, choose “unlimited”, 30, 100 or 365 days.
- *Expire*: shows the selected validity duration of the password.
- *Enable user*: to activate/deactivate access authorisation of the new user.

  This function is switched on by default.

INFORMATION

The user has no access rights and no password can be defined, if this function is deactivated.

- *Logout if inactive:* to switch on/off the automatic logout when inactive after predefined duration.
- *Logout after, min*: to set the expiration time of the automatic logout in minutes.

  This input field is enabled only, when the function is switched on.
- **OK**: to confirm entries.

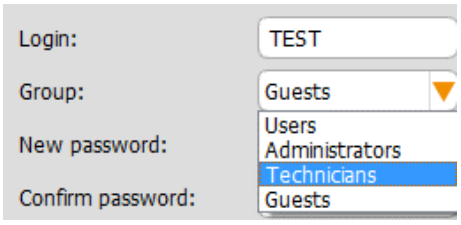
  This button is enabled only after input
- **Cancel**: to cancel without saving.

3. Press ***Login***.

The alphanumeric keyboard appears.

4. Enter desired new user name, e.g. TEST, and confirm with the **OK** key.

Input appears in the Login-field



5. Select the desired user group, e.g. *Technicians*

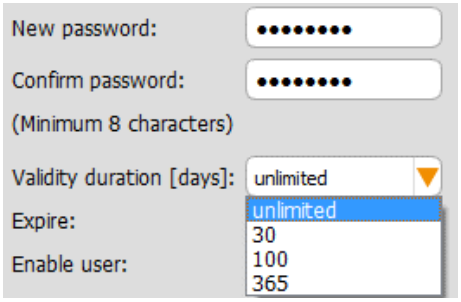
6. Press *Password*.

The alphanumeric keyboard appears.

7. Enter the desired password and confirm with the **OK** key.

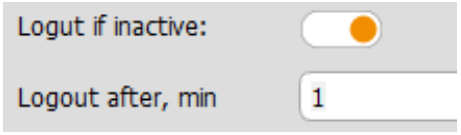
The input appears as dots in input field.

8. Repeat the same procedure with the *Confirm password* input field.



9. Select the validity duration of the password, e.g. validity.

10. Switch on access rights, if necessary.



11. If applicable, set automatic logout, if inactive:

Switch the function on and enter the desired time in minutes.

Once all settings are made:

12. Press **OK**.

The dialogue box disappears, the new user is added and shown in the user selection list.

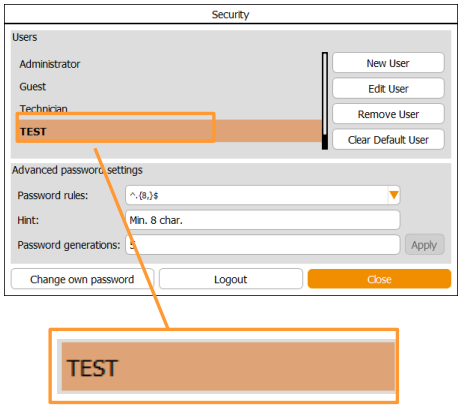
9.3.2.7 Remove User – Deleting a User

To remove a user from the, proceed as follows:

Procedure

1. Log on to the system on user level *Administrator*.

2. Call up submenu *Security*.



3. Select the user to be deleted in the user selection list. The fictitious user *TEST* is used in this example.

4. Press **Remove User**.

The *Confirmation* dialogue box appears with:

- Information *User "TEST" will be removed from user list*:
- Instruction *Press Yes to confirm operation*.
- **OK**: to delete the user.
- **Cancel**: to cancel without changes.

5. Press **OK**.

The dialogue box disappears, the user *TEST* is deleted from the user selection list.

9.3.2.8 Edit User – Editing User Settings

Edit User is used to change the following settings for an existing user:

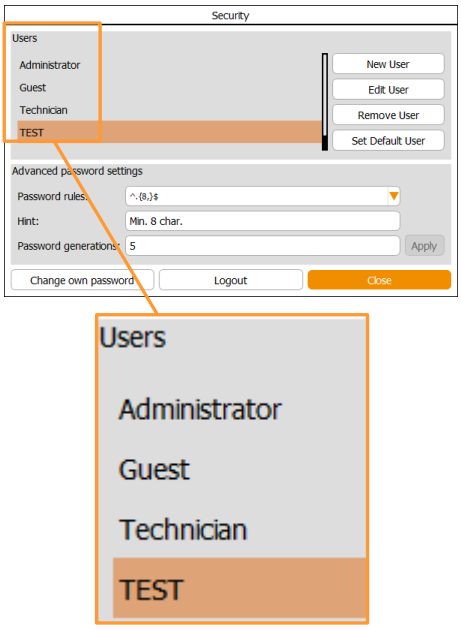
1) Assign new user group.
   See chapter "New User – Adding a New User" for details on the procedure.
2) Change password.
   See chapter "Change Password" for details on the procedure.
3) Automatic user log-out when screen is inactive after a predefined time in minutes has elapsed. The first user level *Guests* is then set automatically.

To edit settings, proceed as follows:

Procedure

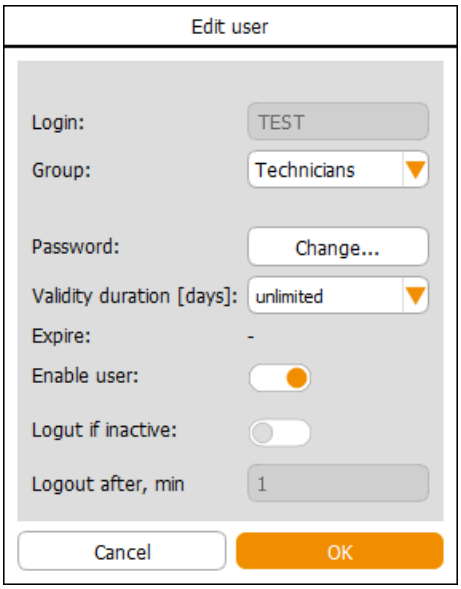
1. Log on to the system on user level *Administrator*.

2. Call up submenu *Security*.



3. Select the desired user from the user selection list, the fictitious user *TEST* is used in this example.

4. Press **Edit User**.



The *Edit User* dialogue box appears with nearly identical input fields, view boxes, ON/OFF switches and buttons as in dialogue box *New User*.

Exceptions:

- *Login*: this function is not enabled here.
- **Change …**: to change the password. The two input fields *New Password* and *Confirm Password* appear after pressing this button.

5. Make required settings.

6. Press **OK**.

Settings are adopted; the dialogue box disappears.

9.3.2.9 Set / Delete Default User – Setting or Deleting an automatic User Login

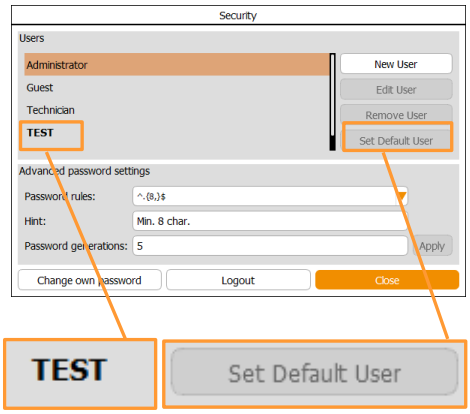
Set Default User is used to set an automatic user login. I.e. a user can be defined who is then automatically logged on to the system the next time it is switched on.

Clear Default User is used to delete the automatic login of a user.

Proceed as follows:

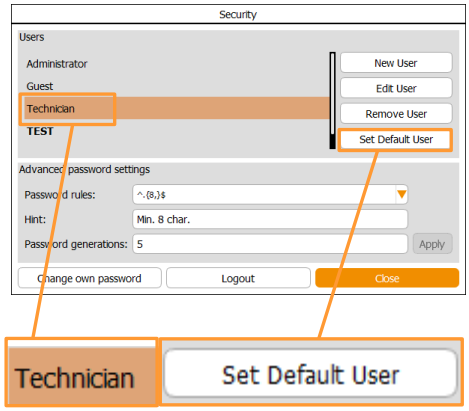
Procedure

1. Log on to the system on user level *Administrator*.
2. Call up submenu *Security.*
3. Touch the desired user in the user selection list. The fictitious user *TEST* is used in this example.
4. Press **Set Default User**.



The selected user *TEST* is displayed in bold letters, the **Set Default User** button is only visible, but not enabled anymore.

Changing the automatic user login

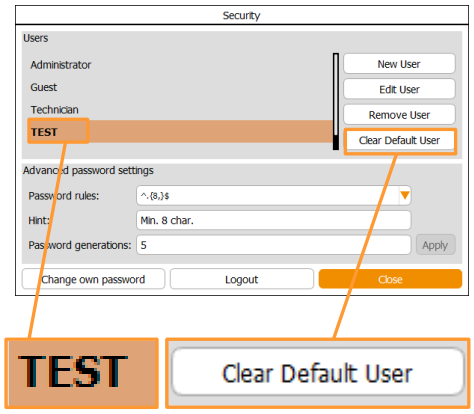


Another user can be defined here for automatic login.

When selecting the desired user in the list, the **Set Default User** button is enabled again.

The new user is adopted for automatic user login after pressing **Set Default User**.

Deleting automatic user login



The automatic user login can be deleted here, too.

When selecting the defined user with the automatic user login setting in the list, the **Clear Default User** button is visible and enabled instead of the **Set Default User** button.

After pressing **Clear Default User**, the automatic user login is deleted.

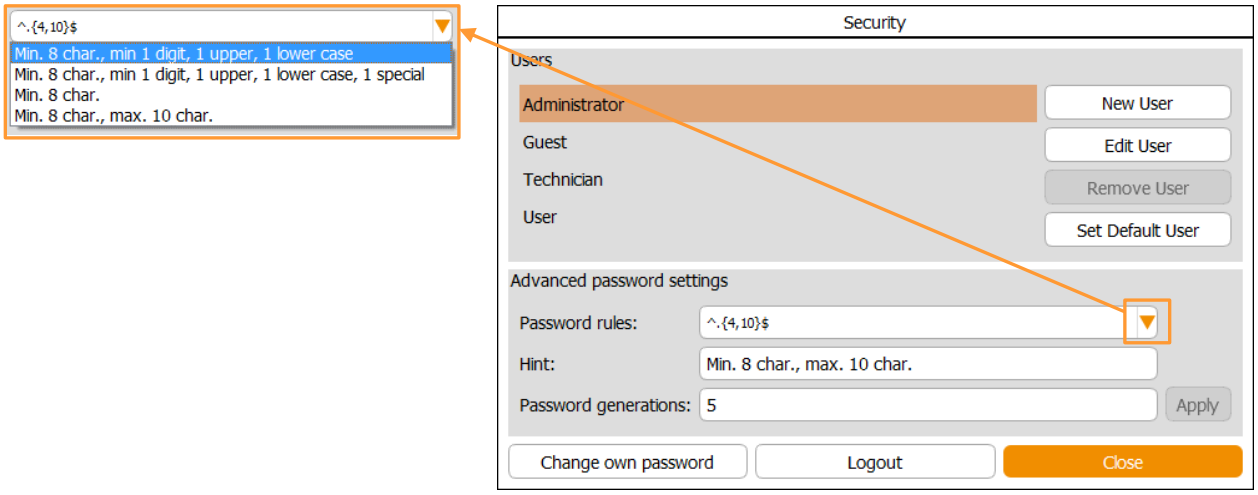
9.3.2.10 Password Security – Configuring Password Rules

The *Advanced password settings* area is visible and enabled from user level *Administrator* in submenu *Security*. Conditions for creating new user passwords can be configured here.

Proceed as follows:

Procedure

1. Login to the system on user level *Administrator*.
2. Call up main menu *System* and press **Security**.
   Submenu *Security* appears with (lower part of the menu):



- *Password rules*: Dropdown menu with choice of four pass word rules (see figure to the top left). The password must have at least:
  - 8 characters, containing at least 1 number, 1 capital letter and 1 lower case letter.
  - 8 characters, containing at least 1 number, 1 capital letter and 1 lower case letter and 1 special character.
  - 8 characters.
  - 8 up to max. 10 characters.
- *Hint*: shows during creation of a new password which rules must be followed.
- *Passwort generations*: defines the number of passwords that must be newly created, before a password may be reused.
- **Apply:** to instantly apply the rule when creating a new password. This button is enabled as soon as a rule is changed.

3. Select the desired rule to apply and the number of new passwords that must be created until reuse of an old password is allowed.

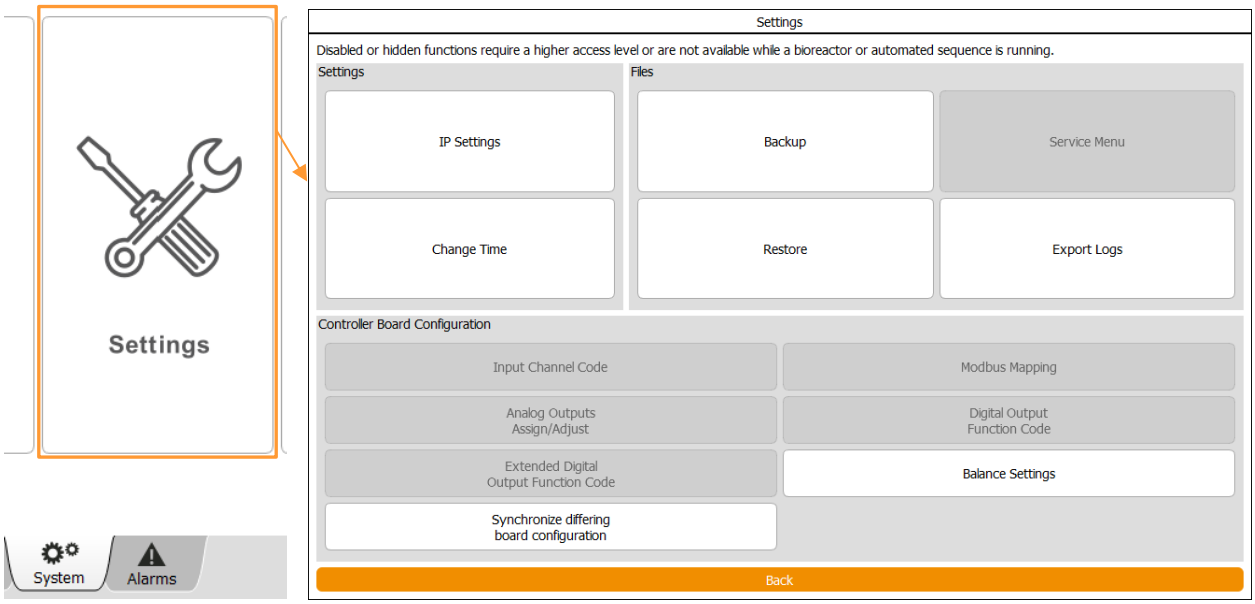
4. Press **Apply**.

   The rule is saved and will be shown when creating the next password.

5. Press **Close**.

   Submenu *Security* disappears.

9.3.3 Settings – Basic Unit Settings



In the submenu *Settings* basic settings for the equipment are made. Depending on the access authorisation, more or less buttons are visible and enabled (for details refer to the tables in chapter “Access Authorisations of User Groups”. The figure above shows the menu on user level *Administrator.*

The menu is divided into three areas with the following functions:

Settings

- **IP Settings**: for network settings
- **Change Time**: to set the date and time

Files

- **Backup**: to save data.
- **Restore**: to restore and upload saved data.
- **Service Menu**: access only for qualified Infors service or licensed dealer.
- **Export Logs**: to export log files.

Controller Board Configuration

- **Input Channel Code**: to set codes for input channels
- **Analog Outputs Assign/Adjust**: to assign/change analogue outputs.
- **Extended Digital Output Function Code**: to set function codes for extended digital outputs.

- **Synchronize differing board configuration**: to synchronize differing board configurations.

> **INFORMATION**
>
> This button is only visible, if the appropriate alarm (*Difference in board configuration!*) has been triggered and is displayed in main menu Alarms after an update of the firmware / change of a control board. For details refer to chapter “System Alarm Difference in oard configuration”.

- **Modbus mapping**: for Modbus settings.
- **Digital Output Function Code**: to set function codes for digital outputs.
- **Balance Settings**: for balance settings.

> **INFORMATION**
>
> None of the functions concerning inputs and outputs, function codes and modbus mappings are described in this manual. These functions are only accessible for Infors service or Infors licensed dealers.

The **Back** button directs back to the main menu *System*.

9.3.3.1 IP Settings – Network Settings

IP Settings is used to establish a network connection. This can be performed either automatically or manually.

> **INFORMATION**
>
> This is only possible, if a network calble is connected.

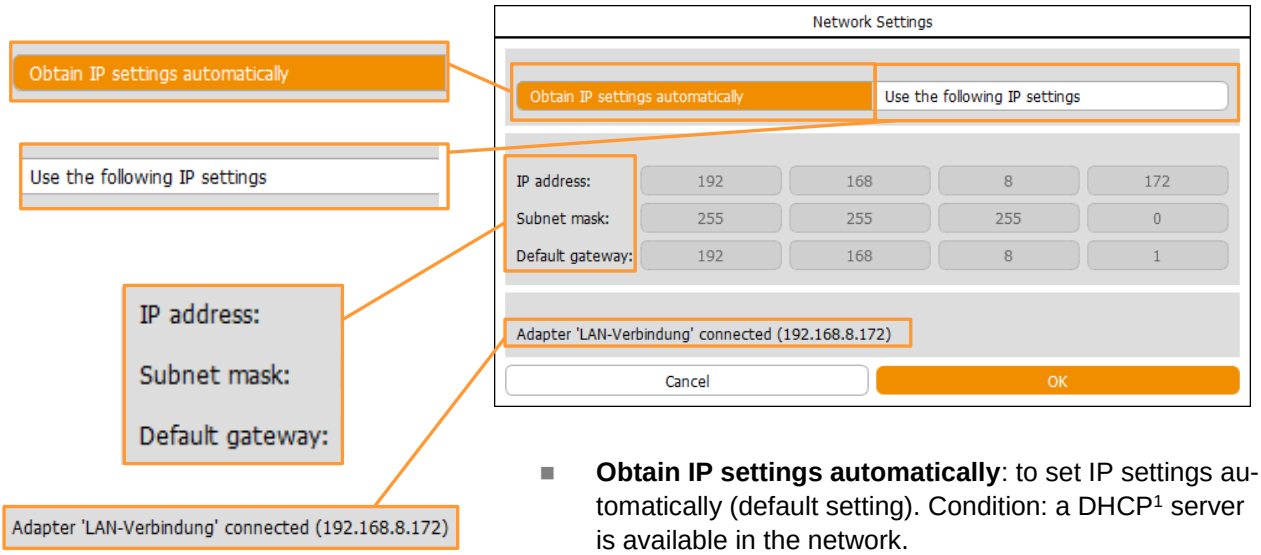
This manual does not describe how to setup a network connection.

To call up the menu to make settings, proceed as follows:

Procedure

1. Log on to the system on user level Administrator.
2. Call up submenu *Settings*.
3. Press **IP-Settings**.

   The *Network Settings* menu appears with:



- **Obtain IP settings automatically**: to set IP settings automatically (default setting). Condition: a DHCP[1] server is available in the network.
- **Use the following IP settings**: to use the following IP settings.

  Only after pressing this button, the following fields are enabled.
- *IP address*: shows current IP address or to enter IP address manually.
- *Subnet mask*: displays default gateway or allows manual input.
- *Default gateway*: shows default gateway or allows manuel input.
- *„….connected*“: status message of the network connection.

INFORMATION

The status message …*connected* indicates that correct network connection is established. If this is not the case (no signal), the message „*No active LAN connection*“ appears.

- **OK**: to save inputs and close the dialogue box.
- **Cancel**: to close the dialogue box without changes.

[1] *Dynamic Host Configuration Protocol*

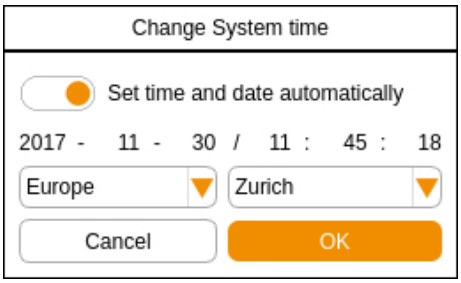
9.3.3.2 Change Time – Changing Date and Time

Change Time enables adjusting the system date and time to the local conditions. The system is set for automatic synchronisation with the time server ex-factory. I.e. the display is corresponding with the selected time zone. Alternatively, these settings can be manually adjusted.

To make settings, proceed as follows:

Procedure

1. Log on to the system on user level *Administrator* and call up the submenu *Settings*.
2. Press **Change Time**.



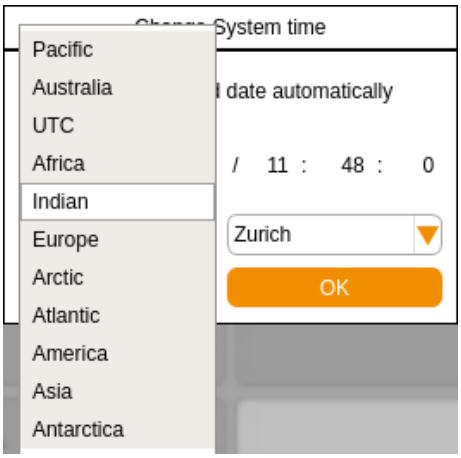
The *Change System time* dialogue box appears with:

- **ON/OFF** switch *Set time and date automatically* is in position **ON.**
- Display (from left to right) for year, month, day, hours, minutes and seconds.
- Dropdown menus for time zone and city: default = Europe / Zurich
- **Cancel**: to close the dialogue box without changes.
- **OK**: to adopt inputs and close the dialogue box.

Changes with automatic adjustment

Proceed as follows:

Procedure



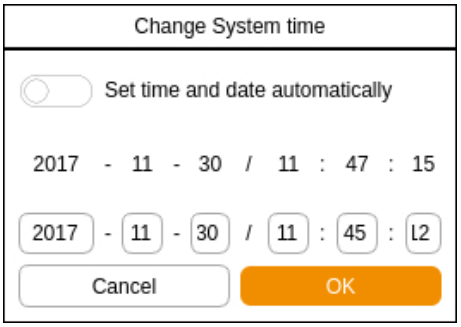
1. Select the time zone and city in the drop down menus.
2. Press **OK**.

Settings are saved, the dialogue box disappears.

Manual changes

Proceed as follows:

Procedure



1. Switch automatic time and date setting **off.**

   Input fields (from left to right) for year, month, day, hours, minutes and seconds appear.

2. Press the desired input field(s), enter the value(s) via appearing numeric keypad and confirm with the **OK** key.

   Inputs are adopted.

3. Press **OK**.

   Inputs are saved, the dialogue box disappears.

9.3.3.3 Backup – Saving Data

The Backup function is used to save the entire settings of the touchscreen software and the control board of the bioreactor. These data can be restored using the Restore function.

Note the following:

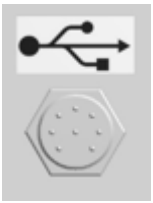
- Data can be saved on the internal memory or on a USB stick.
- A data backup is only executable when all running processes are stopped..

To execute a backup, proceed as follows.

Only when using a USB stick, otherwise go to step 2:

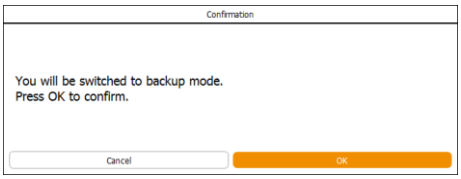
Operation Touch Screen Software

Procedure



1. Use the special cable provided with the equipment and connect it to the appropriate connector (see figure on the left) on the rear side of the operating panel and connect the USB stick.

2. Log on to the system on user level *Administrator*, call up main menu *System* and select submenu *Settings*.
3. Press **Backup** in the *Files* area.

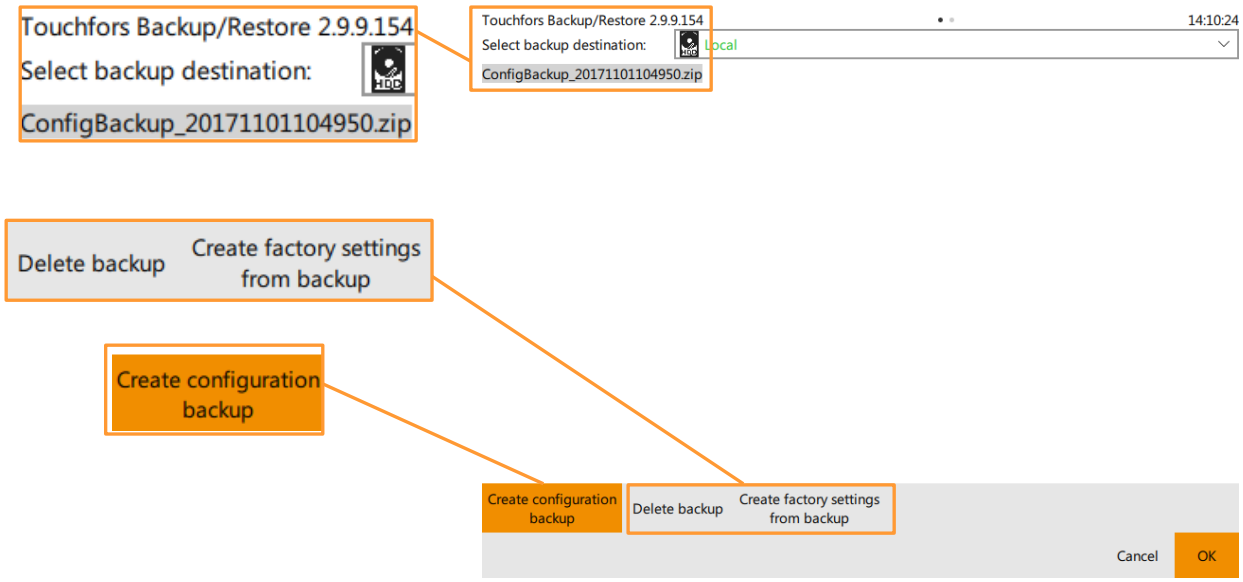


The *Confirmation* dialogue box appears with:

- Information: *You will be switched to backup mode.*
- Instruction: *Press OK to confirm*
- **OK**: to confirm switching to data backup mode.
- **Cancel**: to close the dialogue box without changes.

4. Press **OK**.

   The menu for data backup opens with:

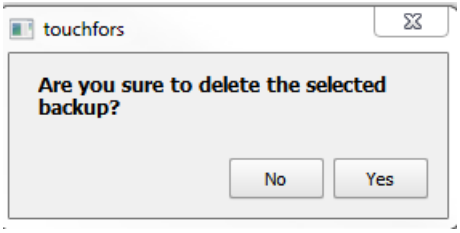


- *Select backup destination*:
  - *local*: to locally save the backup.
  - *external*: to save the backup externally on a detected and connected USB stick.
- **Create configuration backup**: to create the backup.

- **Delete backup**: to delete the backup.
- **Create factory settings from backup**: to create factory settings from the backup.
- **Cancel**: to leave the menu without changes.
- **OK**: to save the backup and leave the menu.

5. Select the backup destination and press **Create configuration backup** to create the backup.
6. Press **OK** to save the backup and leave the menu.

Deleting a backup



Pressing **Delete backup** opens a dialogue box with:

- Question: *Are you sure to delete the selected backup?*
- **No**: to cancel and close the dialogue box without changes.
- **Yes**: to delete the backup and close the dialogue box.

If backup on USB stick:

7. Remove the USB stick and the cable.

9.3.3.4 Restore – Restoring Saved Data or Restoring Factory Settings

The Restore function enables to restore data, which have previously been saved using the Backup function. Data will be uploaded to the system again. It is also possible to restore factory settings using this function.

INFORMATION

Factory settings usually represent the settings of the bioreactor in as-delivered condition. In case of retrofitting of the bioreactor, these settings can be updated, too. Both is exclusively carried out by Infors Service or a licensed dealer.

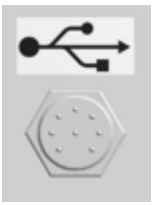
Note the following:

- Data are either restored from the internal memory or from a USB stick, see chapter “Backup – Saving Data”.
- The Restore function is only executable when all running processes are stopped.

To execute the Restore function, proceed as follows:

Operation Touch Screen Software

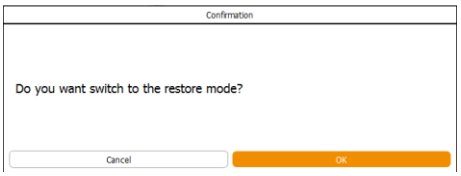
Procedure



Only when using a USB stick, otherwise go to step 2:

1. Use the special cable provided with the equipment and connect it to the appropriate connector on the rear side of the operating panel and connect the USB stick with the saved date (Backup data).

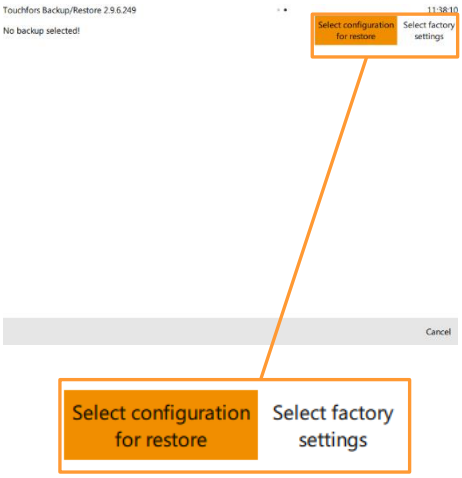
2. Log on to the system on user level *Administrator*, call up main menu *System* and select submenu *Settings*.
3. Press **Restore**.



The *Confirmation* dialogue box appears with:

- Information: *You will be switched to restore mode.*
- Instruction: *Press OK to confirm.*
- **OK**: to confirm switching to restore mode.
- **Cancel**: to close the dialogue box without changing the mode.

4. Press **OK**.



The menu for data restoring appears with:

- **Select Configuration for restore**: to select the backup data for restoring.
- **Select factory settings:** to select factory settings.
- **Cancel**: to leave the menu without changes.
- **OK**: to load the selected backup and restore data.

Executing the backup for data restoring

Pressing **Select configuration for restore** changes the menu display and shows with *Select backup source* the choice of the possible data sources:

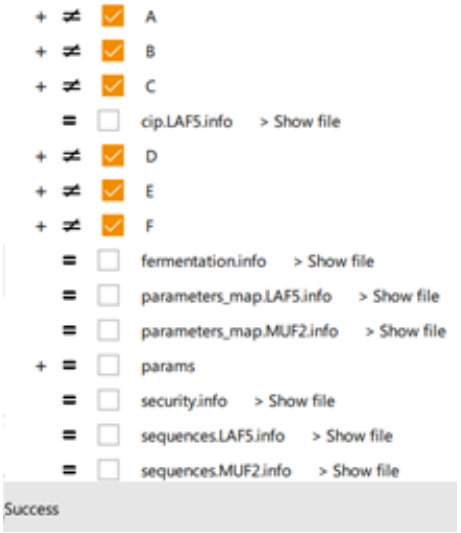
- local: internal memory

- xy (drive) / external: detected and recognised USB stick
- **OK**: To confirm selection

After selection of the data source, a dialogue box appears with:

- *Are you sure to restore the selected backup?*
- **No**: to cancel and close the dialogue box without changes.
- **Yes**: to confirm restoration and start listing data for configuration comparison.

After confirmation via **Yes**, the screen changes and lists data for configuration comparison.



- **≠** signifies a difference between Backup and current configuration.
- **=** No difference between Backup and current configuration.
- **+/-** To open/close tree
- Show file / Show difference: To display file / difference

INFORMATION

This view for showing the difference within a file is for information purposes and mainly foreseen for Infors service or licensed Infors dealers. It shows the differences between the settings of the file to restore and the currently used version in unified format (also *unidiff*).

- **Cancel**: to cancel the backup process and leave the menu.
- **OK**: to execute the backup for restoring data.

9.3.3.5 Export Logs – Exporting Log Files

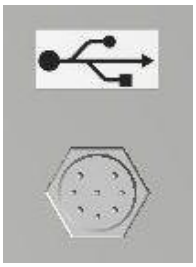
The Export Log functions enables to save all log files (protocol files) as well as alarms and error messages on a USB stick.

Note the following:

- A USB stick is needed for the export.
- Export is only executable when all running processes are stopped.

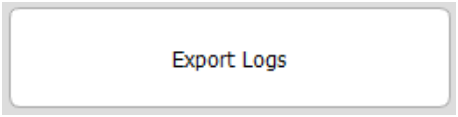
Proceed as follows:

Procedure



1. Use the special cable provided with the equipment and connect it to the appropriate connector (see figure on the left) on the rear side of the operating panel.

2. Connect the USB stick.
3. Log on to the system on user level Technician or Administrator.
4. In main menu *System*, call up submenu *Settings*.



5. Press **Export Logs**.

   Data export is started.

   Once the export is finished, the *Information* dialogue box appears with:

   - Information *Log files successfully exported to: xxxxx*
   - **OK**: To confirm and close the dialogue box.

6. Press **OK**.

   The dialogue box disappears. The Zip file is stored on the USB stick now.

9.3.3.6 Balance Settings

This function is used to configure the connected balances. It is possible to connect up to maximum 7 balances using the equipment manufacturers switchbox.

Note the following:

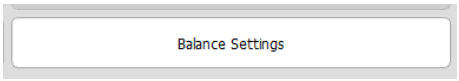
The balance(s) must be configured as follows:

Baud rate 9600, 8 bits, no parity, 2 stop bits.

Proceed as follows:

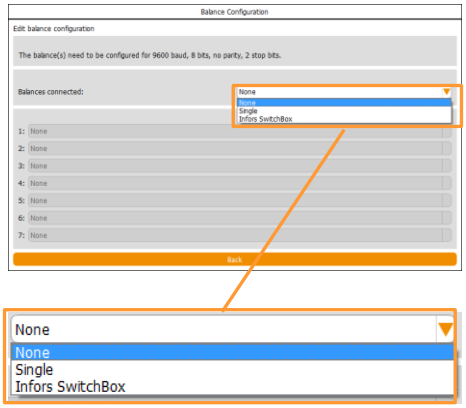
Procedure

1. Connect the balance(s) or switchbox
2. Log on to the system on user level *Administrator*.
3. In main menu *System*, call up submenu *Settings*.



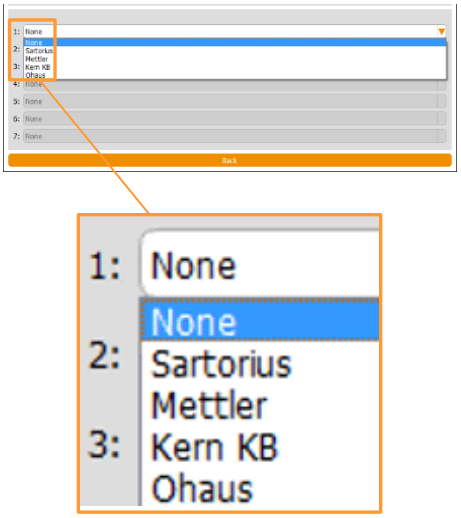
4. Press **Balance Settings**.

The menu *Balance Configuration* appears with:



- Information *The balance(s) need to be configured for 9600 baud, 8 bits, no parity, 2 stop bits*.
- Dropdown menu *balances connected*: to select number of connected balance(s)
  - *None*: no balance
  - *Single*: one balance (without Switchbox)
  - *Infors SwitchBox*
- 7 dropdown menus which are enabled, once one option has been selected.
- **Back**: to save settings and return to submenu *Settings*.

5. Select the desired balance(s).

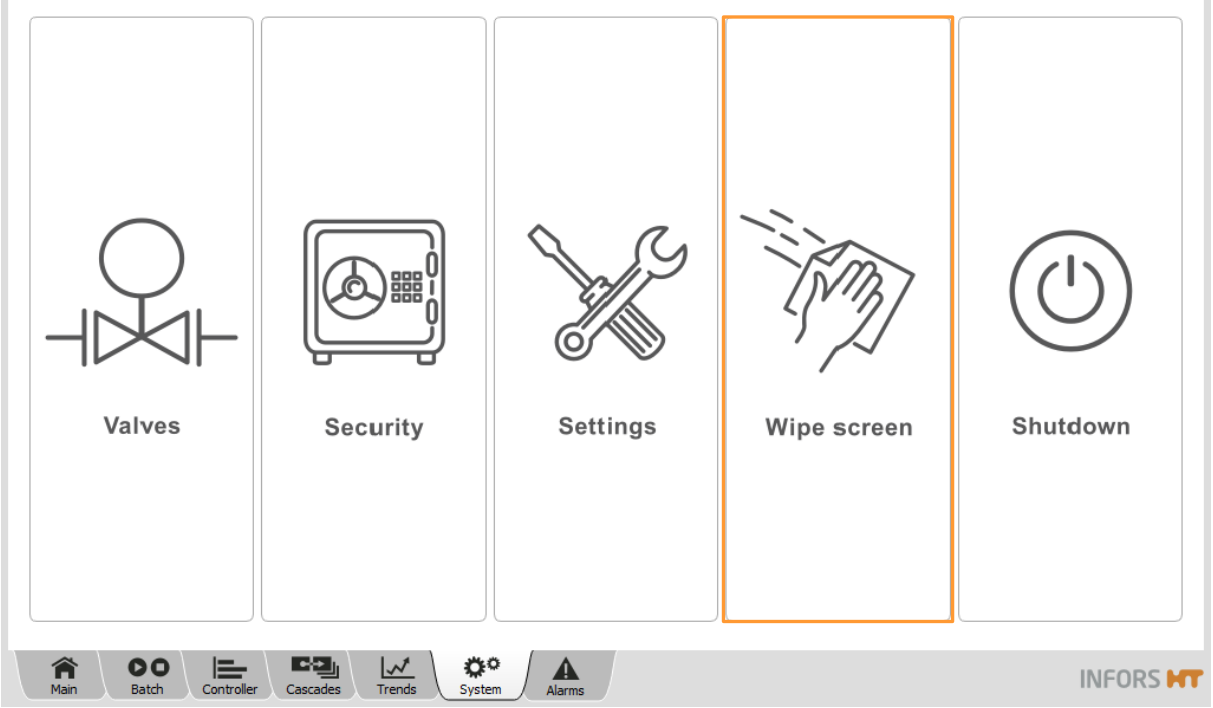


Dropdown menu(s) for selection of the balance type(s) connected appear(s). The choice contains the following types: none (no balance), Sartorius, Mettler, Kern KB und Ohaus

6. Select the balance type(s).
7. Press **Back**.

   Settings are adopted, submenu Settings reappears.

9.3.4 Wipe Screen – (Temporarily) Locking the Screen



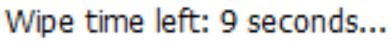
The submenu Wipe Screen has one function only: It locks the screen to prevent any inputs on the screen for 20 seconds. This allows e.g. cleaning the screen for 20 seconds if required.

To activate the temporary screen lock, proceed as follows:

Procedure

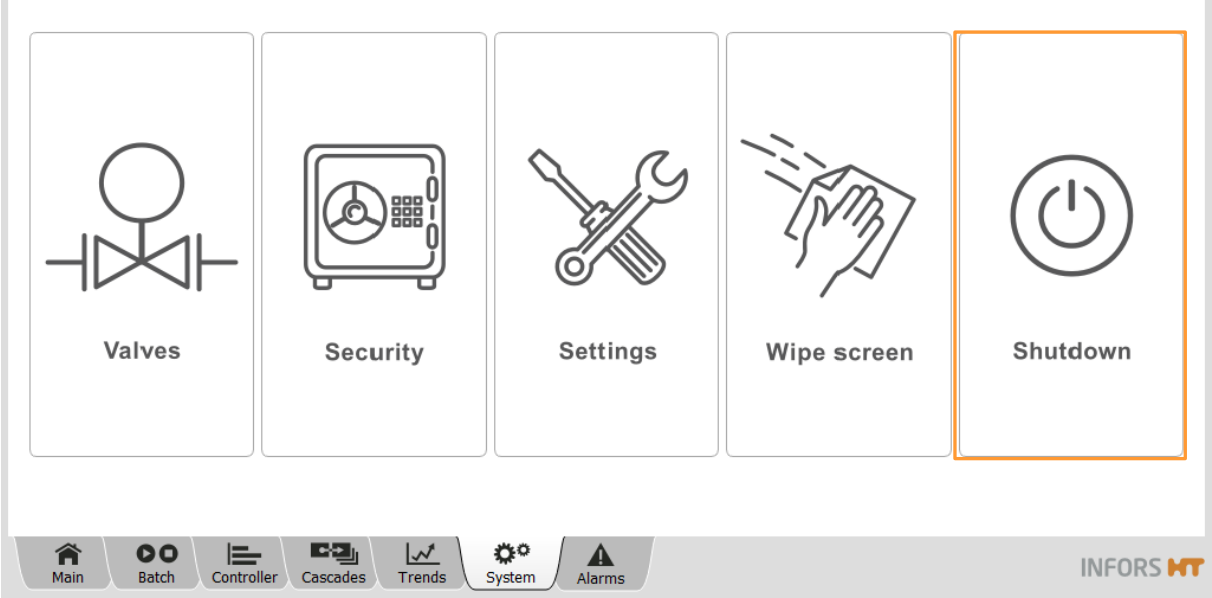
1. In main menu *System*, press **Wipe Screen**.

The screen turns white, the remaining time is displayed in seconds (*Time left: xx seconds*).



Once the time has elapsed, the last screen reappears automatically.

9.3.5 Shutdown – Shutting Down the System

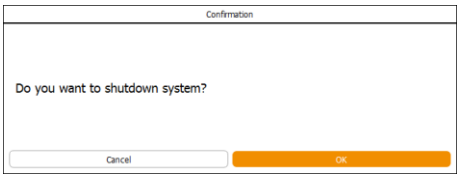


The submenu *Shutdown* has one function only: it shuts down and switches off the system. The system can only shut down and switch off if all bioreactors have been stopped.

Proceed as follows:

Procedure

1. Stop any running process by pressing **Stop** in the main menu *Batch*, if necessary.
2. Call up the main menu *System*.
3. Press **Shutdown**.



The *Confirmation* dialogue box appears with:

- Question *Do you want to shutdown the system?*
- **OK**: To shut down the system
- **Cancel**: To close the dialogue box without changes

4. Press **OK**.

   The system shuts down and switches off.

INFORMATION

ALWAYS shut down the system first, only then switch the equipment off at the main switch.

9.4 Recipes

The various buttons for the Recipes function in main menu *Batch* can be used to load and start, save or delete what are referred to as recipes. This means all parameter settings (including cascade settings) for a fermentation process can be saved and re-used for recurring operating processes later.

INFORMATION

All parameter settings, cascade settings and calibration data of sensors are saved. Pump calibration data are not saved. Calibration data of sensors are not uploaded.

9.4.1 Save Recipe – Saving a Recipe

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

To save a recipe, proceed as follows:

Procedure

1. Log on to the system on user level *Technician* or above.
2. Call up main menu *Batch* and press **Save Recipe**.

The *Save Recipe* dialogue box appears with:

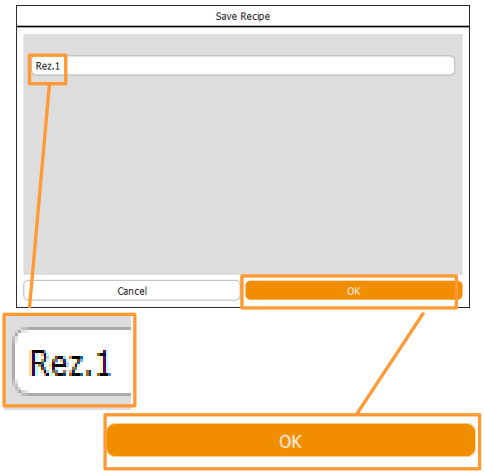
- Input field for the file name of the recipe being saved.
- **OK**: to save the recipe.

  This button is not enabled until a file name has been entered.
- **Cancel**: to cancel the process without saving.

3. Touch the input field.

   The alphanumeric keyboard appears.
4. Enter the desired file name and confirm with the **OK** key.

   The alphanumeric keyboard disappears



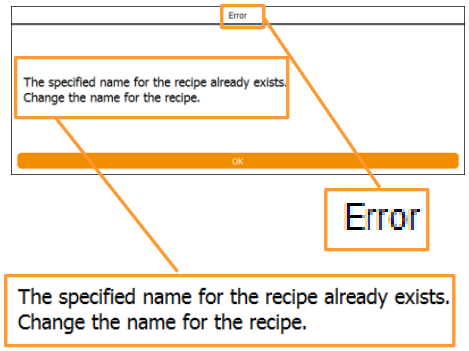
The file name is accepted, **OK** is enabled now.

5. Press **OK**.

The dialogue box disappears, the recipe is saved.

Recipe file name used twice

If the file name for a recipe has been used twice, an *Error* dialogue box appears with:



- *The specified name for the recipe already exists*
- *Change the name for the recipe*.
- **OK**: to close the dialogue box and enter the new name.

9.4.2 Load/Start Recipe – Loading and a Recipe

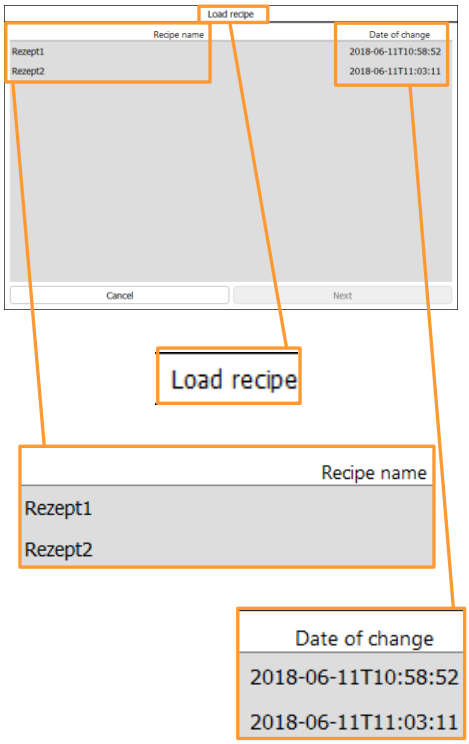
All preparations for a fermentation/cultivaion process should be made before loading and starting a recipe.

To load a recipe, proceed as follows:

Procedure

1. Log on to the system on user level *Technician* or above.

2. Call up main menu *Batch* and press **Load/Start Recipe**.

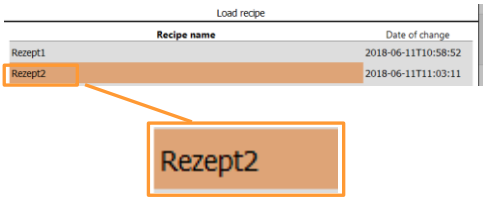


The *Load recipe* dialogue box appears with:

- *Recipe name*: lists all file names of saved recipes.
- *Date of change*: shows date and hour of the saved recipe(s).
- **Next**: to continue.

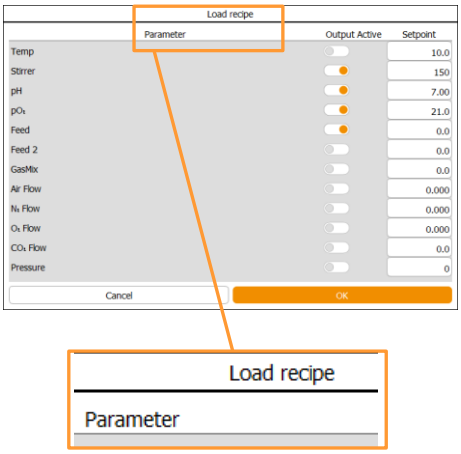
  This button is not enabled until a recipe has been selected.
- **Cancel**: to cancel the process without saving.

3. Select the saved recipe of bioreactor A.



The selected recipe is displayed with an orange background.

4. Press **Next**.



The *Load recipe* dialogue box changes views:

- *Parameter*: lists all the available parameters.
- *Output Active*: to switch parameters on/off.
- *Setpoint*: lists the saved parameter setpoint values of the recipe.

INFORMATION

This is where setpoint values can be subsequently changed here.

- **OK**: to start the bioreactor.
- **Cancel**: to cancel the process without saving.

5. If applicable, change setpoints and/or switch parameters on/off.
6. Press **OK**.

   The dialogue box disappears, the bioreactor starts.

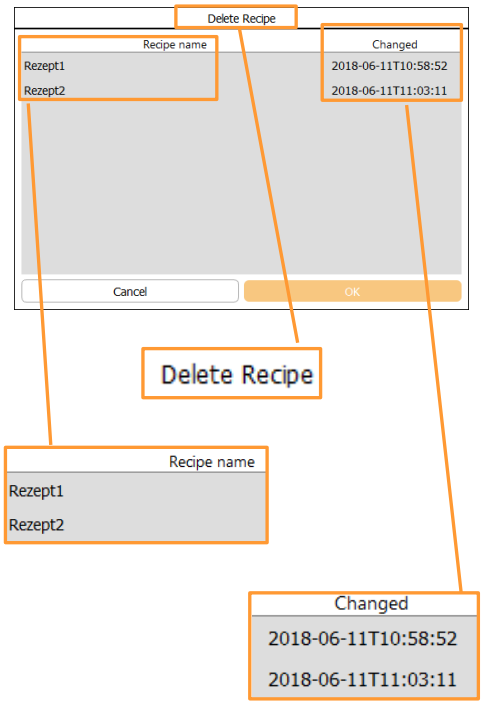
9.4.3 Delete Recipe – Deleting a Recipe

Recipes can only be deleted one by one. Recipes can also be deleted during a running fermentation process.

To delete a recipe, proceed as follows:

Procedure

1. Log on to the system on user level *Technician* or above.
2. Call up main menu *Batch* and press **Delete Recipe**.

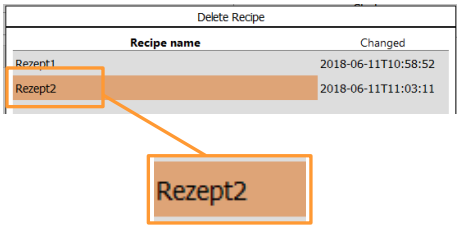


The *Delete Recipe* dialogue box appears with:

- *Recipe name* column: file name of all saved recipes.
- *Changed* column: date and time of the saved recipes.
- **OK**: to delete the selected recipe.

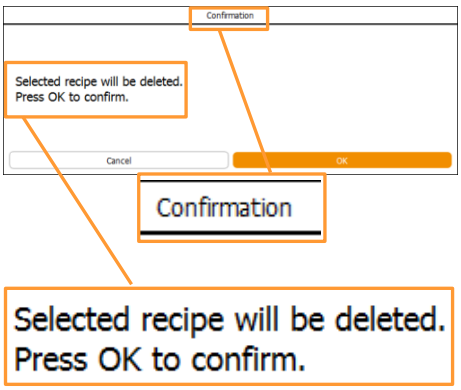
  This button is not enabled until a recipe has been selected.
- **Cancel**: to cancel the process without saving.

3. Select the desired recipe.



The selected recipe is displayed highlighted in orange.

4. Press **OK**.



The *Confirmation* dialogue box appears with:

- *Selected recipe will be deleted*
- *Press OK to confirm*
- **OK**: to delete the recipe and close the dialogue box.
- **Cancel**: to cancel the process without saving.

5. Press **OK**.

The dialogue box disappears; the recipe is deleted.

9.5 Parameters – Short Description

The following sections provide a short description of the equipment's parameters which are functional. This means, the appropriate hardware of the Techfors-S bioreactor is present and configured accordingly.

9.5.1 Temp

Measures and controls the temperature in the vessel. The measured values are recorded by a platinum resistor temperature sensor.

9.5.2 Stirrer

Measures and controls the rotation speed of the stirrer shaft. This depends on factors such as the type of vessel volume, drive system, culture viscosity and number and kind of impellers and can be found in the gassing specifications of the equipment.

9.5.3 pH

Measures and controls the pH in the culture vessel in a range of pH 2 to 12. The measured values are recorded by a traditional pH sensor (potential measurement against reference) manufactured by METTLER TOLEDO

The pH is controlled as standard by adding acid and base via the two digital peristaltic pumps *Acid* and *Base*. The activity of the pumps is time dependent. This means that they always operate in start/stop mode at the same speed. Control is made by a PID loop. A dead band can be used to prevent unwanted rapid dosing.

Temperature compensation is a special function of the pH parameter. This function must be switched on during fermentation so that the temperature dependency of the measurement principle is corrected.

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

For details about technical data, use and maintenance of the sensor see the separate documentation from the sensor manufacturer METTLER TOLEDO.

9.5.4 pO2

Measures the saturation of dissolved oxygen in the culture. The measuring system is configured for the use of a traditional amperometric/polarographic pO_2 sensor manufactured by METTLER TOLEDO.

In comparison, for example, with pH measurement which is calibrated to absolute measurements, calibrating the oxygen measurement is always performed to a relative reference point. To do this the calibration is to 100 % relative oxygen saturation, generally determined with air to a max. stirrer speed and maximum gassing rate.

The actual concentration of dissolved oxygen in mmol/L can therefore differ for 100 % saturation depending on the process.

The PID controller output from pO_2 is generally cascaded to other parameters such as *Stirrer*, *Flow*, *Feed* or *Gasmix*.

For details about technical data, use and maintenance of the sensor see the separate documentation from the manufacturer METTLER TOLEDO.

9.5.5 Antifoam

Measures the fill level or the foam formation and regulates the addition of antifoam reagent via the digital peristaltic pump *Antifoam* in the vessel. The antifoam pump is activated as soon as the antifoam sensor comes into contact with foam / liquid.

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.

9.5.6 Feed

The addition of the feed solution (feed) is regulated via the analogue peristaltic pump *Feed*. Pump speed is adjustable and can be set in steps of 0.1 % within a range of 0 % to 100 %.

9.5.7 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.

Example

2-gas-mix system with air and oxygen, supplied via a magnetic valve:

Settings

- cycle duration: 10 seconds
  (visible in the input field *Eval. Time (s)* in the option *PID* of the *GasMix* parameter)
- 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 ≙ 10 seconds

Setpoint 20 ≙ 2 seconds

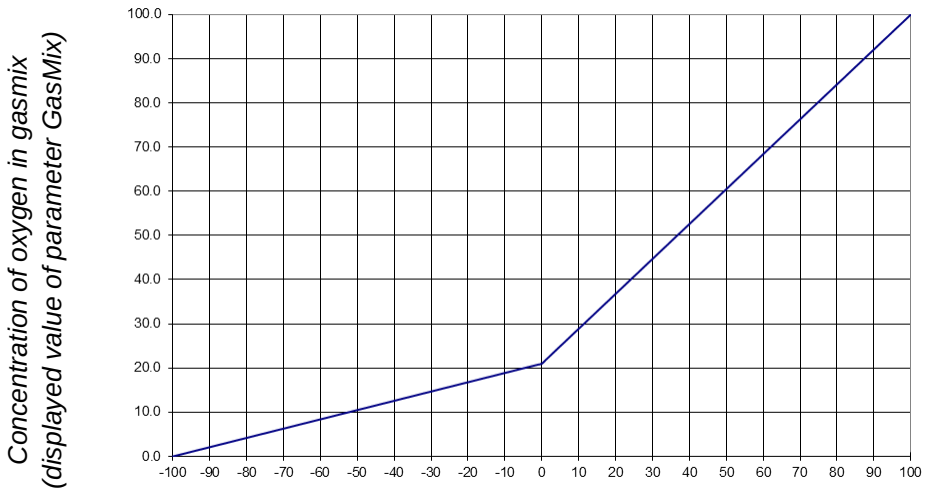
INFORMATION

For this described configuration of the 2-gas-mix system with air + oxygen with two solenoid valves, the oxygen portion of the gas mixture cannot fall below 20.95 %.

For a 3-gas-mix system the displayed value is the percentage of oxygen in the gas mixture.

However, for entering the setpoint the following applies:

- -100 = only nitrogen ≙ 0 % O_2 content
- 0 = only air ≙ 21 % O_2 content
- 100 = only oxygen ≙ 100 % O_2 content



Setpoint Parameter GasMix

If the parameter *GasMix* combined with the parameter *GM Flow* and the parameters *Air Flow*, *O2 Flow* and/or *N2 Flow* is installed and configured, the specified parameters are preconfigured by the equipment manufacturer in an advanced cascade for pO_2 control.

ATTENTION

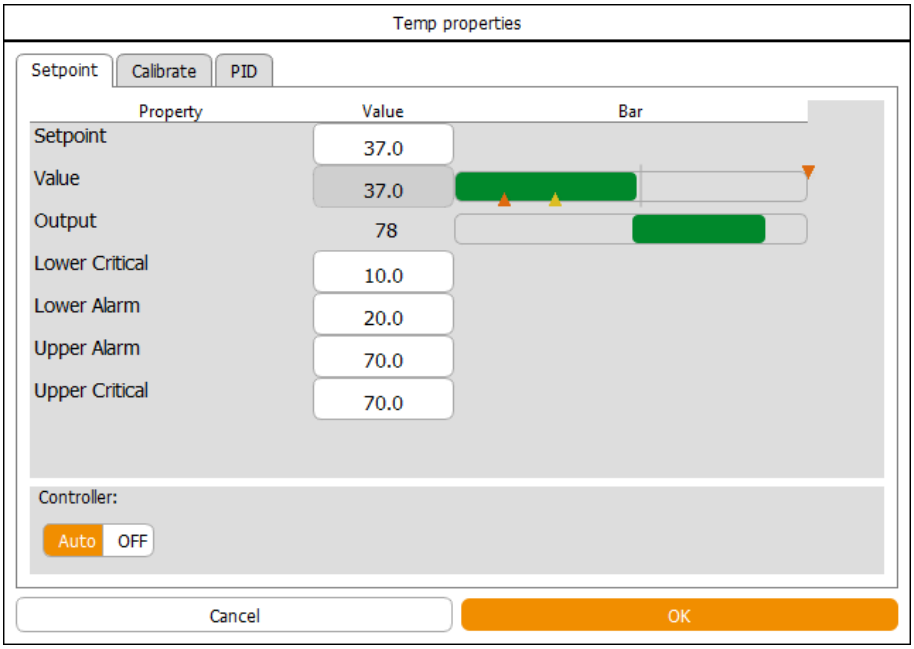
Changes to a cascade that has been preset by the equipment manufacturer may cause controller errors!

9.5.8 Flow

Measures and regulates the flow of two or more process gases in the culture vessel via a single mass flow controller (thermal mass meter with integrated control valve). The measurement system is entirely electronic and the measurement is displayed according to the present configuration in L/min.

If the parameter *Flow* is available this means that the individual process gas lines are equipped with solenoid valves, which are switched using the *Gasmix* parameter.

9.6 Parameter Options



Parameter options are setting menus for the parameters. They are shown as tab pages in the *Properties* dialogue box for the selected parameter. The figure above shows the example of the *Temp properties* dialogue box (temperature parameter).

The parameters and their options (setting menus) for each individual bioreactor are called up in main menu *Controller*.

Depending on the access authorisation and the type of the parameter, more or less options may be available.

For details on user levels and their access authorisations see the chapter “Access Authorisation of User Groups”.

Every *properties* dialogue box for each parameter has two buttons:

- **OK**: saves inputs, closes dialogue box
- **Cancel**: closes the dialogue box without changes

Most parameters have the following options:

- *Setpoint*: this is where setpoint values, alarm values and critical values can be set and where parameters can be switched on and off.
- *Calibrate*: this is where the sensors’ measured values are calibrated.

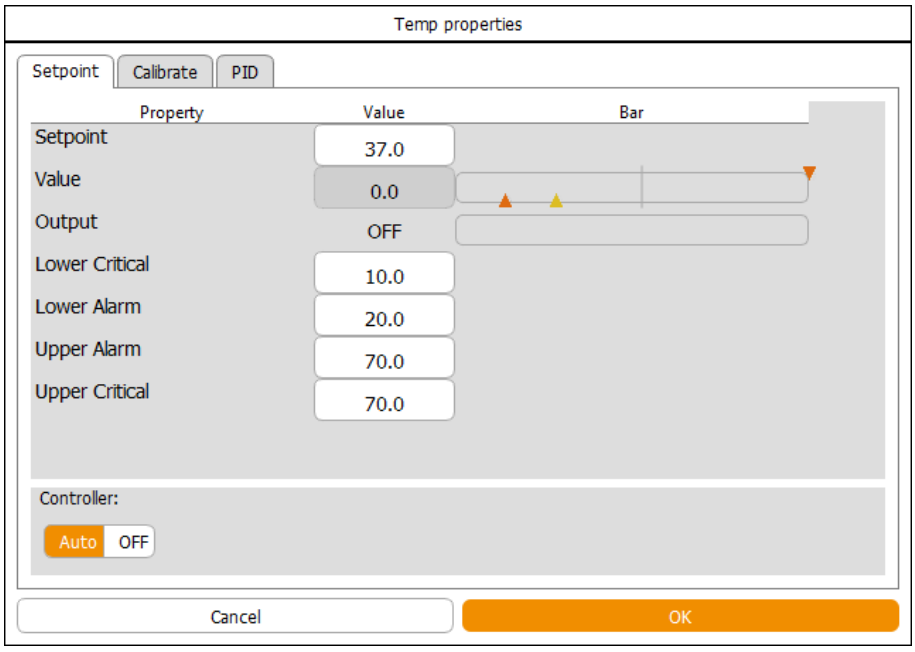
This option is only available for calibration of the measured values of the pH, pO2 and turbidity sensors (OPTEK system) on user levels *User* and *Technician*. All other calibration menus are only accessible on user level Administrator and above.

- *PID*: This is where controller settings are made.
- *Options*: This is where the basic parameter settings are made.

  This option is only accessible to the manufacturer's qualified personnel. This option is not visible or enabled at any other user level.

The following chapters describe the content and function of the individual tab pages, i.e. parameter menus. Each menu description is followed by either detailed setting instructions or a cross reference to the respective corresponding in these operating instructions.

9.6.1 Setpoint



The tab page for the *Setpoint* option is divided up into a three-column main area with input fields and view boxes and a *Controller* area.

Columns

- *Property*: designation of the input fields and view boxes
- *Value*: values of the input fields and view boxes

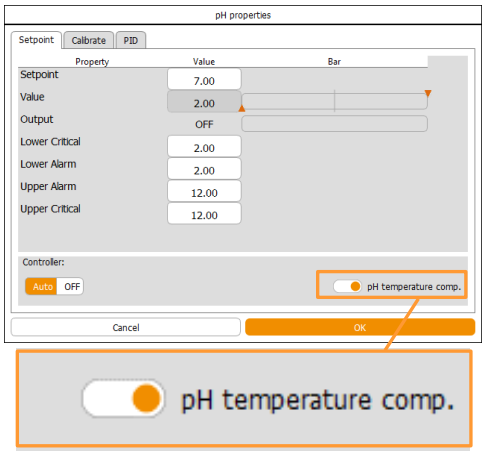
- *Bar*: graphic display of the values as in main menu Controller. For details refer to chapter “Main Menus”, “Controller – Value Display”.

Input fields and view boxes

- *Setpoint*: to enter the setpoint
- *Value*: displays the current value
- *Output*: Shows the controller output as a percentage.
- *Lower Critical*: to enter the lower critical value
- *Lower Alarm*: to enter the lower alarm value
- *Upper Alarm*: to enter the upper alarm value
- *Upper Critical*: to enter the upper critical value

Controller

- **Auto**: to switch on the parameter into automatic mode. In this mode, it is possible to switch the parameter on or off by touching the controller output (displayed value *OFF* or %) in main menu *Controller* during a running fermentation/cultivation.
- **OFF**: to switch off the parameter. This mode deactivates the controller output in main menu *Controller*, too.



The pH parameter has the additional function *pH temperature comp*. (pH temperature compensation). It has to be switched on during a fermentation/cultivation process so that temperature-compensated values can be generated. That means, the temperature dependency of the measuring principle will be corrected.

pH of liquids is temperature-dependent, too. Therefore pH will still be responsive to temperature variation, although temperature compensation is switched on.

This function also has to be switched on to calibrate the pH sensor whilst simultaneously measuring the temperature of the pH buffer solution or manually entering the temperature of the buffer solution.

INFORMATION

Temperature compensation is only relevant when the analogue measuring system is configured for the use of pH sensors from the manufacturer METTLER. The digital measuring system which uses pH sensors from the manufacturer HAMILTON this function is integrated into the sensor, and is therefore not used in the touch screen software.

9.6.1.1 Setting Setpoint Values, Switching Parameters ON / OFF

Parameter setpoint values are basically set in the configuration dialogue for the bioreactor. Once the bioreactor is running, setpoint values can be changed then via main menu *Controller*.

Parameters can be switched on or off in the configuration dialogue or via main menu *Controller* once the bioreactor is running, if their controller output is set to automatic mode (*Auto*) in the *Setpoint* option of the parameter.

In stopped state of the bioreactor, all its parameters are automatically switched off and cannot be switched on.

INFORMATION

The bioreactor is always started with the settings in the configuration dialogue. Changes to these settings are saved and transferred to the next configuration dialogue. If setpoint values are changed or parameters are switched on/off whilst the bioreactor is running, these settings are only adopted for the current fermentation process.

Note the following when setting setpoints:

When using a lightly foaming medium, set the setpoints in parameters *Stirrer* (stirrer speed) and the different *Flow* parameter(s) as low as possible if this does not have a negative effect on the oxygen supply to the culture. If there is still heavy foaming, a chemical antifoaming agent will need to be used. In this case the *Dose time* and *Wait time* in the parameter *Antifoam* has to be set accordingly.

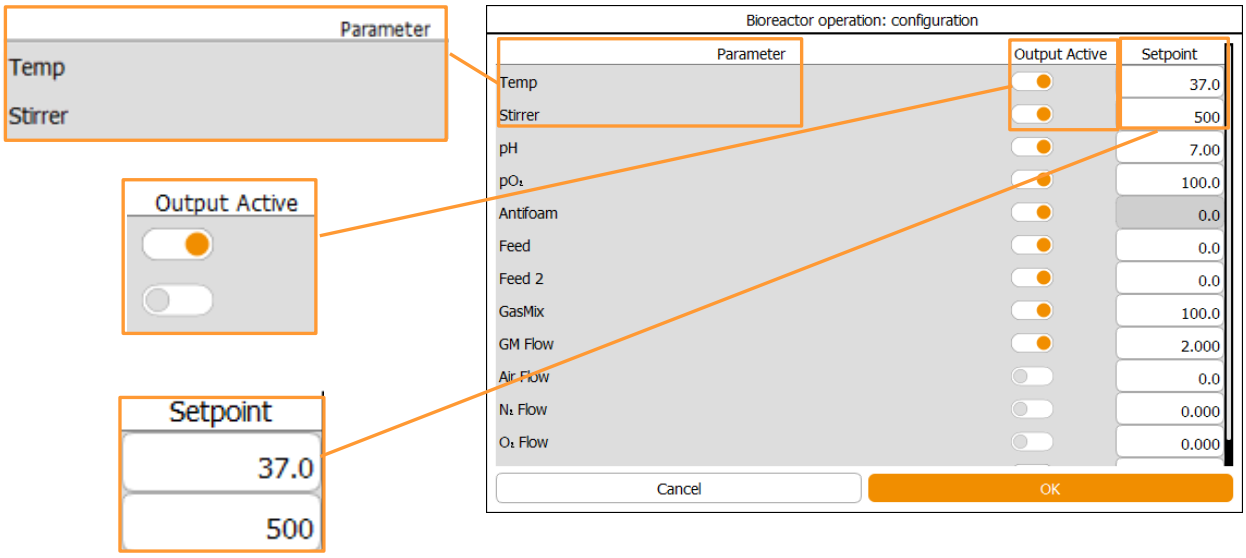
Settings in the configuration dialogue

To make the settings in the configuration dialogue, proceed as follows:

Procedure

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

The *Configuration bioreactor operation* dialogue box appears with:



- *Parameter*: lists all the available (depending on the equipment configuration) parameters
- *Output Active*: to switch each parameter individually on or off, if the *Controller* in the *Setpoint* option of the parameter is set to automatic (*Auto*) mode.
- *Setpoint*: lists all parameter setpoint values with which the bioreactor is started. Setpoint values can be changed here.
- **OK**: to save inputs and start the bioreactor (fermentation/cultivation)
- **Cancel**: to close the dialogue box without changes

2. Press ***Setpoint*** of the desired parameter, e.g. *Stirrer*.

   The numeric keypad appears.
3. Type in the desired setpoint value, e.g. **300**, and confirm with the **OK** key.

   The numeric keypad disappears; the value is accepted for the *Setpoint* view box/input field.
4. Repeat the same procedure for all desired parameters.
5. Switch on/off parameters as required.
6. Press **OK**.

   The dialogue box disappears, the settings are saved, and the bioreactor (fermentation/cultivation) is started.

   Changed settings are transferred to the next configuration dialogue.

Settings on the running bioreactor

To make the settings on the running bioreactor, the following two options are available:

a) Directly via the *Setpoint* input field/view boxes and the controller output buttons in the *Output* column of the main menu *Controller*.

b) In the *Setpoint* menu of the selected parameter in the *Parameter* column of the main menu *Controller*.

INFORMATION

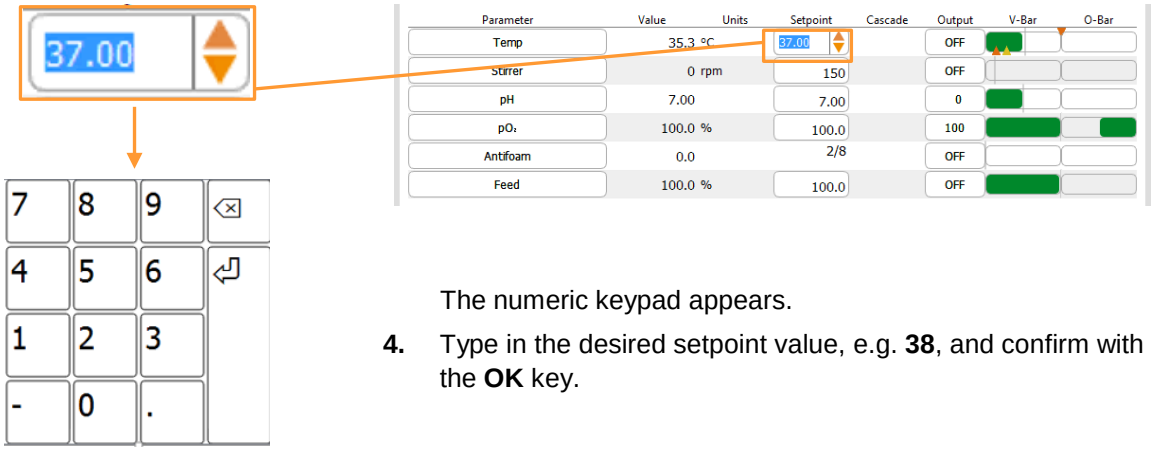
Changed settings are adopted for the fermentation/cultivation process in progress only.

Proceed as follows:

Variant a)

Procedure

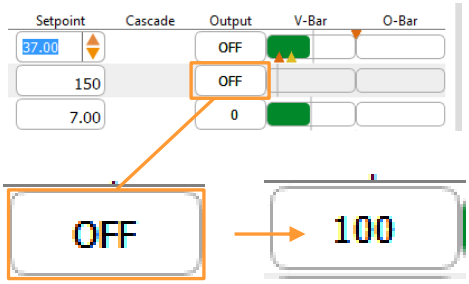
1. Select the desired bioreactor from the selection bar, e.g. bioreactor A.
2. Call up main menu *Controller*.
3. Press the *Setpoint* input field/view box of the desired parameter, e.g. *Temp.*



The numeric keypad appears.

4. Type in the desired setpoint value, e.g. **38**, and confirm with the **OK** key.

The numeric keypad disappears; the value is accepted for the *Setpoint* view box/input field.



5. Press the controller output button of the parameter.

The parameter is switched on, the controller output changes from *OFF* to the display of the corresponding numeric value in %.

INFORMATION

To switch the parameter i.e. controller output on or off here, is only possible, if the controller of the parameter is set to automatic (Auto) mode in its *Setpoint* option. See also next procedure in variant b).

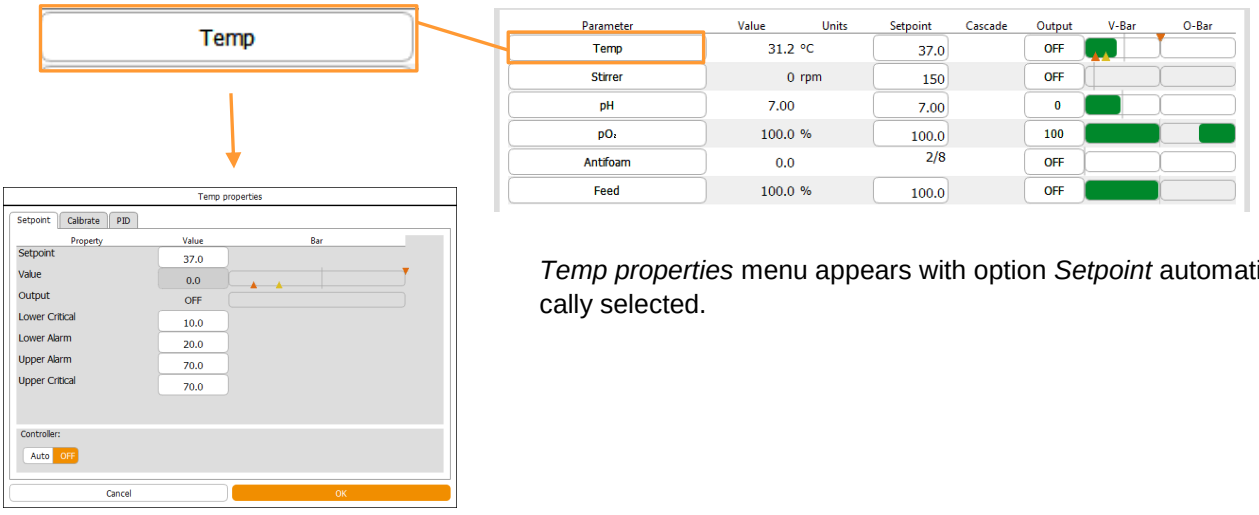
6. Repeat the same procedure for all desired parameters.

Variant b)

Procedure

1. Call up main menu *Controller*..

2. Press the desired parameter button, e.g. **Temp**, in the *Parameter* column.



Temp properties menu appears with option *Setpoint* automatically selected.

3. Press ***Setpoint***.

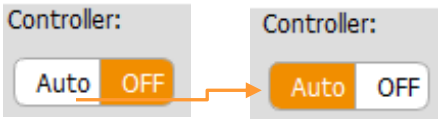
The numeric keypad appears.

Type in the desired setpoint value, e.g.**38**, and confirm with the **OK** key.

The numeric keypad disappears; the value is accepted for the *Setpoint* input field**.**

4. Change alarm values and critical values as required.

For details about alarm value and critical value settings refer to chapter „Setting Alarm Values and Critical Values”.



5. Ensure the controller output is switched to automatic mode (**Auto)**, change setting as necessary.

   The parameter is set switched on now.

6. Press **OK**.

   The dialogue box disappears, the settings are saved.

7. Repeat the same procedure for all desired parameters.

9.6.1.2 Setting Alarm Values and Critical Values

Alarm values and critical values can be set symmetrically or asymmetrically.

- Symmetrically: The difference between the setpoint value and the upper alarm value or the upper critical value = the difference between the setpoint value and the lower alarm value or the lower critical value.
- Asymmetrically: The difference between the setpoint value and the upper alarm value or the upper critical value ≠ the difference between the setpoint value and the lower alarm value or the lower critical value.

Upper alarm values can be set ≤ upper critical values. Lower alarm values can be set ≥ lower critical values.

A parameter alarm is triggered as soon as a value drops below the lower alarm value or exceeds the upper alarm value. For details see the chapter “Alarms – Parameter Alarms, User Alarms, System Alarms”, “Parameter Alarms”.

INFORMATION

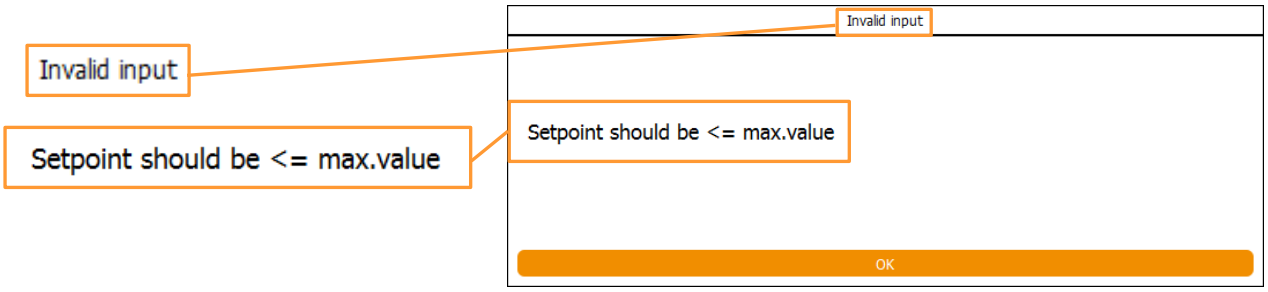
Alarm values and critical values have to be set by selecting the desired parameter in the main menu Controller and calling up its *Setpoint* option menu. The setting procedure remains the same as for setpoint values. The bioreactor can be in stopped or running state while entering these values.

Invalid setpoint value or alarm limit input

When an invalid setpoint, alarm or critical alarm value is entered, a corresponding *Invalid input* dialogue box appears after confirming the entered value via OK key.

Example with input of setpoint > max. value

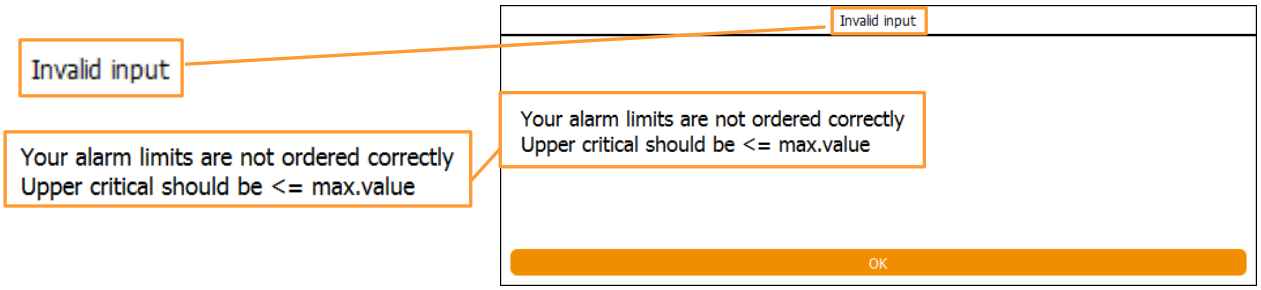
Invalid input dialogue box appears with:



- *Setpoint should be <= max. value*
- **OK**: To close the dialogue box without changes and enter a new setpoint.

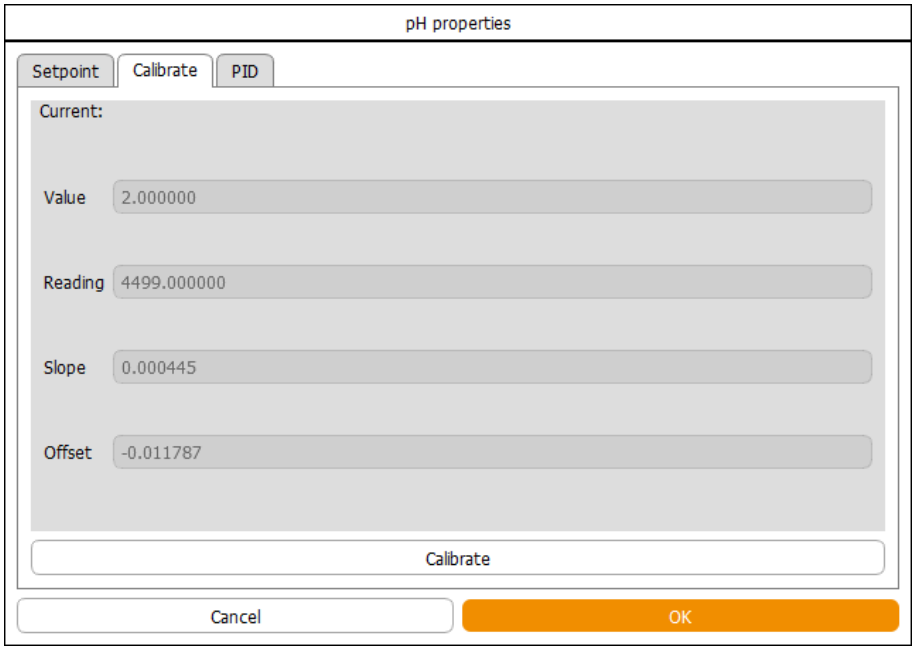
Example with input of upper critical value > max. value

Invalid input dialogue box appears with:



- *Your alarm limits are not ordered correctly. Upper critical should be <= max. value*.
- **OK**: To close the dialogue box without changes and enter a new value.

9.6.2 Calibrate



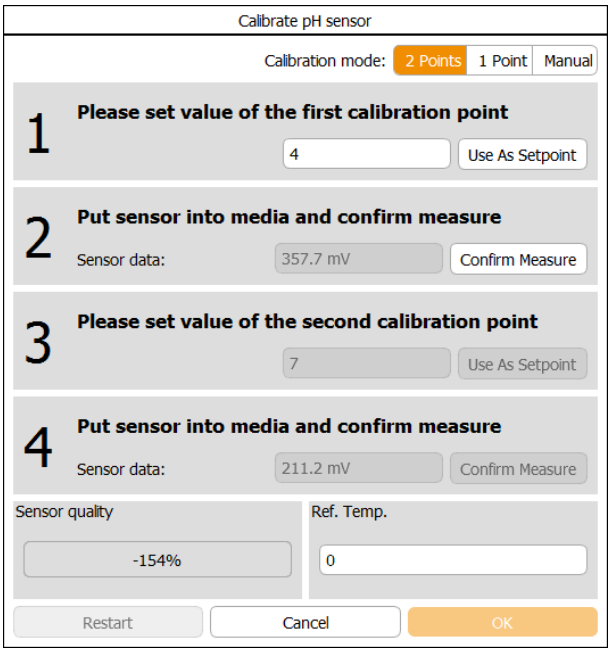
The tab page for the *Calibrate* option contains four view boxes and a button:

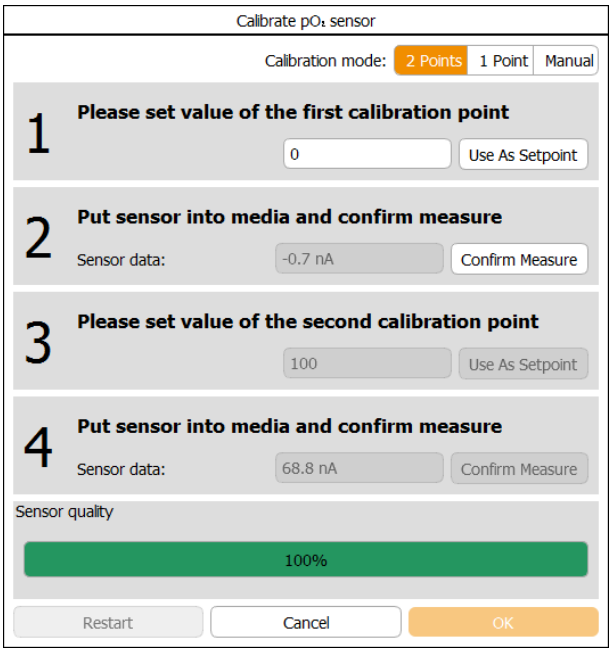
- *Reading*: shows the current measured value in digital units
- *Value*: shows the current measured value depending on the last calibration
- *Slope*: shows the digital value of the calculated slope of the calibration line
- *Offset*: describes the intersection point of the calibration line with the X axis
- **Calibrate**: to open the calibration menu

The calibration menus for pH and pO_2 can also be called up directly via **Calibrate pH** and **Calibrate pO2** in the main menu *Batch*. These two menus are described in the following chapter in detail.

9.6.3 Calibration Menus pH and pO2 Sensors

The below figures show the calibration menu for METTLER pH sensors on the left-hand side and on the right, the calibration menu for METTLER pO_2 sensors. Both menus look essentially the same, small differences are explained in the following menu description.





The calibration menu contains the following:

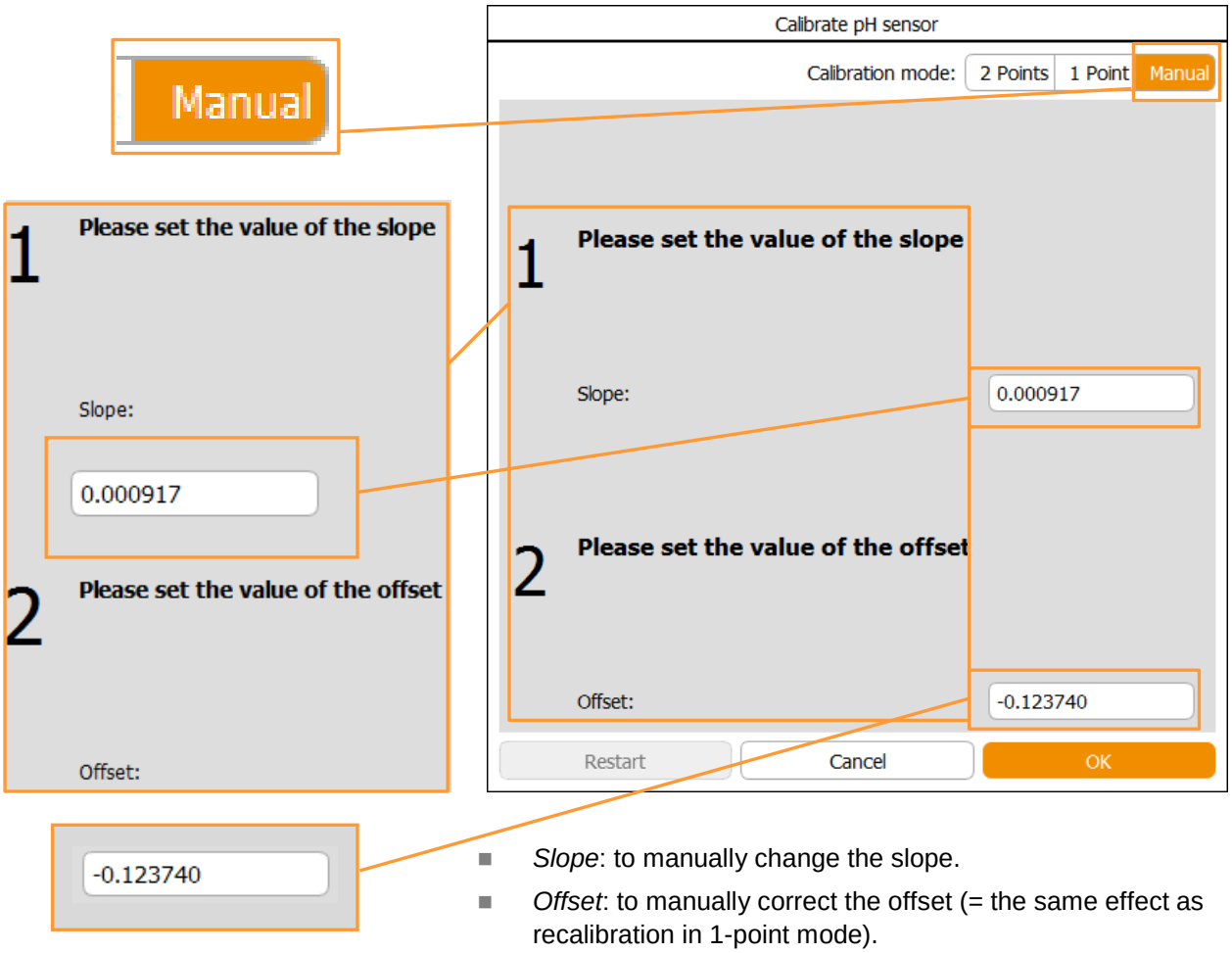
Header: Calibration mode

- **2 point**: to select 2-point calibration mode.

  This mode is automatically selected in the calibration menu for pH sensor calibration.
- **1 point**: to select 1-point calibration mode.

  If the pH sensor has to be recalibrated, this is carried out in 1-point calibration mode.
- **Manual:** to select manual calibration mode

  This mode is only relevant to the user for parameter pH. The menu contains:



- *Slope*: to manually change the slope.
- *Offset*: to manually correct the offset (= the same effect as recalibration in 1-point mode).

  For details on recalibration see the chapter “Recalibrating the pH Sensor”.

INFORMATION

For all other parameters the manual button is only relevant to the manufacturer’s service specialists. The necessary full menu can only be accessed at the service level.

Main section: Line 1 and 3

- Instruction: *Please set value of the first / of the second calibration point*.
- **Use As Setpoint (pO2):** this function is only relevant and can only be used under certain circumstances at the *Technician* user level. For details see the chapter “Special Function USE AS SETPOINT”.

INFORMATION

For all other parameters the USE AS SETPOINT button is only relevant to the manufacturer's service specialists.

Main section: Line 2 and 4

- Instruction: *Put sensor into media and confirm measure.* For the pH sensor this is the buffer solution.
- *Sensor data*: displays the measurement.
- **Confirm Measure**: to confirm measurement.

INFORMATION

The input fields and buttons in line 3 and 4 are only available once the first measurement has been confirmed. Line 3 and 4 are faded out in 1-point calibration mode.

Lower section

- *Sensor quality* display bar: charts the quality of the sensor.

  If the green colour in the display bar is barely or not at all visible:

  - pH sensor: replace the sensor.
  - pO_2 sensor: replace the membrane body of the sensor in accordance with the sensor manufacturer's instructions in separate documentation.

  If the green colour fills less than half of the display bar:

  - pO_2 sensor, recommended: replace the sensor in accordance with the sensor manufacturer's instructions in separate documentation.
- *Ref. Temp*: displays the measured temperature of the reference buffer solution, or is used as an input field to manually enter the temperature of the reference buffer solution.

INFORMATION

This field is only relevant for the pH sensor. It is only visible and available if the temperature compensation function in the setpoint menu has been switched on.

Footer

- **Restart calibration**: to restart the calibration.
- **Cancel calibration**: to abort calibration.
- **OK**: to confirm calibration, close calibration menu

OK and **Restart** are only available once at least one measurement has been confirmed.

9.6.3.1 Calibrating the pH Sensor – General Information

The bioreactor system is equipped and preconfigured ex-factory with the measuring system for the use of the analogue pH sensors from the manufacturer METTLER.

For all pH sensors it generally applies that a reliable pH measurement always needs a 2-point calibration with a high and low reference buffer. It also applies that the calibration should be performed again before each fermentation/cultivation process. Calibration must be performed prior to sterilisation, in other words before inserting the pH sensor in the vessel.

The sequence that the two reference points are calibrated is irrelevant for the existing bioreactor measurement system.

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 equipment during calibration. Another option is to measure the temperature externally and enter the value manually in the touch screen software. If not measured or manually input, the buffer temperature is assumed to be 20 °C.

Detailed information on the calibration of the pH sensors and of the pH buffers supported by the sensors can be found in separate documentation provided by the sensor manufacturer.

The following describes a 2-point calibration of a METTLER pH sensor with manual entry of buffer solution temperature. This means that the calibration takes place with temperature compensation switched on.

INFORMATION

This corrects 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.

9.6.3.2 Calibrating the pH Sensor - Procedure

To calibrate the pH sensor, proceed as follows:

Procedure

1. Connect the sensor cable.

Ensure the cable is not buckled or twisted.

ATTENTION

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

2. Call up main menu *Controller*, select parameter *pH* and call up Option *Setpoint*.

3. Switch pH temperature compensation on.

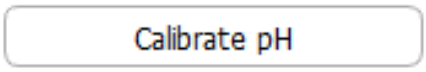
4. Press **OK**.

   The dialogue box disappears, the setting is stored.

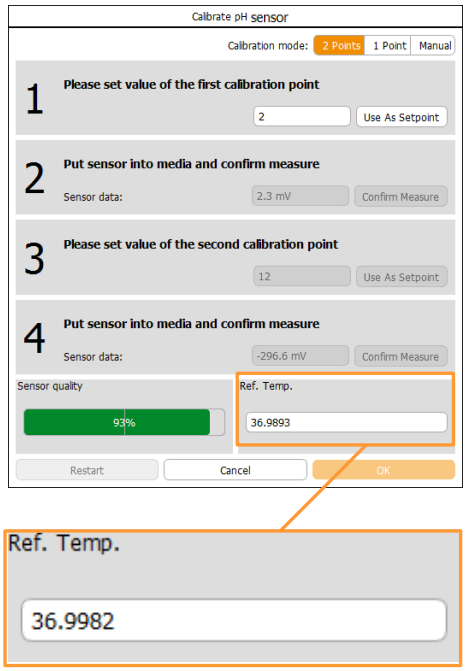
5. Carefully remove the watering cap from the pH sensor and rinse the pH sensor with distilled water, do not rub!

ATTENTION

Dry wiping or rubbing a pH sensor after rinsing can cause electrostatic charge. This can greatly increase the response time and generate incorrect measurements. At most, gently dab a pH sensor after rinsing, **NEVER** rub or wipe it!



6. Call up main menu *Batch* and press **Calibrate pH**.



The calibration menu *Calibrate pH sensor* appears.

The 2-point calibration mode is automatically selected. The *Ref. Temp* input field/view box is displayed.

INFORMATION

Without switching pH temperature compensation on before, this field is not visible.

7. Press the input field in line 1.

   The numeric keypad appears.

8. Type in the value of the low (or high) reference buffer confirm with the **OK** key.

INFORMATION

The order in which the reference points are calibrated is irrelevant.

The numeric keypad disappears, the value is adopted.

9. Press the ***Ref. Temp*** view box/input field.

   The numeric keypad appears.

10. Enter the temperature value of the buffer solution and confirm with the **OK** key.

    The numeric keypad disappears; the value is adopted.

11. Hold the pH sensor into the relevant buffer solution.

    The measurement (in mV) is displayed in line 2 in *Sensor data*.

    As soon as the measurement is stable:

12. Press **Confirm Measure** in line 2.

    The calibration value is accepted. The input fields and buttons in line 3 and 4 are available now.

INFORMATION

The signal characteristics are asymmetric. In other words, the closer the signal comes to the real value, the slower the change. The calibration is inaccurate, if the measurement is confirmed with OK before the sensor signal has completely stabilised. Wait a few minutes before confirming with OK and check the reading again, if in doubt.

13. Rinse the pH sensor with distilled water, do not rub!

14. Press the input field in line 3.

The numeric keypad appears.

15. Type in the value of the high (or low) reference buffer and confirm with the **OK** key.

INFORMATION

The order in which the reference points are calibrated is irrelevant.

The numeric keypad disappears; the value is adopted.

16. Put the pH sensor into the relevant buffer solution.

The measurement (in mV) is displayed in line 4 in *Sensor data*.

As soon as the measurement is stable:

17. Press **Confirm Measure** in line 4.

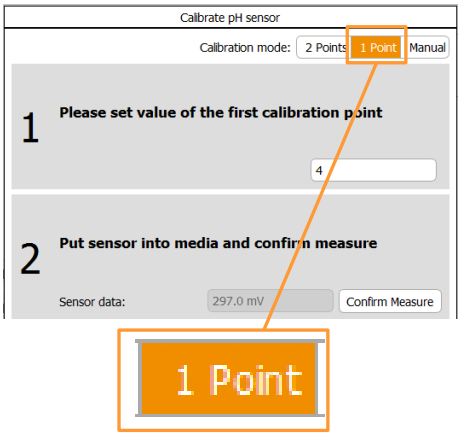
The calibration value is accepted.

18. Press **OK**.

The dialogue box disappears, the calibration values are stored.

19. Rinse the pH sensor with distilled water, do not rub!

9.6.3.3 Recalibrating a METTLER pH Sensor



To compensate for a deviation (drift) in the measurement over a long-term fermentation, it is possible and sufficient to recalibrate with a 1-point calibration. This means that the pH of a sample measured using an external measurement device is accepted as the new reference value in 1-point calibration mode.

The same effect is achieved by manually correcting the offset (deviation). In other words, the difference between the externally determined measurement and the displayed measurement in the culture needs to be added to or subtracted from the last calculated offset value depending on the result. The correction is made in manual calibration mode.

9.6.3.4 Polarising the pO_2 Sensor (METTLER)

Polarographic pO_2 sensors must be polarised at initial operation or after disconnection from the voltage source. Correct calibration is not possible otherwise. This means that the pO_2 sensor must be polarised before calibration.

For polarisation, the sensor cable must simply be connected to the pO_2 sensor and the equipment must be switched on at the main switch.

Duration of polarisation (= polarisation time) depends on how long the pO_2 sensor has been disconnected from the voltage source (= depolarisation time)

As a general rule: if depolarisation time > 30 minutes, the minimum polarisation time is 360 minutes.

More details about polarisation can be found in the separate documentation form the manufacturer METTLER TOLEDO.

9.6.3.5 Calibrating the pO_2 Sensor – General Information

The bioreactor system is equipped and preconfigured ex-factory with the measuring system for the use of analogue, polarographic METTLER pO_2 sensors.

Generally it applies that: calibrating the pO_2 sensor should be performed after sterilisation because sterilisation can change the gradient of the pO_2 sensor. A 1-point calibration to 100 % is generally sufficient for an exact measurement and should be carried out again before each fermentation.

The zero point (0 % calibration) should be checked at regular intervals of about 6 months.

When performing a 2-point calibration, the 0 % calibration must always be performed before the 100 % calibration.

The polarographic METTLER pO_2 sensors need to be polarised before calibration. For details on this see the chapter “Polarising the pO_2 Sensor”.

Detailed information on the polarisation, calibration, use, maintenance and servicing can be found in the separate sensor documentation of the manufacturer.

100 % calibration conditions

The 100 % calibration of the pO_2 sensor is performed under the following conditions:

- in the medium
- at the operating temperature
- at the maximum expected stirrer speed
- at the maximum expected gassing rate with air or the oxygen-containing gas(es) provided for fermentation/cultivation

0 % calibration conditions

The operating conditions of the 0 % calibration are the same as the 100 % calibration. One exception is the gassing.

To displace oxygen out of the medium, the medium has to be gassed before and during the 0 % calibration with nitrogen instead of with air or the gas(es) used for fermentation/cultivation.

9.6.3.6 Calibrating the pO_2 Sensor - Procedure

The following example describes a 2-point calibration of a (polarographic analogue) METTLER pO_2 sensor. This needs to take place in the correct sequence. This means that the first calibration point is 0 % (zero point), the second calibration point is 100 %.

Proceed as follows:

Procedure

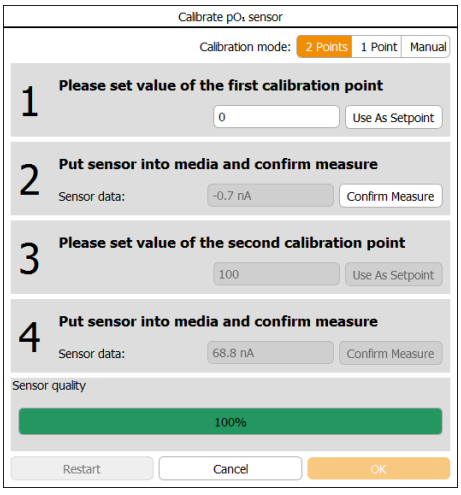
1. Connect the gassing line to nitrogen. In doing so, leave the gas supply turned off.

INFORMATION

Depending on the equipment configuration, there may already be a nitrogen gas line. In this case you only need to adjust the gas supply accordingly.

2. In main menu *Batch*, call up the bioreactor configuration menu (**Start** button).
3. Set the temperature setpoint and switch on the parameter.
4. Set the maximum expected stirrer speed during fermentation and switch on the parameter.
5. Start the bioreactor.
6. Slowly turn on the nitrogen supply and gas the medium.
7. Wait until the required stirrer speed and operating temperature are reached and the oxygen is displaced out of the medium.

8. Call up main menu *Batch* and press **Calibrate pO2**.



The calibration menu *Calibrate pO2 sensor* appears.

The 2-point calibration mode is automatically selected.

INFORMATION

The Use As Setpoint button is not relevant for this calibration.

If the value in the first input field is not set to 0 (zero for zero point = 0 %):

9. Press the first input field (…*first calibration point*) in line 1.

   The numeric keypad appears.
10. Type in the value 0 confirm with the **OK** key.

The numeric keypad disappears; the value is adopted.

As soon as the measurement (line 2, *Sensor data*) is stable:

11. Press **Confirm Measure** in line 2.

The value is accepted as 0 % oxygen.

12. Switch off the nitrogen gassing and switch on normal gassing.

13. Set the maximal expected gassing value during fermentation/cultivation.

If the value in the second input field is not set to 100 (for 100 %):

14. Press the second input field (…*second calibration point)* in line 3.

The numeric keypad appears.

15. Type in the value 100 and confirm with the **OK** key.

The numeric keypad disappears; the value is adopted.

16. Wait until the medium is saturated with oxygen.

As soon as the measurement (line 4, *Sensor data*) is stable:

17. Press **Confirm Measure** in line 4.

The value is accepted as 100 % oxygen saturation.

18. Press **OK**.

The dialogue box disappears, the calibration is stored.

Special Function USE AS SETPOINT

The special function *USE AS SETPOINT* is for users of the *Technicians* user level and is only relevant in the calibration menu of the pO_2 parameter when using METTLER sensors.

It can only be used if a three-fold gas mixture (air/O_2/N_2) is installed and the parameter *Gasmix* is configured in a cascade for the pO_2 regulation.

INFORMATION

For all other parameters the USE AS SETPOINT button is only relevant to the manufacturer's service specialists.

How it works

In the calibration menu of the *pO2* parameter (METTLER sensors):

a) 0 % calibration

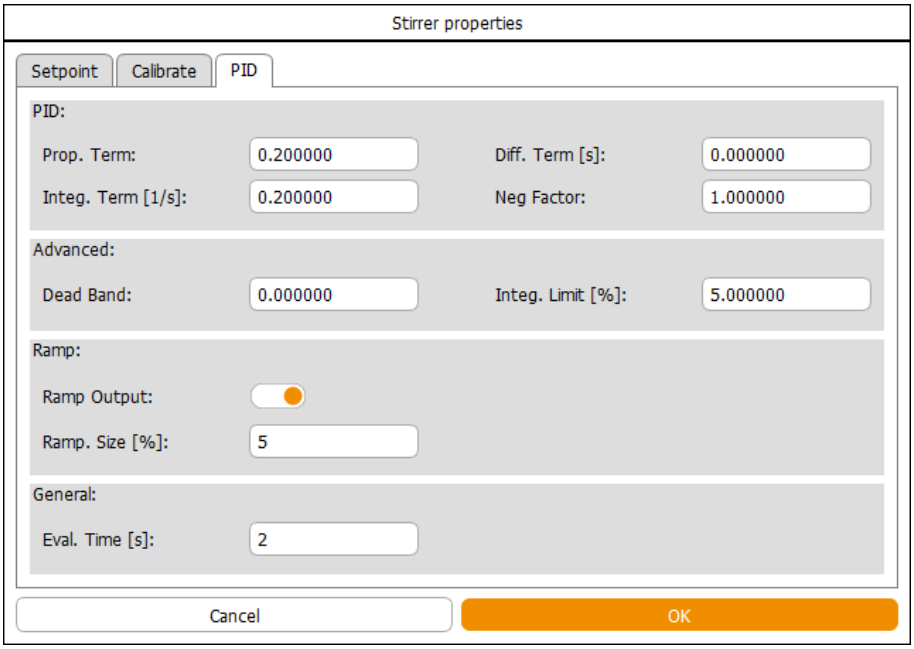
The input ***0*** (%) in the input field of the first calibration point and touching the **USE AS SETPOINT** button causes the *Gasmix* parameter to switch to nitrogen for this value.

b) 100 % calibration

(2nd point), before entering the ***100*** value:

The input ***21*** (%) in the input field of the second calibration point and touching the **USE AS SETPOINT** button causes the *Gasmix* parameter to switch to air for this value. The value can then be changed to ***100*** (%) in the input field and the calibration completed.

9.7 PID (Control)



The *PID* tab page is split into four horizontal areas and contains input fields for PID control settings. The following table explains the function of the individual setting values in more detail.

A detailed explanation of PID control with important notes for its settings can be found in the following chapters.

Note the following:

- In the case of parameters which are not controlled but only measured, only the value in the Eval Time (s) input field is relevant. This value is always > 0.
- If the ramp output is switched off, the value in the Ramp Size % input field is not relevant.

Operation Touch Screen Software

Setting value	Description
Prop. Term	Proportional factor: The greater the discrepancy between the set-point value and the actual value the greater the controller output.
Integ. Term [1/s]	The integral factor aggregates all errors over the time. If the setpoint is not achieved using the proportional factor, the integral factor adjusts the output successively until the setpoint value is achieved. An integral factor set too high will lead to oscillation of the control loop.
Diff Term [s]	The differential quotient calculates the change in the actual value over the time and counteracts this change to limit any overshoot.
Neg. Factor	The negative factor can be used to add weighting to two-sided control (+100 to -100 %) (e.g. heavy acid, light alkali). In the process 1 is the balance and 0.5 or 2 equate to the half or double the controller output accordingly. Example: Nitrogen influences the pO_2 value less than oxygen, thus a negative factor of 2 can compensate for the reaction of the controller.
Dead Band	If a dead band is entered, no control is implemented within this value at either side of the setpoint value (symmetrically, + / -). I.e. the controller output is = 0. The dead band is used for pH control.
Integ. Limit [%]	The integral influence is used to ensure that the integral factor cannot increase over an indefinite period. This limits erroneous accumulation. The integral influence is set between 0 and 100 % of the controller output.
Ramp output	In order to perform changes slowly or step-by-step, a ramp can be introduced. This is useful above all for the stirrer speed or a mass flow valve.
Ramp Size [%]	The ramp size is a percentage value with which the controller output is increased step-by-step and evenly over a set time. For the set time see the value (in seconds) in the Eval Time input field.
Eval Time [s]	The evaluation time determines the intervals in seconds at which the PID value is recalculated. The controller speed is defined this way. A scanning time of 10 seconds is a good average value.

9.7.1 Explanations of PID Control

The PID function is based on a generic formula provided as example:

$$Error_n = \frac{Set - Act}{Max.Value - Min.Value}$$

$$Output_n = P.Term * \left\{ Error_n + I.Term \cdot \int_{i=0}^{n} Error_i + D.Term \cdot (Error_n - Error_{n-1}) \right\}$$

Explanation of the formula

- Error = deviation between setpoint value and actual value.
- P = proportional factor, proportional response to an error, used to reach a setpoint.
  The bigger the value, the sharper the control.
- I = integral factor, integration of the error in 1/second.
  A typical integral factor is < 0.05.
- D = differential quotient, derivative of the error, set in seconds (mostly to 0).

Be aware of the following relating to the individual factors:

Proportional factor

The change of the proportional factor has a considerable effect on a running process.

If the proportional factor is increased excessively, this causes oscillations in the control loop around the setpoint value.

Example, the pH parameter

To achieve the setpoint value, a little acid, then a little base, acid again, then base etc. is added.

If the proportional factor is reduced excessively, the controller hardly reacts to the deviations and never achieves the setpoint value.

Integral factor

The integral factor should have a low value and only be changed a little in small steps with long pauses.

The ideal approach is to switch off the equipment briefly after changing the integral factor in order to delete the pending error calculation.

A typical integral factor is < 0.05. It should equate to the reciprocal value of double to quadruple the system's cycle duration. The higher the entered value, the less the time (in seconds) remains for control.

A higher value than 0.05 is generally of no use as it exceeds the time minimum for which the control is required. This causes fluctuations in the control circuit.

Example of calculation of the integral factor

The cycle duration of system oscillations is measured at 50 seconds from amplitude to amplitude. The integral factor is thus calculated as follows:

1 / (50 sec x 2) = 0.01 1/sec

1 / (50 sec x 4) = 0.005 1/sec

Integral factor	Seconds
0.1	10
0.05	20
0.001	100
0.005	200

Differential quotient

The differential quotient is rarely required. It is set to 0 (zero) at the beginning.

A high value is only necessary if major changes are made in quick succession. In all circumstances it causes the controller output to react stronger.

9.7.2 Changing the PID Controller Settings

When making changes to the PID controller settings proceed as follows:

Procedure

1. Make a note of the factory settings, i.e. make sure they can be restored, if necessary.
2. For readjustment of a PID controller, start with the setting for the proportional factor. Select a proportional band width as large as possible.
3. Reset the integral factor and the differential quotient to zero.
4. Increase the proportional factor until the controller causes the actual value to oscillate.

5. Measure the oscillation duration. E.g. with the diagram of the parameter in the software from the equipment manufacturer.
6. Halve the proportional factor and vary the integral factor between the reciprocal value of the doubled and quadrupled oscillation duration.

9.8 Cascade Control

The main menu *Cascade* provides the option of setting up a cascade control of a process parameter – mostly pO2. This means that the controller output parameter (=Output) of the master controller (e.g. pO2) is used as a master parameter for the slave controller(s).

INFORMATION

The master controller and slave controllers are also called master and slave.

Serial cascade

A deviation of the setpoint of the parameter to be controlled (master controller) influences the setpoint of the first parameter (slave controller) in the cascade.

If the first parameter in the cascade reaches its maximum or minimum setpoint and the setpoint of the parameter being controlled is not yet achieved, the next parameter in the serial cascade is activated and so it continues.

In the example of the left-hand figure:
The parameter *Stirrer,* the 1st slave controller, is activated first in the cascade, to control the pO_2 parameter, the master controller.
The parameter *AirFlow,* the 2nd slave controller, is only activated when the setpoint of parameter pO_2 has not been achieved by the *Stirrer* parameter.

Parallel cascade

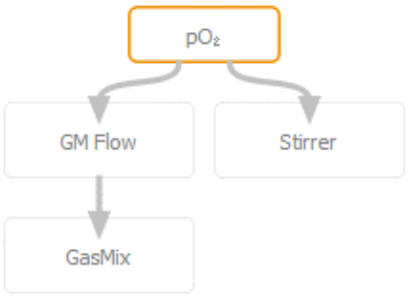
A deviation of the setpoint of the parameter to be controlled (master controller) influences the setpoint of all parameters (slave controllers) that are in the cascade.

In the example of the left-hand figure:
The parameters *Stirrer* and *Air Flow*, both slave controllers, are activated at the same time to control the *pO_2* parameter, the master controller.

Parallel serial cascade

A deviation of the setpoint of the parameter to be controlled (master controller) influences the setpoint of all parameters (slave controllers) that are parallel and the first element in the cascade.

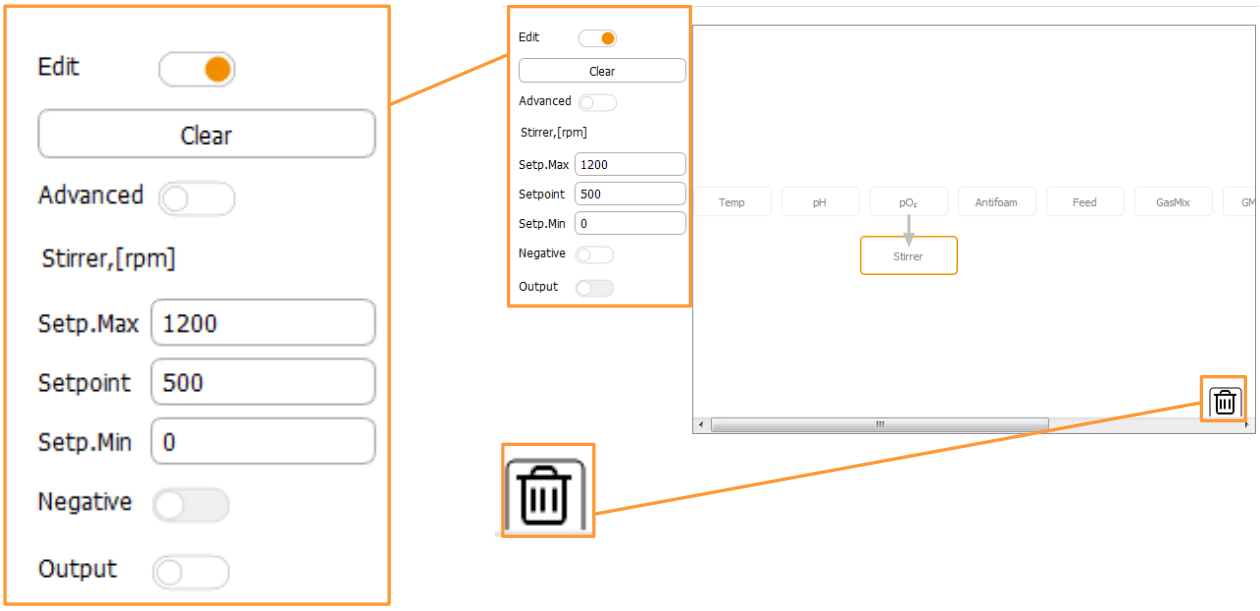
If the parameters that are connected in parallel reach their maximum or minimum setpoint and the setpoint of the parameter being controlled is not yet achieved, the next parameter(s) in the cascade is/are activated.



In the example of the left-hand figure:
The parameters *Stirrer* and *Air Flow* (master controller) are activated at the same time to control the pO_2 parameter.
The parameter *GasMix* (slave controller) is only activated when the setpoint of parameter *pO_2* has not been achieved by the *Stirrer* and *AirFlow* parameters.

9.8.1 Setting a Cascade

The different cascade settings are made in the left-hand side of the main menu *Cascade*. The process parameters can be merged to a cascade in the main area of the menu using drag & drop.



Cascade elements (parameters) can be removed and dropped off in the recycle bin using drag&drop.

- *Edit*: to switch on/off the edit function of the cascade.

  Switching off this function will also deactivate the display of the present process parameters in the main area of the menu.

  Once the edit function is switched on, all parameters can be merged to one or even several cascades using drag&drop.

  Each parameter can only be used once and in one cascade only.
- **Clear**: to call up warning dialogue and delete cascade after confirmation.
- *Advanced*: to switch on/off the setting mode for advanced cascade.

INFORMATION

Advanced cascades are used for customised equipment configurations. They are only set from the equipment manufacturer at the factory. Their settings and possible adjustments are equipment-specific saved at the factory. If required, they may be obtained upon request from the manufacturer.

- Parameter name, (e.g. *Stirrer*): selected parameter with unit.

  The selected parameter visually stands out from the other parameters in the main screen area. The input fields for min./ max. and setpoint values are visible and enabled at the same time to the left-hand side.
- *Setp. Max*. und *Setp. Min*.: factory settings for min. and max. setpoint values which define the adjustable value range of the selected parameter in which the cascade can change the setpoint of the cascaded parameter to control the setpoint of the master controller. These values are adjustable within this predefined value range.
- *Setpoint*: setpoint of the parameter.
  - Master controller: the setpoint to be controlled.
  - Slave controller: the starting setpoint of the parameter from which the setpoint of the parameter of the cascade can be varied within the value range of *Setp. Min. up to Setp. Max.*

INFORMATION

In most cases, it is recommended to set the setpoint for the slave controller to the lower end of the value range (Setp. Min.)

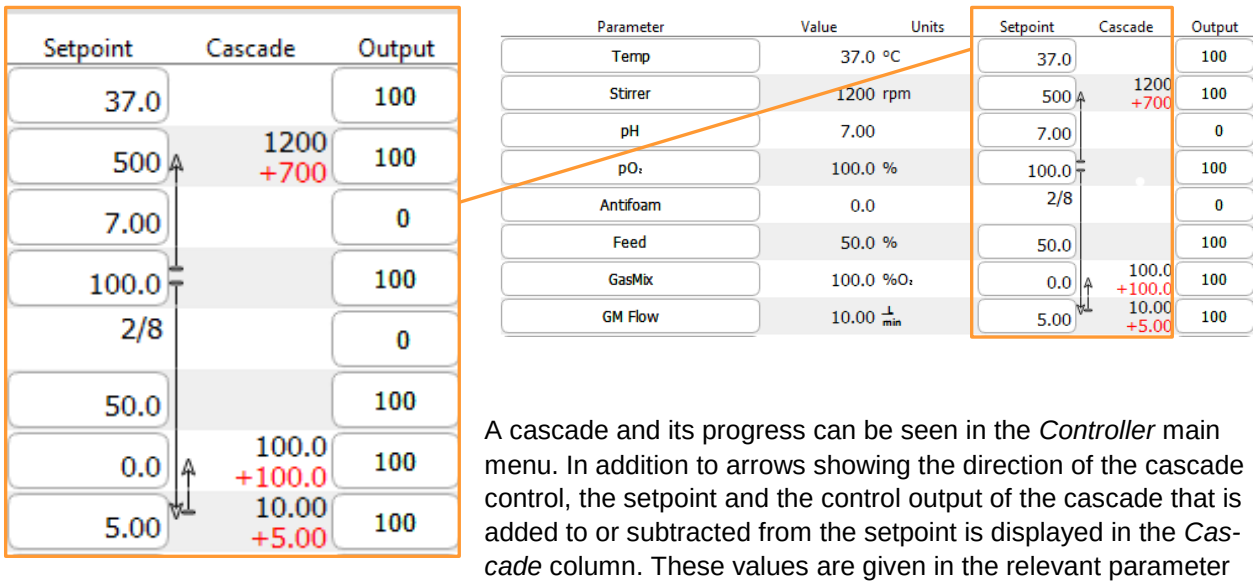
- *Negative*: to switch on/off the negative function of a cascade. Can be used for slave controller, if an increase of the setpoint of the slave controller leads to a decrease of the current value of the slave controller.
- *Output*: to switch on/off the cascade and all used parameters in the cascade hereby.

  Each parameter in the cascade must be switched on (*Output ON*) for the cascade to function.

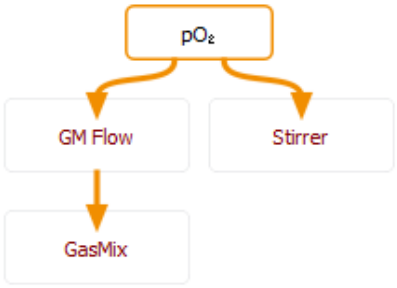
  The parameters can also be switched on and off in the *Controller* main menu.

  If a parameter is switched off (*Output OFF*), all of the following parameters are uncoupled from the cascade.

Cascade progress display



A cascade and its progress can be seen in the *Controller* main menu. In addition to arrows showing the direction of the cascade control, the setpoint and the control output of the cascade that is added to or subtracted from the setpoint is displayed in the *Cascade* column. These values are given in the relevant parameter unit.



The colour of the added/subtracted setpoint in the *Controller* menu and the name of the parameter in the *Cascade* menu indicates the progress of the cascade and the remaining scope of the cascade within the value range of a slave controller to control the master controller according to the following scheme:

Colour	Utilisation of value range
Grey	Inactive
Green	0 – 90 %
Yellow	90 – 99 %
Red	100 %
Blue	0 %

Example of calculation

Stirrer, e.g. for slave controller from setpoint to max. setpoint.

- Setpoint: 500
- Setpoint max. 1200
- Value range: 1200 – 500 = 700

700 = 100 % / 630 = 90 %

500 + 630 = 1130 = setpoint, from which 90 % of the value range are reached.

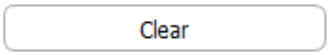
This means for the display according the colour scheme mentioned:

- Green: up to 1130
- Yellow: up to 1193
- Red: at 1200

9.8.2 Deleting a Cascade

To delete all settings of a cascade (does not apply to advanced cascade), proceed as follows:

Procedure



1. In main menu *Cascade*, press **Clear**.

A warning dialogue box appears with:

- Warning / Instruction: *All information NOT created manually with Advanced Cascades will be lost*. *Press OK to confirm*:
- **OK**: to confirm delete of the cascade and close the dialogue box.
- **Cancel**: to close dialogue box without changes.

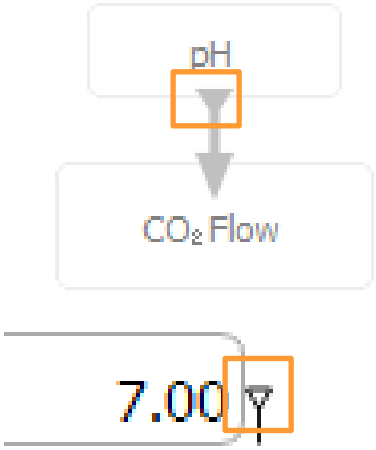
2. Press **OK**.

Cascade is deleted.

9.8.3 Negative Function of a Cascade

The *Negative* function causes a change in sign of the controller output.
This means, a negative controller output causes the addition of a positive value for the set point of the cascaded parameter and vice versa.

The pH regulation with base and CO_2 instead of acid is a classic example of this: to reduce the pH, the CO_2 flow rate (*CO2Flow* parameter) needs to increase.



The fact that the *Negative* function has been switched on is illustrated by the triangle symbol on the arrow that indicates the direction of the cascade control.

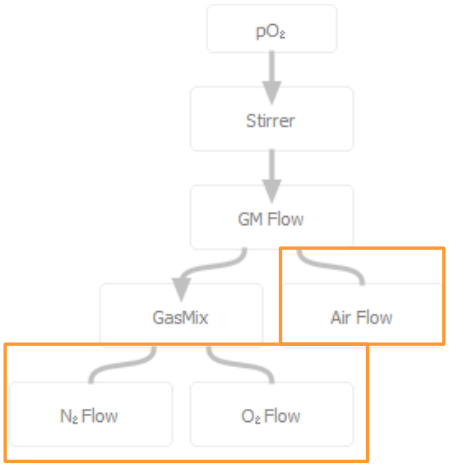
This arrow shape can be seen both in the *Cascade* menu as well as in the *Controller* menu.

9.8.4 Special Configurations

For bioreactors with gassing strategy “High End” (configuration with several mass flow controllers for flow control and gas mix) the gases to be used e.g. *Air Flow*, *N2 Flow* and *O2 Flow*, must be assigned to both parameters that control the gas mixture, i.e. parameters *GasMix* and *GM Flow*, in the cascade configuration.

For this purpose, setup the following cascades additionally to the desired cascade configuration, if the appropriate parameters are present:

- Parameter *Air Flow* as slave controller to parameter *GM Flow*
- Parameter *O2 Flow* as slave controller to parameter *GasMix*
- Parameter *N2 Flow* as slave controller parameter *GasMix*



If parameters *O2 Flow* and *N2 Flow* are present, then they are setup as a parallel cascade below parameter *GasMix*.

To make a distinction between the allocation of these parameters and regular cascade elements, the connections are shown without arrow.

9.9 Pumps

The pumps are controlled in accordance with the corresponding parameters:

Standard

- *Acid* pump (digital): in accordance with the *pH* parameter
- *Base* pump (digital): in accordance with the *pH* parameter
- *Antifoam* pump (digital): in accordance with the *Antifoam* parameter
- *Feed* pump (analogue): in accordance with the *Feed* parameter

Optional

- *Feed 2* pump (analogue): in accordance with the *Feed 2* parameter

Digital pumps have a set speed and are time controlled. I.e., they always run at the same speed in start/stop mode. Analogue pumps have a variable speed (0 % to 100 %). Both digital and analogue pumps are controlled within a range of 0 % to 100 %.

Example

- Analogue: 50 % of the maximum feed rate = pump runs at half speed.
- Digital: 50 % of the maximum feed rate = pump runs during half the time

The following pump settings are possible:

- Setting the pump speed for feed pump(s) and dosing/waiting time for the antifoam pump
- Calibrating the pumps
- Resetting the delivery rate manually to zero
- Filling or emptying the pump hoses automatically

INFORMATION

This function is only present for the four standard pumps.

For details on how to change the settings for the feed pump(s) and the antifoam pump refer to the appropriate chapters in chapter “Parameters”. Calibration, pump counter and automatic filling and emptying is described in detail in the following chapters.

9.9.1 Calibrating a Pump

Calibrating a pump makes it possible to display and record the actual delivered volume. The delivery rate is indicated in millilitres.

Not the following points:

- Always use hoses of the same kind with the same dimensions for calibration and pumping media.
- Pump calibration must be executed before sterilisation.

Aid

- Graduated measuring cylinder/jug or scale/balance and an empty vessel
- Reagent bottle equipped with silicone hose, filled with the reagent to be delivered, the feed or a liquid which has the same viscosity

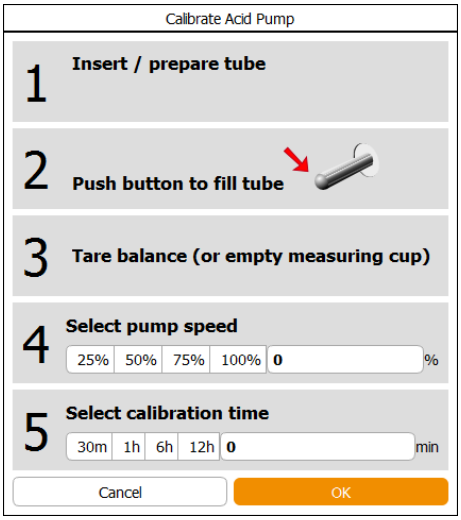
INFORMATION

To obtain precise results, the reagent bottle should be put on a scale which is linked to the bioreactor or to the bioprocess platform software eve® installed on a PC or laptop.

In order to calibrate a pump, e.g. the acid pump, proceed as follows:

Procedure

1. Connect the reagent bottle to the pump.
2. Place the output end of the hose in a measuring cylinder/jug. Or: Place the reagent bottle on a scale and tare to zero, place the output end of the hose in an empty vessel
3. Completely fill the hose using the rocker switch of the base pump.
4. Call up the main menu *Batch* and press **Calibrate Acid**.



The *Calibrate Acid Pump* dialogue box appears with:

- Line 1, instruction on: *Insert/prepare tube.*
- Line 2, instruction: *Push button to fill tube*.
- Line 3, instruction: *Tare balance (or empty measuring cup)*.
- Line 4, instruction: *Select pump speed*.

  25%, **50%**, **75%** and **100%** and input field *%*: to select the pump speed in percent or enter another value in %. After selecting one of the buttons, the **Other** button appears instead of the % input field. Selection can be cancelled using this button.
- Line 5, instruction: *Select calibration time*.

  30m, **1h**, **6h**, **12h** and input field *min*: to select the calibration duration or enter another calibration duration in minutes.
- **OK**: to confirm entries and start calibration.
- **Cancel**: to cancel procedure and close the dialogue box without changes.

5. Select the desired pump speed in % or enter it via numeric keypad.

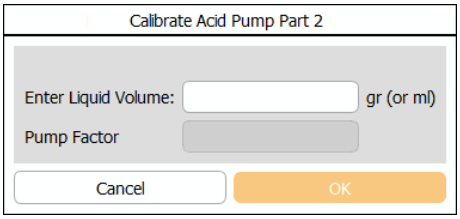
INFORMATION

To obtain most accurate results, the pump should be calibrated at the same speed as it is to be expected to run during fermentation/cultivation.

6. Select calibration duration or enter it manually via numeric keypad.
7. Press **OK**.

Calibration is started. This is indicated by *In progress*… and *time left*…. in h/min/s shows elapsing time next to the now enabled **Stop** button..

Once the time has elapsed:



the *Calibrate Acid Pump Part 2* dialogue box appears with:

- *Enter Liquid Volume gr (or ml)*: to enter the delivered volume in mL or g.
- *Pump Factor*: displays the calculated pump factor after entry of the delivered volume.

  The pump factor is always ≠ 1 with a calibrated pump.
- **OK**: to confirm entries.
- **CANCEL**: to cancel calibration and close the dialogue box without changes.

8. Enter the delivered liquid in mL or g via numeric keypad.

   The pump factor is calculated automatically and displayed in the *Pump Factor* view box.
9. Press **OK**.

   The dialogue box disappears; the calibration value is saved.

   Done at with date and time next to the **Stop** button indicates that and when the pump was calibrated.

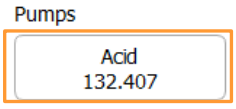
9.9.2 Resetting the Pump Counter to Zero

The number of pump revolutions and the delivered quantity (in mL) of calibrated pumps are displayed constantly during a running fermentation/cultivation process. The display remains in place after completion of the process (when the bioreactor is stopped) until a new fermentation / cultivation process is started again (when the bioreactor is started).

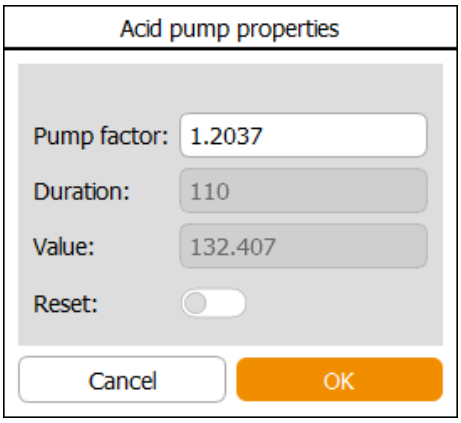
The counter can also be reset to zero manually, proceed as follows:

Procedure

1. Call up the main menu *Main*.



2. Press the desired pump button, e.g. **Acid**.



The *Acid pump properties* dialogue box appears with:

- *Pump factor*: displays the pump factor or allows to be changed manually.
  The pump factor is always ≠ 1 with a calibrated pump.

INFORMATION

Manual change of the pump factor leads to rejection of the previous calibration value.

- *Duration*: displays number of pump revolutions
- *Value*: displays delivered quantity in mL
- *Reset*: to switch on the reset of the pump counter.
- **Cancel**: to close the dialogue box without changes.
- **OK**: to confirm entry and close the dialogue box.

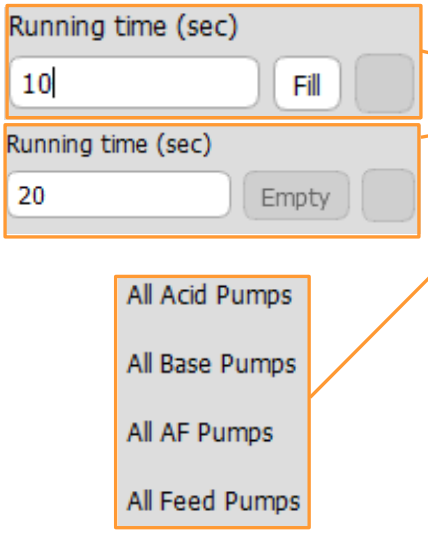
3. Activate the counter reset via *Reset*.
   The function is switched on.
4. Press **OK**.
   The counter is reset to zero and the count starts from the beginning, as soon as the bioreactor is started.

9.9.3 Automatically Filling/Emptying Pump Hoses

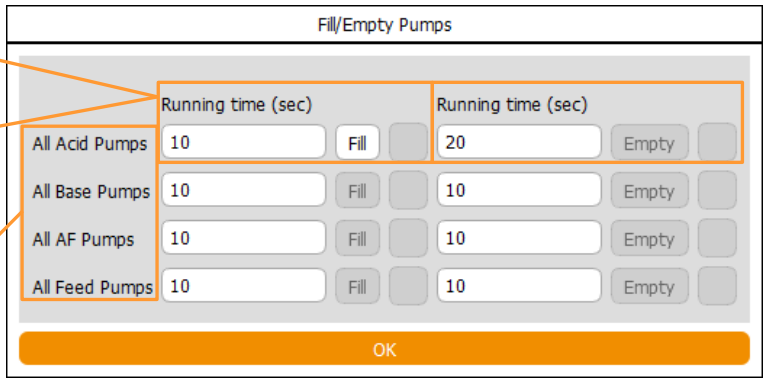
Fill/Empty Pumps in main menu Batch allows the automatic filling or emptying of the pump hoses of the four standard pumps when the bioreactor is in stopped state. For each pump, an individual filling/emptying duration can be defined.

Note the following:

- The pump duration of a pump should preferably be tested with the liquid which has the same or similar viscosity as the liquid to be pumped.
- Observe hose lengths and hose sizes of the pumps and, if necessary, test the pump duration of each pump considering the same conditions mentioned above.



Content of Fill/Empty Pumps Menu



All pumps (*All Acid Pumps* etc.) listed on four lines, divided in two columns with:

- Input fields *Running time (sec)*: to enter the running duration of the pump in seconds, either for filling or for emptying.
- **Fill**: to start automatic filling of the selected pump.
- **Empty**: to start automatic emptying of the selected pump.

  Stop buttons are provided next to each of these buttons for immediately stopping the filling or emptying process.
- **OK**: to close the menu.

INFORMATION

If a filling or emptying procedure is active, the remaining filling or emptying duration is displayed. The menu cannot be closed while at least one filling or emptying procedure is active.

9.10 SIP – Sterilisation in Place

Sterilisation is always carried out according to the application and user specifications.

General information about in situ sterilisation and possible methods are described in main chapter “Preparations before Fermentation/Cultivation”, chapter “In situ Sterilisation – General Information”.

The following chapters describe the SIP processes (Sterilisation in Place) which are started on the touch screen software.

WARNING

The vessel is under pressure during sterilisation!

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

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

CAUTION

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

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

INFORMATION

The following chapters describe full sterilisation process and the sterilisation process of the harvest/sample valve as built and configured on the pilot bioreactor Techfors-S with serial number S-129020. Sterilisation processes of the optional sample valve and the resterilisable feed line are not described here.

9.10.1 Full Sterilisation – Vessel Sterilisation

The water in the vessel jacket is heated up by steam injection for full sterilisation of the vessel. The steam generated by the liquid in the vessel sterilises the filters for inlet air and exit gas at the same time.

The harvest/sample valve (bottom valve) is sterilised separately, see chapter “SIP Harvest/Sample Valve - Sterilisation of the Harvest/Sample Valve”.

9.10.1.1 Process Sequences

The following table shows the different process sequences in the left column and describes the dialogue boxes and status messages which will appear in the touch screen software in the right column.

Sequence	Description
Configuration	Dialogue box *Full sterilisation: configuration* for process configuration (see next chapter)
User interaction required	Dialogue box *Full sterilisation: user interaction required* with instruction(s)
Start delay	Status: *starting inhibitor + time left* in h:min:s Sequence is skipped, if function is switched off.
Heating up to degassing temperature	Status: *heating up to degas. temp*. + setpoint temperature in °C Sequence is skipped, if value for degassing time = 0.
Degassing at degassing temperature	Status: *degassing at temp*. + setpoint temperature in °C + *time left* in h:min:s Sequence is skipped, if value for degassing time = 0.
Heating up to sterilisation temperature	Status: *heating up to steril. temp.*
Sterilisation at sterilisation temperature	Status: *sterilising at temp*. + setpoint temperature in °C + *time left* in h:min:s
Cooling down to 103 °C	Status: *cooling down to 103 °C*
Cooling down to 80 °C	Status: *cooling down to 80 °C* Immediate process abortion is possible at temperature < 80 °C.
Cooling down +10 °C above inoculation temperature	Status: *cooling down to inoc. temp. +10 °C*
Holding phase	Status: *holding inoc. temp*. + setpoint temperature in °C Holds inoculation temperature until fermentation/cultivation is started or full sterilisation is stopped.
Process end	Status: *STOP activated at* OR *fermentation started at* with date and time.

Degassing

All liquids contain some physically dissolved air at room temperature, which escapes when heating up. Liquid is free of gas at 121 °C. If the medium is quickly and continuously heated up to the selected sterilisation temperature, the escaping gas in the medium cannot escape fast enough, so that foam will strongly build up during sterilisation.

Foam can be prevented or reduced by systematic degassing. Duration time and temperature at which the medium shall be degassed are defined in the configuration dialogue, see chapter “Process Configuration”.

General information about the process sequences

All buttons for processes that cannot be simultaneously running are deactivated. Depending on the current phase of the process, values change and are displayed in the main menu *Controller*.

The actual state of valves, actuators, in and outputs is displayed in the submenu *Valves*.

INFORMATION

Should the sterilisation temperature fall below the set point, the message *temp low* will appear. The countdown stops until the temperature has reached the set point again to proceed with the process.

9.10.1.2 Process Configuration

Input field	Value range	Unit
Stirrer speed	10 to 1000	min[1]
Sterilisation temperature	110 to 125	°C
Sterilisation time	10 to 60	min
Degassing temperature	to 98	°C
Degassing time	0 to 60	min
Cooling flow Cooling flow during cooling phase to prevent vacuum in the vessel.	10.0 to 20.0	L/min
Inoculation flow Air flow during inoculation phase (holding phase)	0 / 0.2 to 20.0	L/min
Inoculation temperature	up to 79	°C
Delay Start (Process start delay)	ON / OFF	
Hours	0 to 99	h
Minutes	0 to 59	min
(Starting process in … hours … minutes)		

9.10.1.3 Process Start

Before starting the process, check and ensure that:

- All required services are available and activated.
- All services have the correct connection pressure.
- The mechanical seal is lubricated.

ATTENTION

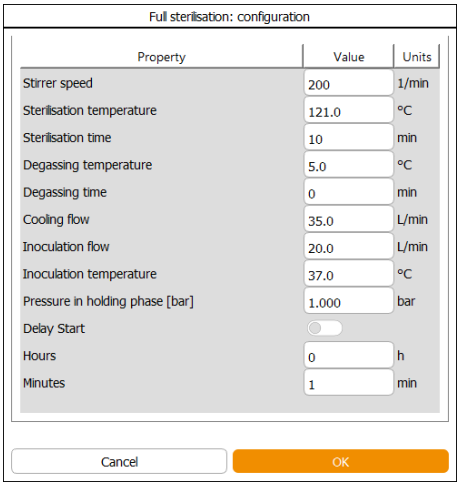
A mechanical seal, which has not been adequately lubricated is destroyed when running dry.

- Antifoam sensor is removed.
- Inoculation needle(s) is/are removed.
- Push valve(s) is/are closed.

To start the process, proceed as follows:

Procedure

1. Call up main menu *Batch* and press **Full Sterilisation**.



The configuration dialogue box appears.

INFORMATION

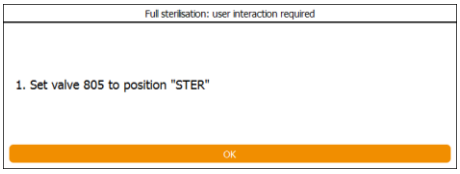
The configuration dialogue contains more or less input fields depending on the equipment's configuration. The figure to the left serves as an example.

2. Enter the desired values via numeric keypad and activate delayed start, where appropriate.

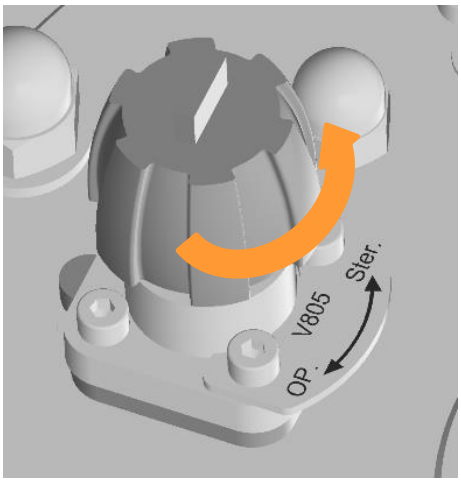
Once all values are entered:

3. Press **OK**.

4. Enter the desired values via numeric keypad and activate delayed start, where appropriate



The *Full sterilisation: user interaction required* dialogue box appears with the instruction, to execute the following step in the procedure:



a) Turn valve **805** in Position *STER*.

Once executed:

5. Press **OK**.

The program automatically runs through the different process sequences until the holding phase of the configured inoculation temperature.

9.10.1.4 Process End

Inoculation temperature is held until the sterilisation is stopped via the **Stop** button or by starting the bioreactor (fermentation/cultivation) via the **Start** button. The process end is either indicated by *STOP activated at* or *fermentation started at* with date and time.

9.10.1.5 Process Abortion

The process is aborted by pressing the **Stop** button next to the **Full Sterilisation** button.

For safety reasons, the process can only be aborted immediately at a temperature < 98 °C. This means, if the temperature is ≥ 98 °C, the cooling sequence will start first and be indicated appropriately. Process abortion is indicated by *aborted at* with date and time.

9.10.2 SIP Harvest/Sample Valve – Sterilisation of the Harvest/Sample Valve

The harvest/sample valve can be sterilised as often as required with clean steam. This procedure is independent of the full sterilisation process. Approximately 10 to 20 minutes of sterilisation before and after sampling are usually sufficient. After sterilisation, the harvest/sample valve should cool down before sampling.

The process is started and stopped in the touch screen software and the sterilisation duration is entered in the configuration dialogue. But steam inlet is manually regulated via valve **203**, which is located on the steam hose line of the harvest/sample valve.

INFORMATION

All buttons for processes that cannot be simultaneously running are deactivated during the process.

9.10.2.1 Process Sequences and Process Configuration

The following table shows the different process sequences in the left column and describes the dialogue boxes and status messages which will appear in the touch screen software in the right column.

Sequence	Description
Configuration	Dialogue box *Sterilisation harvest/sample valve: configuration*
User interaction required	Dialogue box *Sterilisation harvest/sample valve: user interaction required* with instructions
Sterilisation	Status: *sterilisation* + *time left* in h:min:s
User interaction required	Dialogue box *Sterilisation harvest/sample valve: user interaction required* with instruction
End of sterilisation	Status: *finished after* + time in h:min:s

Duration of sterilisation is set in the configuration dialogue box:

Input field	Value range	Unit
Sterilisation time	10 to 60	min

9.10.2.2 Process Start and End

Before starting the process, check and ensure that:

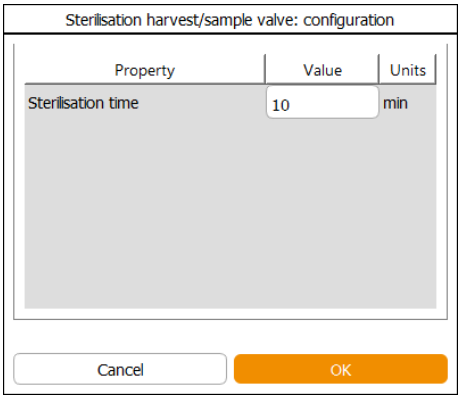
- All required services are available and activated.
- All services have the correct connection pressure.

- Harvest/sample valve **201** is closed.
- Steam hose is connected to valve **203**.

To start the process, proceed as follows:

Procedure

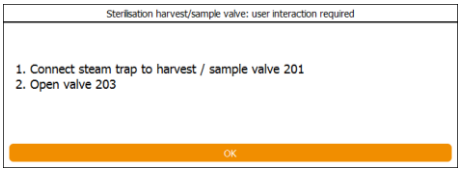
1. Call up main menu *Batch* and press **SIP Harvest/Sample Valve**.



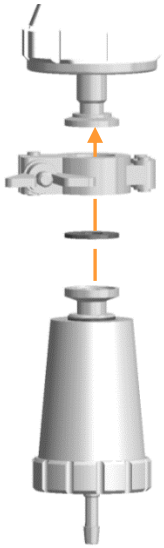
The configuration dialogue box appears.

2. Enter the desired values via numeric keypad.

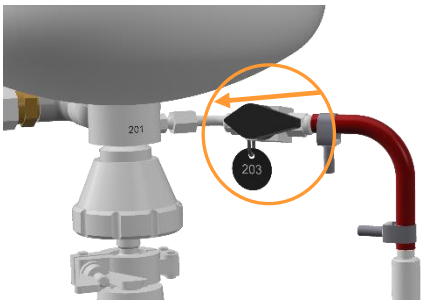
3. Press **OK**.



The *Sterilisation harvest/sample valve: user interaction required* dialogue box appears with instructions, to execute the following steps in the procedure:



a) Connect the steam trap to harvest/sample valve **201**.

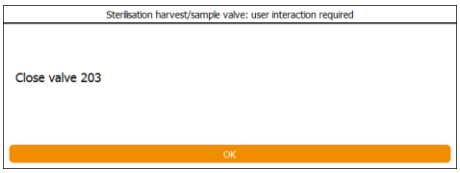


b) Open valve **203** (*Steam harvest/sample valve*).

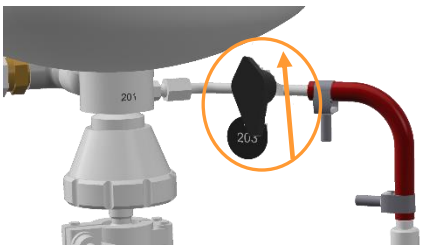
Once executed:

4. Press **OK**.

The sterilisation sequence (countdown) begins.



Once sterilisation time has elapsed, the second *Sterilisation harvest/sample valve: user interaction required* dialogue box appears with the instruction to execute the following step in the procedure:



a) Close valve **203** (*Steam harvest/sample valve*).

Once executed:

5. Press **OK**.

The process is finished.

9.10.2.3 Process Abortion

The process can be aborted any time by pressing the **Stop** button next to the **SIP Harvest/Sample Valve** button. The same dialogue box like for the process end appears with the instruction for closing valve **203**. That the process has been aborted and after how much time is indicated with *aborted after* + time in h/min/s.

9.11 Starting & Stopping the Bioreactor, Shutting Down the System

9.11.1 Starting the Bioreactor (Fermentation/Cultivation)

Before you start the process, check and ensure that:

- All required services are available and activated.
- All services have the correct connection pressure.
- The mechanical seal is lubricated.

ATTENTION

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

- Inoculation needle(s) is/are mounted
- Push valve(s) is open

To start the bioreactor, proceed as follows:

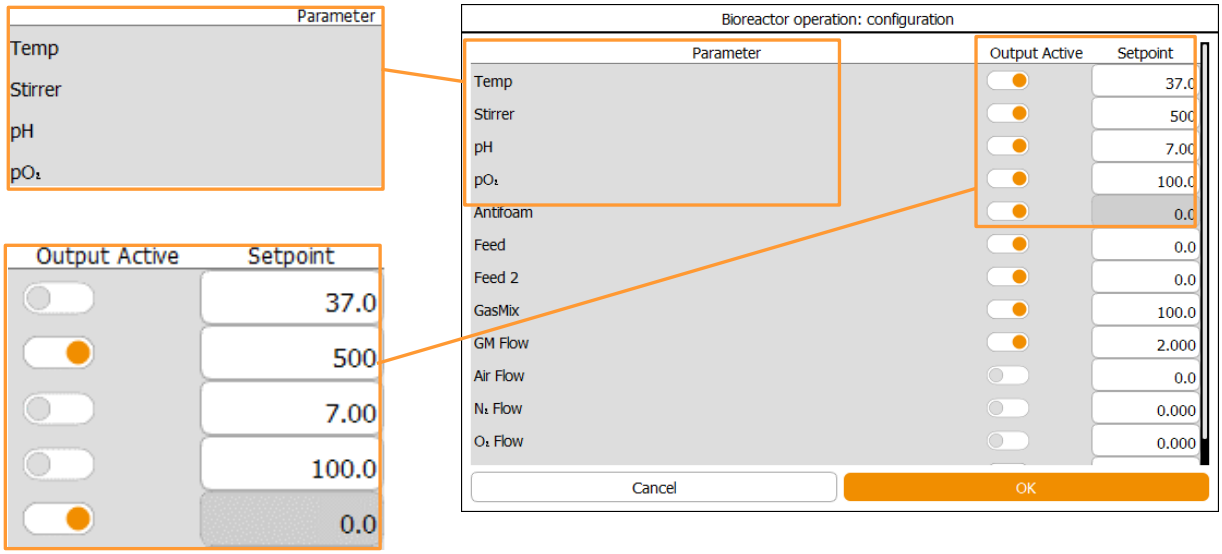
Procedure

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

The configuration dialogue box appears containing the controlled parameters. Setpoint settings of the previous fermentation/cultivation are visible here.

INFORMATION

The configuration dialogue box contains more or less process parameters depending on the equipment's configuration. The figure below serves as an example.

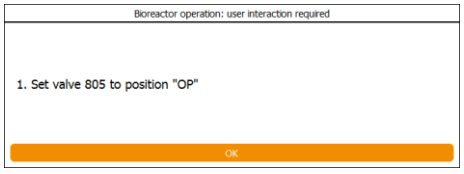


2. Change setpoint settings, if necessary and switch parameters on.

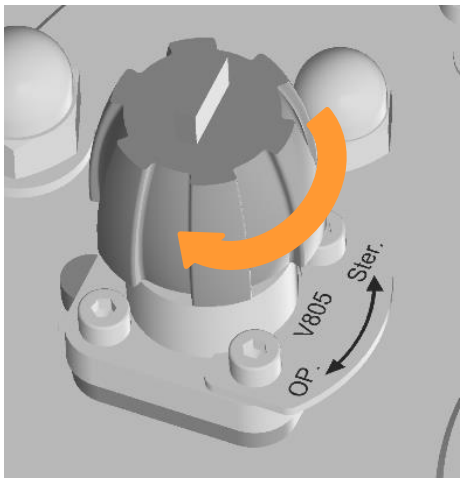
> **INFORMATION**
>
> The bioreactor is started with the settings in the configuration dialogue box. Changes to these settings are saved and transferred to the next configuration dialogue box. If setpoint values are changed or parameters are switched on /off whilst the bioreactor is running, these settings are only adopted for the current fermentation/cultivation process.

Once all settings are made:

3. Press **OK**.



The *Bioreactor: user interaction required* dialogue box appears with the instruction to execute the following step in the procedure:



a) Turn valve **805** in position *OP* (= operation).

Once executed:

4. Press **OK**.

Once the bioreactor (fermentation/cultivation) is started, the status message *in progress since* indicates that and since when (days/hours/minutes/seconds) the bioreactor is running.

All buttons for starting processes that cannot be simultaneously running are deactivated.

⚠ CAUTION

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

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

- Current values and controller outputs are visible in the main menu *Controller*.
- A recording of the current values and a diagram are visible in the main menu *Trends.*

⚠ WARNING

The vessel may be under pressure during operation!

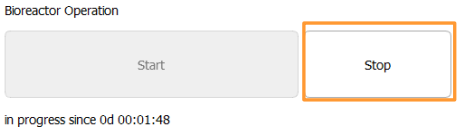
Removing mounting parts or the vessel top plate lead to spurting out of liquids and/or rapid exhausting of gasses. This may cause severe chemical burns, burns or intoxication.

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

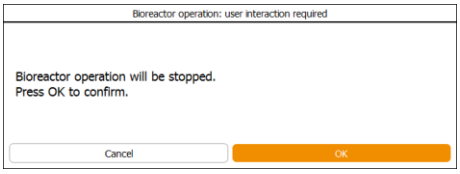
9.11.2 Stopping the Bioreactor

To stop the bioreactor, proceed as follows:

Procedure



1. Call up main menu Batch and press Stop next to the Start button.



The *Bioreactor operation: user interaction required* dialogue box appears with:

- Instructions *Bioreactor operation will be stopped* and *Press OK to confirm*.
- **OK**: to stop the bioreactor and close the dialogue box.
- **Cancel**: to close the dialogue box without changes.

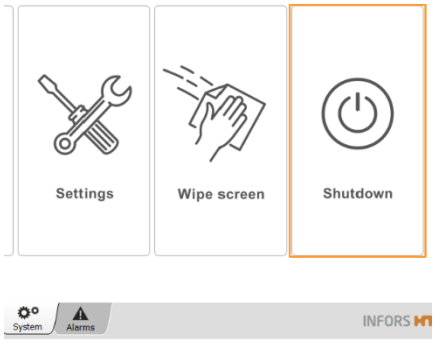
2. Press **OK**.

The bioreactor is stopped. *Stopped after* with display of d/h/min/s below **Start** indicates after how much running time the bioreactor was stopped.

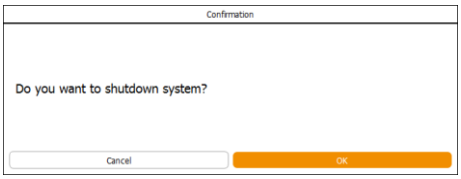
9.11.3 Shutting Down the System, Switching Off the Equipment

To shut down the system and to switch off the equipment, proceed as follows:

Procedure



1. In main menu System, press **Shutdown**.



Dialogue box *Confirmation* appears with:

- Question: *Do you want to shutdown the system?*
- **OK**: to shut down the system.
- **Cancel**: to close the dialogue box without changes

2. Press **OK**.

   The system is shut down and switched off.

ATTENTION

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

When the screen is dark:

3. Turn the main switch counter clockwise (quarter turn) in position **0/OFF**.
4. Close/shut off supply lines and ensure they are pressure-free.

WARNING

The vessel may be still pressurised after switching off at the main switched due to stored energy!

Check the vessel pressure on the manometer and, if required, put the vessel into non-pressurised condition before every manipulation on the vessel and its components

10 Cleaning and Maintenance

The following chapters describe in detail how the vessel, the top plate and accessories are cleaned and, as required, stored.

Furthermore, the chapter contains a maintenance plan and corresponding descriptions for the procedures to be performed by the operator.

10.1 Cleaning Agent and Disinfectant

Intended use	Allowed products/tools
For vessel with slight contamination	Water
Cleaning agent for denaturation of proteins	0.1 N NaOH
Cleaning agent for smaller component parts (e.g. exit gas cooler)	Ultrasonic bath
Cleaning agent for surfaces	Water
Disinfectant for surfaces	Ethanol, 70 %

10.2 Cleaning the Vessel

After ending fermentation/cultivation followed by in situ sterilisation for decontamination (depending on user specifications), the vessel should be cleaned.

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

Procedure

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

   Temperatures of e.g. 40 up to 60 °C improve the cleaning action, prolong stirring duration as necessary.

5. Stop the bioreactor, shut down the system and switch off the equipment.
6. Empty the vessel.
7. Thoroughly rinse the vessel with water.

   Repeat the procedure, if necessary.

If the vessel is not used again for the next fermentation right after, sufficient air circulation in the vessel should be ensured.

10.3 Cleaning the Vessel Top Plate

Depending on the application, separate cleaning of the vessel top plate may be necessary. To clean the vessel top plate thoroughly, proceed as follows:

Procedure

1. Lift up and remove the vessel top plate and put it onto an appropriate storage area.

> **INFORMATION**
>
> A detailed description how to remove the vessel top plate can be found in chapter “Removing the Vessel Top Plate” of the main chapter “Preparations before Fermentation/Cultivation”. Observe the safety advice and follow the instructions stated in there.

2. Dismantle component parts.
3. Carefully rinse all component parts with water.

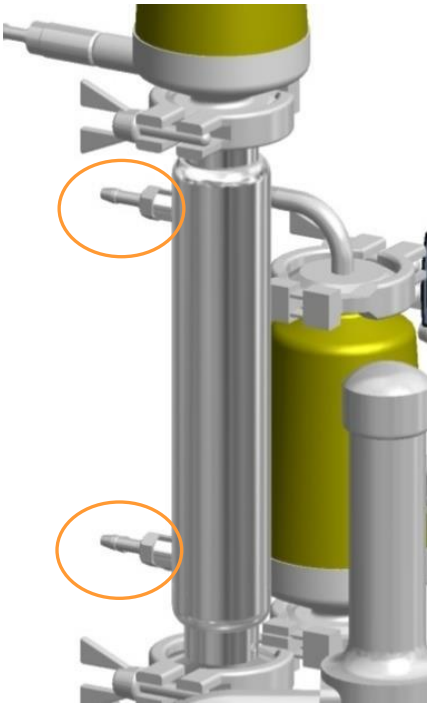
   Use 0.1 N caustic soda solution as necessary.
4. Carefully rinse the vessel to plate with water or wipe it with a damp cloth or sponge.

   Use 0.1 N caustic soda solution as necessary.
5. Check vessel top plate sealing (O-ring) and O-rings of mounting parts on damages and replace them as necessary.
6. Leave the vessel top plate and the mounting parts to dry or dry wipe them.
7. Re-assemble clean and dry mounting parts into the also clean and dry vessel top plate.
8. Store the vessel top plate clean and dry in a location where it is secure and unable to fall or be damaged in passing, if not used right after for next fermentation/cultivation.

10.4 Dismantling and Cleaning the Exit Gas Cooler

To remove the exit gas cooler from the vessel top plate in order to dismantle and clean it, proceed as follows:

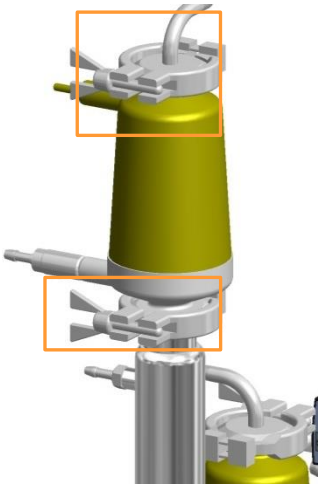
Procedure



1. Remove the red pressure hoses from the exit gas cooler (the red pressure hoses are not visible on the picture to the left).

INFORMATION

The pressure hoses for water inlet/outlet of the exit gas cooler are secured with hose clamps.



2. Remove the two clamps before and after the exit gas filter along with the exit gas filter itself.

Cleaning and Maintenance

Ensure that the flat gaskets between the flanges do not get lost.

3. Remove the clamp between the bottom flange of the exit gas cooler and the flange on the vessel top plate
4. Remove the exit gas cooler from the vessel top plate and put it aside on a work space, where it cannot fall off.

   Ensure the flat gasket does not get lost.

5. Carefully lift the inner plates out of the main body of the exit gas cooler.

6. Put the disassembled exit gas cooler (inner plates and main body) into 0.1 N NaOH for 4 hours.
7. Thoroughly rinse the exit gas cooler with water.
8. Put the exit gas cooler into an ultrasonic bath for 2 to 5 minutes.
9. Wash the exit gas cooler through with 70 % Ethanol.
10. Thoroughly rinse the exit gas cooler with distilled water.
11. Let it dry in a clean place and re-assemble when dry.

10.5 Cleaning Reagent Bottles, Hoses and Component Parts

Reagent bottles and hoses are separately autoclaved before cleaning. For details refer to main chapter “Fermentation/Cultivation”, chapter “Sterilisation after Fermentation/Cultivation”

After autoclaving and cooling down, proceed as follows:

Procedure

1. If appropriate, carefully empty the reagent bottles, and dispose of the liquid respecting the internal safety regulations.
2. Thoroughly rinse reagent bottles, hoses and component parts such as e.g. inoculation needles, push valves etc. with water.
3. Check silicone and pump hoses on damage and replace as necessary.

INFORMATION

Depending on user specifications, the hoses are replaced after every use.

4. Check reagent bottles and its components on damage and replace as necessary.
5. Check O-rings on component parts and lid seals on the reagent bottles on damage and replace as necessary.
6. Leave to dry the reagent bottles, hoses and component parts on a clean surface.

10.6 Cleaning the Sensors

Cleaning and storage of the sensors is described in the separate documentation of the corresponding sensor manufacturer. Strictly follow these instructions.

The antifoam and/or level sensor from the equipment manufacturer is cleaned and maintained like any other component part (inoculation needles, push valves etc.).

If not used for next fermentation/cultivation, it is stored when clean and dry.

10.7 Cleaning Surfaces of the Instrumentation Cabinet and Operating Unit

If required, the surfaces of the instrumentation cabinet and the operating unit can be cleaned.

ATTENTION

Take the protection classes IP43 (instrumentation cabinet) and IP66 (operating unit) into account when cleaning!

Proceed as follows:

Procedure

1. Ensure the equipment is switched off at the main switch, switch off, where applicable.
2. Disconnect from mains supply.
3. Wipe the surface of the instrumentation cabinet and of the operating unit with a soft, damp cloth.

   Use an appropriate (non-aggressive!) disinfectant as necessary.
4. Clean the screen of the operating unit with a wipe suitable for computer or laptop screens.

10.8 Maintenance Plan

WARNING

Non-compliance of this maintenance plan contains a high risk!

It is the responsibility of the user, that this maintenance plan is complied with. Non-compliance will lead to exclusion of liability (see General Terms and Conditions).

The required maintenance for reliable operation is described in the following chapters.

Reduce the maintenance intervals in case increased abrasion is detected during regular checks.

Contact the manufacturer for questions concerning maintenance. For contact details, see page 2.

To be carried out by operator	
Interval	**Maintenance work**
Before every operation	Check hose lines and connections.
	Check all O-rings and rubber seals and replace if necessary.
	Check the reagent bottles and any other work tool made of glass on intactness; replace if necessary.
	Lubricate the mechanical seal.
	Check the filters with a filter test device, if available.
After every fermentation/cultivation	Sterilise and clean the vessel, the vessel top plate, built in parts of the vessel top plate, reagent hoses and bottles. Proactively replace silicone hoses (frequency depends on application).
After 20 – 50 sterilisations (rough recommendation)	Replace air filters. Reduce or enhance maintenance interval as necessary.
Every 6 months	Replace all pump and silicone hoses on the reagent bottles.
As required	Clean the surfaces of the instrumentation cabinet and the operating unit.

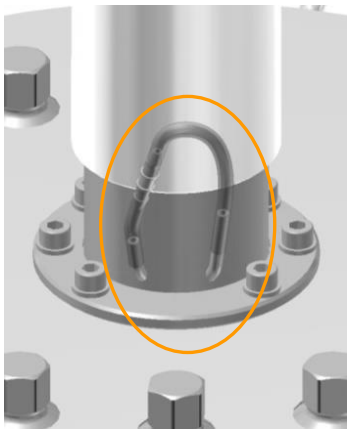
To be carried out by qualified personnel	
Interval	**Maintenance work**
Every 6 months	Check and calibrate measuring sections (temperature, pH, etc.) with a simulator.
	Replace all O-rings and rubber seals, reduce maintenance interval as necessary.
As required	Replace hoses and hose connections.

To be carried out by qualified personnel from the manufacturer	
Interval	**Maintenance work**
When signs of wear or damage are apparent or at maintenance intervals defined by the operator of the equipment.	Replace mechanical seal.

INFORMATION

For details about maintenance of parts and peripheral devices not made by the equipment manufacturer refer to the separate documentation from the manufacturer of these components. Read these and strictly follow instructions stated in there.

10.9 Lubricating the Mechanical Seal



The silicone hose on the drive hub must always be filled with liquid (glycerine!) to ensure the mechanical seal is lubricated.

ATTENTION

Risk of loss of property due to the mechanical seal running dry!

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

To lubricate the mechanical seal proceed as follows:

Procedure

1. Pull off the longer piece of hose from the coupling on the shorter piece.
2. Fill a syringe with glycerine
3. Plug the syringe onto the open hose end.
4. Fill glycerine into the hose.
5. Plug the longer piece of hose onto the coupling of the shorter piece.

   If glycerine has come off the hose, wipe off as necessary.

The following points need to be observed

- A small loss of glycerine is normal during operation of the vessel. For this reason, it is recommended to top up with glycerine regularly, e.g. after several fermentations or every time the top plate is removed for cleaning. Provided the mechanical seal is in normal operational order, after topping up of a few cubic centimetres of glycerine will be visible in the hose where the glycerine is added.
- Due to normal wear of the mechanical seal – which is made of hard carbon and silicon carbide – the glycerine will show a dark discoloration which is visible in the silicone hose. This discoloration is perfectly normal and should not be understood as a sign of progressive wear of the mechanical seal.
- If glycerine loss is significant during or between fermentations, this might indicate a misaligned or defective mechanical seal. A significant glycerine loss can be detected if much more glycerine than usual is necessary for topping up the chamber and/or sudden dark discoloration of the culture liquid, due to glycerine running down the stirrer shaft.
- If a significant loss of glycerine is observed, the manufacturer must be contacted to have the seal checked by qualified personnel from the manufacturer or local dealer to re-align or replace the seal.
- When replacing the top plate after cleaning, leave it for some time before checking the level of the glycerine in the mechanical seal. This allows for any possibility that tilting of the top plate has temporarily drained some glycerine from its correct location.

11 Interferences

The following section describes possible reasons for interferences and how to resolve them. Reduce the service intervals in correspondence with the actual loads if interferences become increasingly common. Contact the manufacturer for interferences that cannot be resolved by following the above instructions. For service contact details, see page 2.

11.1 Interferences Basic Operation and Operating Unit

Interference		
Equipment does not work, power display ***POWER*** is not illuminated, no display.		
Possible Causes	**Remedy**	**By**
Power cable not connected.	Connect power cable.	Operator
Main switch switched off.	Switch main switch on.	Operator
Fuses blown	Check fuses of mains connection. Check fuses of basic unit.	Qualified electrician
Break in power connections.	Check power plug. Check power cable on damages or kinks. Check socket and cable on basic unit.	Qualified electrician

Interference		
Power display ***POWER*** is illuminated, no display.		
Possible Causes	**Trouble shooting**	**By**
Monitor of operating unit is switched off at the ON/OFF key.	Switch the monitor of the operating unit on at the ON/OFF key.	Operator
Power supply cable not connected to the operating unit.	Plug the power supply cable in at the DC socket on the rear side of the operating unit	Operator
Power supply cable not connected to controller inside the instrumentation cabinet.	Connect the power supply cable to the controller inside the instrumentation cabinet.	Qualified electrician

Interference		
No communication between equipment and operating unit. Alarm *no communication.*		
Possible Causes	**Remedy**	**By**
iDDC-bus cable (display cable) not connected to the operating unit.	Plug the round connector of the iDDC-bus cable in at the COM1 socket (labelled with RS-485) on the rear side of the operating unit.	Operator
iDDC-bus cable (display cable) is not connected to the controller inside the instrumentation cabinet.	Connect the iDDC-bus cable (display cable) to the controller inside the instrumentation cabinet.	Qualified electrician

11.2 Interferences Drive System

Interference		
Motor does not start		
Possible Causes	**Remedy**	**By**
Parameter *Stirrer* is not switched on.	Switch parameter *Stirrer* on.	Operator
Stirrer setpoint = 0.	Set *Stirrer* setpoint > 0 Check value in *Deadband* of parameter option *PID*: Value must be = 0 (zero)	Operator
Parameter *pO2* is switched on and set to work with stirrer. (Option *Cascade* in parameter *pO2*)	Switch *Cascade* off and test operation via parameter *Stirrer*.	Operator

Interference		
Motor does not start, parameter Stirrer is turned on, Cascade in pO_2 is not activated.		
Possible Causes	**Remedy**	**By**
Motor cable not properly connected	Check motor cable connection, connect properly as necessary.	Qualified personnel
Motor is/was overheated or mains voltage of the motor is too low.	Turn the equipment off at the main switch. Wait for approx. 20 seconds. Turn the equipment on at the main switch. If this does not resolve the problem, see next section.	Operator
	Turn the stirrer drive (parameter *Stirrer*) off at the operating panel. Open the instrumentation cabinet. Check the LED display of the motor controller: ■ Error Code M: motor overheated ■ Error Code Z: low mains voltage. Press the **Reset** button of the frequency converter. Close the instrumentation cabinet. Turn on parameter *Stirrer*.	Qualified electrician

Interference		
Motor control is erratic		
Possible Causes	**Remedy**	**By**
Wrong settings in *PID* option of parameter *Stirrer*	Reset default settings in *PID* menu.	Operator

11.3 Interferences Temperature Control System

Interference		
No temperature control.		
Possible Causes	**Remedy**	**By**
Parameter *Temp* (temperature) is not switched on	Switch parameter *Temp* (temperature) on	Operator

Interference		
No cooling or inadequate cooling.		
Possible Causes	**Remedy**	**By**
No water supply or inadequate flow.	Ensure water supply is turned on and flow is sufficient.	Operator
Incorrect Neg. factor (negative factor) in option *PID* of parameter *Temp* (temperature)	Check *Neg. factor* (negative factor) in option *PID* of parameter Temp (temperature): Value must be positive	Operator

Interference		
Temperature drifts up or down over time		
Possible Causes	**Remedy**	**By**
Incorrect settings in option *PID* of parameter Temp (temperature)	Check settings in option *PID* of parameter *Temp* (temperature) and adjust as necessary (especially *P-term*).	Operator

Interference		
Alarm *no water detected in temperature control system*. Temperature control is switched off, circulation pump and heating are deactivated, and active process continues running.		
Possible Causes	**Remedy**	**By**
Temperature control circuit is not filled	Fill the temperature control circuit	Qualified personnel

Interference		
Negative temperature value		
Possible Causes	**Remedy**	**By**
Broken cable or faulty sensor	Replace temperature sensor	Infors service technician or licensed dealer

11.4 Interferences pH System

Interference		
No display or incorrect display of pH		
Possible Causes	**Remedy**	**By**
Sensor cable is twisted or kinked or not properly connected.	Check and ensure that the sensor cable is not kinked or twisted. Connect the sensor cable properly as necessary.	Operator
pH sensor is not calibrated	Test calibration with pH4 and pH7 buffers	Operator
Temperature compensation function is switched off.	Switch temperature compensation function on in normal use.	Operator
pH drift during long-term fermentation	Recalibrate pH with offline values (“pH Sensor Recalibration”).	Operator
Faulty pH sensor	Read documentation from sensor manufacturer	Operator

Interference		
No pH control		
Possible Causes	**Remedy**	**By**
Parameter *pH* is not switched on.	Switch parameter *pH* on.	Operator
No control in *Deadband* in option *PID*	Check *Deadband* in option *PID* of parameter *pH*: switch off or enter a small value.	Operator
No corrective reagents.	Check and refill bottles, if necessary Check connection with vessel. Connect properly, if necessary. Ensure that reagent hose line(s) is/are not clamped off. Remove clamp(s), if necessary. If working with push valve(s): Check and ensure that the push valve(s) is/are open, open as necessary.	Operator
Acid or/and *Base* pump(s) does/do not operate properly.	Check operation of the pump using the rocker switch. Check pump hose type and replace if necessary.	Operator

Interference		
pH value drifts up and down over time or acid and base are added almost continuously in turn.		
Possible Causes	**Remedy**	**By**
Incorrect settings in option *PID*	Check settings in option *PID* of parameter *pH* and adjust as necessary (especially *P-term*).	Operator
Incorrect strength of reagents.	Ensure that reagents are of roughly equal strengths in terms of effect (i.e. 0.1 to 2.0 molar).	Operator

11.5 Interferences pO2 System (Dissolved Oxygen)

Interference		
No display or incorrect display of pO2		
Possible Causes	**Remedy**	**By**
Sensor cable is twisted or kinked or not properly connected.	Check and ensure that the sensor cable is not kinked or twisted. Connect the sensor cable properly as necessary.	Operator
pO2 sensor is not polarised.	Polarise the pO_2 sensor	Operator
Faulty sensor	Check the calibration of the pO_2 sensor. Consult the documentation of the sensor manufacturer.	Operator

Interference		
No pO2 control		
Possible Causes	**Remedy**	**By**
Parameter *pO_2* is not switched on.	Switch parameter *pO_2* on.	Operator
Incorrect settings in option *Cascade* of parameter *pO_2*	Check set up of cascade, adjust settings, if necessary.	Operator
No gas flow into vessel.	Check supply connections. Check and ensure that gas supply is turned on. Turn on, if necessary. If present, check and ensure that the rotameter valve is fully open. If present, ensure the *Flow* parameter(s) is/are switched on and flow rate is not set too low a value, adjust as necessary.	Operator

Interference		
pO_2 control is unstable		
Possible Causes	**Remedy**	**By**
Incorrect settings in option *PID* of parameter *pO_2*	Check settings and adjust as necessary, especially *P-term* and *Deadband*. *Deadband* must be 0.	Operator

11.6 Interferences Antifoam Control

Interference		
Foam is not sensed		
Possible Causes	**Remedy**	**By**
Sensor cables are not properly connected	Connect properly as necessary.	Operator

Interference		
Foam is always/frequently detected		
Possible Causes	**Remedy**	**By**
Sensor cables are not properly connected	Connect properly as necessary.	Operator
Transparent insulation of antifoam sensor damaged	Replace transparent insulation of antifoam sensor	Qualified personnel from the manufacturer

Interference		
Antifoam pump does not work		
Possible Causes	**Remedy**	**By**
Parameter *Antifoam* is not switched on.	Switch the parameter on.	Operator
Dosing time of parameter *Antifoam* = 0 (zero).	Set dosing time of parameter > 0.	Operator

Interference		
No or inadequate reagent.		
Possible Causes	**Remedy**	**By**
Reagent bottle empty	Refill bottle, if necessary.	Operator
Wrong antifoam agent or wrong concentration	Replace agent, if necessary.	Operator
Hose line blocked or clamped off.	Check hose line connection between reagent bottle and vessel, connect properly as necessary. Open/remove hose clamp, if necessary.	Operator
If working with push valve: valve closed	Open the push valve as necessary.	Operator
Antifoam pump does not operate properly	Check operation using the rocker switch. Check hose type and replace if necessary.	Operator

11.7 Interferences Feed and Pump

Interference		
No feed inlet		
Possible Causes	**Remedy**	**By**
Feed parameter is/are not switched on.	Switch *Feed* parameter(s) on.	Operator
Setpoint of *Feed* parameter(s) = 0 (zero).	Enter setpoint of *Feed* parameter(s) > 0	Operator
Reagent bottle empty	Check and refill bottle, if necessary.	Operator
Feed hose line blocked	Check connection with vessel. Connect properly if necessary. Check and ensure that hose line is not clamped off. Remove clamp, if necessary.	Operator
If working with push valve: valve is closed	Open the push valve	Operator
Feed pump does not operate properly	Check pump operation using the rocker switch. Check hose type and replace if necessary.	Operator

11.8 Interferences Gassing System

Interferences		
No gassing		
Possible cause	**Remedy**	**By**
The in-house gas supply has been interrupted.	Stop the bioreactor (fermentation/cultivation). Check the in-house gas supply and switch it on, if necessary.	Operator
Gasmix and/or *Flow* parameter(s) is/are not activated. Setpoint(s) in the *Gasmix* and/or *Flow* parameter(s) = 0	Activate the *Gasmix* and/or *Flow* parameter(s) as necessary. Set the setpoint(s) of the *Gasmix* and/or *Flow* parameter(s) > 0 as necessary.	Operator
Inlet air or exit gas escapes via twist valves on the filters.	Check whether the twist valves are closed, close as necessary.	Operator
Inlet air filter blocked.	Replace the inlet air filter under sterile conditions.	Operator

Interference		
The desired gas flow rate is not reached.		
Possible cause	**Remedy**	**By**
Inlet air or exit gas filter blocked.	Replace the filter under sterile conditions.	Operator
Wrong connection pressure of gas(es).	Check connection pressure of gas, adjust as necessary.	Operator

Interference		
Sudden increase in evaporation losses in the culture vessel.		
Possible cause	**Remedy**	**By**
The exit gas cooler does not cool.	Check the water supply to the exit gas cooler, restore it if necessary. Check and ensure that the *Cooler* valve (118) in main menu *Main* is open (valve symbol is green) and set to automatic (*Auto*)	Operator

11.9 Returning for Repair

The provider must return the equipment or the faulty component part(s) to the manufacturer if, after consulting the service department of the local dealer or the manufacturer, on-site diagnosis and/or repair is not possible.

INFORMATION

When returning the equipment, the component part or accessory for repair, it is required for the safety of all parties involved and because of legal provisions that a lawful declaration of decontamination is present. Refer to main chapter “Safety and Responsibility”, chapter “Declaration of Contamination” for details.

12 Disassembly and Disposal

The equipment must be disassembled and disposed of in an environmentally friendly manner if it is no longer in use.

INFORMATION

When returning the equipment for disassembly or disposal, it is required for the safety of all parties involved and because of legal provisions that a lawful declaration of decontamination is present. Refer to main chapter “Safety and Responsibility”, chapter “Declaration of Contamination” for details.

12.1 Disassembly

Prior to disassembly:

- Switch off the equipment and lock any isolation switch in the ‘off’ position.
- Physically disconnect the main energy supply from the equipment and wait for components to fully discharge.
- Remove and dispose of all additional consumable items, auxiliary components and/or spent processing material in an environmentally acceptable manner.

Clean and disassemble component parts professionally with regard to any local regulations concerning employment and environmental protection. If possible, separate materials.

12.2 Disposal

Recycle disassembled components if no agreement is made concerning reclaim or disposal.

- Send metals for scrap.
- Send plastic components for recycling.
- Sort and dispose of the remaining components according their material composition.

WARNING

Electronic waste, electronic components, lubricants or other auxiliary materials/supplies are subject to hazardous waste regulations and may only be disposed of by registered specialist disposal firms.

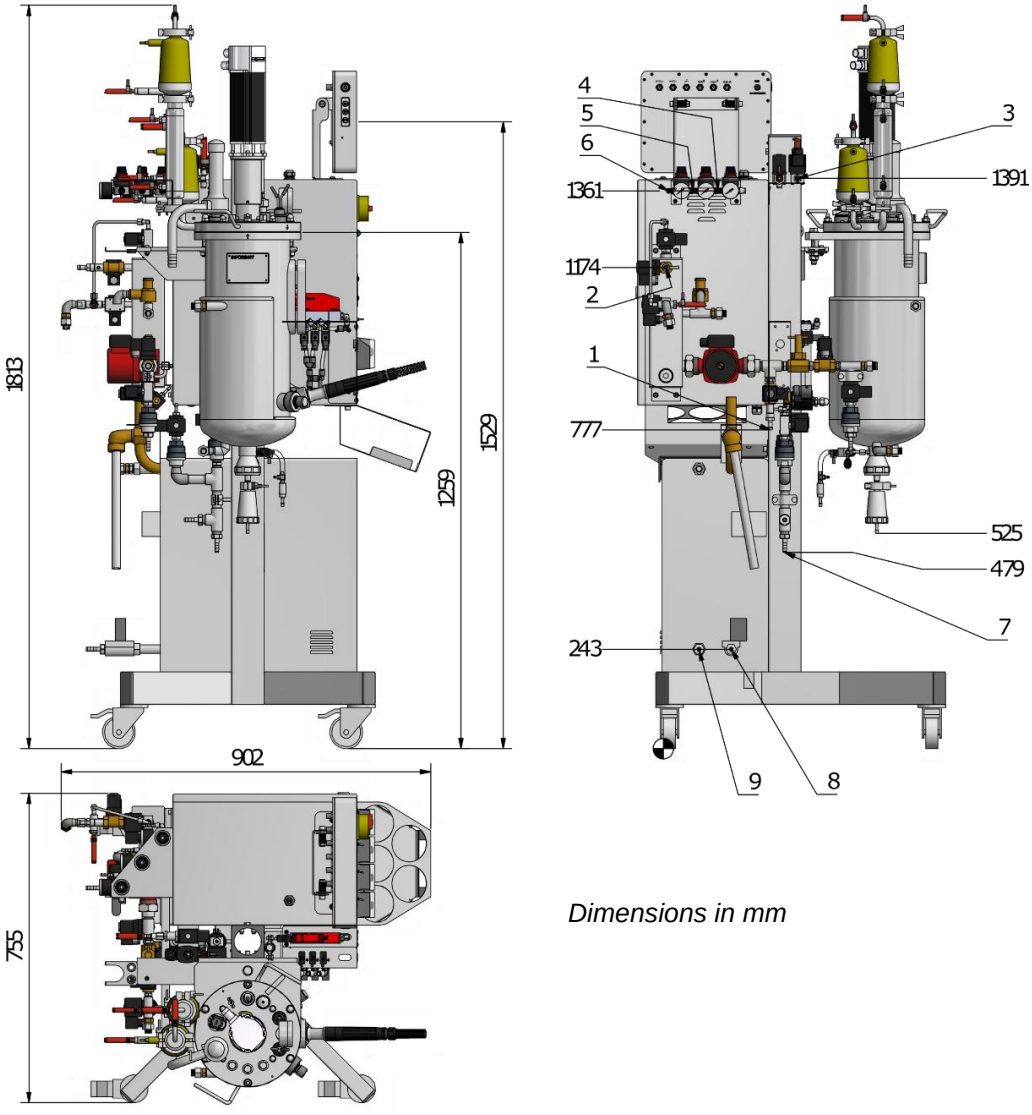
For disposal, the system units are to be disassembled and dismantled into individual material groups. These materials are to be disposed of according to the applicable national and local legislation.

Local authorities or specialist disposal firms can provide information regarding environmentally acceptable disposal.

If no special arrangements have been made for return, INFORS HT units with the required declaration of decontamination can be sent back to the manufacturer for disposal.

13 Technical Data

13.1 Dimensions, Connections & Connection Values



Dimensions in mm

1 Cooling water in (male adapter DN10) / 2.0 ± 0.5 bar

2 Cooling water out (male adapter DN10) / pressureless

3 Air out (male adaptor DN10) / pressureless

4 Air in (male adapter DN06) / ± 2.5 bar

5 O_2 in (male adapter DN06) / ± 2.5 bar

6 N_2 in (male adapter DN06) / ± 2.5 bar

7 Contaminated condensate out (male adapter DN09) / pressureless

8 Water in steam generator (male adapter DN09) / min. 3.0 bar (*Water quality: $CaCO_3$ concentration 0 mmol L^{-1} to max. 0.53497mmol L^{-1})*

9 Total emptying steam generator (male adapter DN09) / pressureless

13.2 Electrical Power Supply

WARNING

High leakage current!

Earth connection essential before connecting supply!

Bioreactor

Description	Value	Unit
Voltage 1 phase L1 + N (neutral) + PE (earth)	230 (± 5 %)	V
Frequency range	50	Hz
Max. current	16	A
Leakage current	> 3.5	mA

Steam Generator

Description	Value	Unit
Voltage 3 phases L1 + L2 + L3 + N (neutral) + PE (earth)	400 (± 5 %)	V
Frequency range	50	Hz
Max. current	16	A

INFORMATION

The power supply of both, the bioreactor and the steam generator, must be individually made safe by the use of an FI-switch (or RCD – Residual Current Device) of the kind RCCB, Type B on the installation site.

Detailed information about connection conditions as well as technical data, operation and maintenance of the **steam generator** can be found in the separate documentation from its manufacturer. Read the manual before initial operation of the equipment and strictly follow instructions stated in there.

13.3 Specifications

13.3.1 Instrumentation Cabinet

Description	Value
Dimensions	W = 320 mm D = 450 mm H = 550 mm
Protection class	IP43
Material	1.4301
Peristaltic pumps	*Acid*, *Base*, *Antifoam*, digital *Feed, analogue*

13.3.2 Operating Unit

Description	Value
HMI	Colour touch screen 12"
Protection	IP 66

13.3.3 Vessel

Description	Value
Volume total	Vessel: 30 L Vessel jacket: 2.0 L
Working volume vessel	Max. 20 L Min. 6.1 L
Dimensions	Height: 643 mm Inner diameter: 250 mm Ratio H/D: 2.5 : 1
Pressure range	Vessel inside: -1 up to +3 bar Vessel jacket: 0 up to +3 bar
Temperature range	Vessel inside: -10 up to +150 °C Vessel jacket: -10 up to +150 °C
Material in contact with media	stainless steel 1.4404 or 1.4435 = AISI 316L with finish Ra ≤0.6 µm, electropolished
Material not in contact with media	stainless steel 1.4301 = AISI 304 with finish Ra ≤1.0 µm, electropolished

Technical Data

Vessel top plate assembly	■ 8 x 19 mm ports with Rd28x1/8" ■ 2 Tri-Clamp DN10 ports, 1 for air inlet incl. diaphragm valve **805**, 1 for exit gas cooler ■ 1 x 10 mm port for temperature sensor (PT100) ■ 1 connection flange for motor ■ 4 recessed holes D = 8 mm for the baffles ■ 2 x 4 mm holes for negative lead of the antifoam sensor ■ 2 lifting handles ■ 6 hexagon capped nuts and metal washers for fixing the vessel top plate
Vessel upper section	■ 2 INGOLD standard ports iD = 25 mm / G1-1/4", angled (3°) ■ 2 Tri-Clamp 1-1/2” ports for CIP lances
Vessel flange	6 threaded bolts M10 for fixing the vessel top plate
Vessel jacket and INGOLD ports	■ 1 INGOLD standard port iD = 25 mm / G1-1/4", horizontal ■ 3 INGOLD standard ports iD = 25 mm / G1-1/4", angled (15°) ■ 2 connections for the water in- and outlet
Vessel bottom	1 threaded nozzle for the harvest / sample valve
Accessories	■ 1 sight glass (115 x 15 mm) ■ 1 vessel identification plate ■ 4 baffles, removable, width 25 mm ■ 1 ring sparger
Harvest- /sample valve (bottom valve)	Type NW25.5 incl. steam connection (ISO G1/8")

13.3.4 Temperature

Description	Value	
Heating / Cooling	Steam heating provided by integrated steam generator [1)] Tap water cooling (on site)	
Sterilisation	Automatic with steam provided by integrated steam generator	
Temperature range	Sterilisation	110 °C to 125 °C
	Fermentation [2)]	20 °C to 79 °C
Sensor	Pt-100 class B, 1/3 DIN	
Accuracy temperature measuring & control (Fermentation)	± 0.3 °C at 10 to 60 °C ± 0.5 °C at > 60 °C	

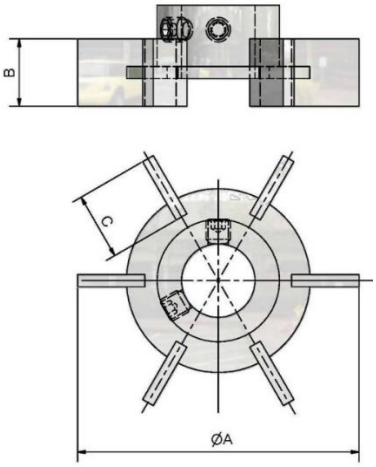
1) *Detailed information about technical specifications, operation and maintenance of the steam generator can be found in the separate documentation from its manufacturer.*

2) *Min. fermentation temperature depends on ambient temperature, used cooling system, stirrer rotation speed and medium viscosity.*

13.3.5 Stirrer

Description	Value
Drive	Top drive, with single mechanical seal
Direction of rotation of drive shaft	Clockwise (top view)
Motor type	AC servomotor, brushless
Range of rotation speed [1)]	10 to 1500 min^{-1}
Accuracy control	± 5 min^{-1} at 10 to 1000 min^{-1} 1 % setpoint at > 1000 min^{-1}

1) *Valid for liquid with viscosity similar to water, without gassing, with 2 Rushton impellers.*



Impellers

Description	Value
Number /Type	3 impellers, type Rushton, 6 blades, adjustable in height
Dimensions	A = 66 mm B = 13 mm C = 16 mm
Material	316L, electropolished, Ra 0.8 µm

13.3.6 Gassing

Description	Value
Gas(es) and entry	Air, O_2, N_2 Gasmix entry via ring sparger or head room (deviation by means of valve **805**) Solenoid valves
Control	Gas flow: 1 MFC Gasmix: 3 solenoid valves
Mass Flow Controller (MFC) **FIC801**	Thermal mass flow controller Manufacturer: Vögtlin Instruments Type: red-y smart series Range: 0.2 – 20 L/min Accuracy: ± 3 % FS Connection thread: 1/4"
Filter	Manufacturer: Pall Type: Novasip, steam sterilisable Model: C3PFRP1A Max. pressure: 6.5 bar Max. temperature: +142 °C Retention rate: 0.2 µm
Steam trap	Type: balanced pressure thermostatic steam trap Material: stainless steel

A detailed documentation about the filter body & element can be found in the separate documentation of the filter's manufacturer PALL.

13.3.7 Exit Gas

Description	Value
Outlet	Via exit gas cooler and exit gas filter into atmosphere
Exit gas cooler	Material: Stainless steel
Filter	Manufacturer: Pall Type: Novasip, steam sterilisable Model: C3PFRP1A Max. pressure: 6.5 bar Max. temperature: +142 °C Retention rate: 0.2 µm
Steam trap	Type: balanced pressure thermostatic steam trap Material: stainless steel

Detailed information about the filter body & element can be found in the separate documentation from the manufacturer PALL.

13.3.8 pH

Description	Value
Control	Peristaltic pumps acid & base
Control range	pH 2 - 12
Measuring accuracy	pH ± 0.1
Measuring system, analogue	
Type of sensor	Conventional pH sensor potential measurement against reference
Manufacturer	METTLER TOLEDO
Measuring range of sensor	pH 2 - 12

For details about technical data, use and maintenance of the sensor see the separate documentation from the sensor manufacturer METTLER TOLEDO.

13.3.9 pO2

Description	Value
Control	Cascaded stirrer Cascaded air flow Cascaded gasmix Cascaded O_2 flow *The functionality of the parameters depends on the hardware configuration of the equipment*
Control range	0 – 100 %
Measuring accuracy	1 % FS
Measuring system, analogue	
Type of sensor	Traditional amperometric/polarographic pO2 sensor
Manufacturer	METTLER TOLEDO
Measuring range sensor	0 % up to 150 %

For details about technical data, use and maintenance of the sensor see the separate documentation from the sensor manufacturer METTLER TOLEDO.

13.3.10 Antifoam

Description	Value
Sensor	Conductive with dosing needle, adjustable in height
Control	Peristaltic pump (*Antifoam*)
Range	0 / 100 % (OFF/ON)

Sensor

Description	Value
Length	350 mm
Material	■ Parts in contact with medium: 316L ■ Surface finish of steel parts in contact with media: 0.8 µm, electropolished
O-rings	EPDM

13.3.11 Pumps

Description	Value	
Type	Peristaltic	
Digital	3 pieces	Acid Base Antifoam
Analogue	1 piece	Feed
Rotation speed	Digital	150 min^{-1} / fixed rotation speed
	Analogue	150 min^{-1} / max. rotation speed, adjustable within range of 0 % up to 100 %
Accuracy	± 1 min^{-1}	

13.3.12 Push Valve

Description	Value
Process connection	Rd28x1/8" (19 mm port in vessel top plate)
Parts in contact with medium	Material: 316L, stainless steel Surface roughness: 0.8 µm, electro polished
O-ring	EPDM

13.3.13 Pressure Indication Vessel

Description	Value
Type	Manometer
Connection	19 mm port in vessel top plate
Range	0 – 4.0 bar
O-ring	EPDM

13.3.14 Pressure: Safety Valves

Description	Value
Safety valve vessel	Triggering pressure: 3 bar g Manufacturer: Ramseyer
Safety valve temperature control circuit	Triggering pressure: 3 bar g Manufacturer: Ramseyer

For details about technical data, use and maintenance of the safety valves refer to the separate documentation from the manufacturer Ramseyer.

13.4 Operating Conditions

Description	Value
Temperature range	5 °C – 35 °C
Relative air humidity, non-condensing	20 % - 90 %
Min. distance from walls, ceilings [1)] and other appliances	150 mm

1) *The distance from the ceiling must be chosen in such a way that the vessel top plate including its built-in parts can easily be lifted from the vessel.*

13.5 Operating Materials

Application	Permitted products
Lubricant for the single mechanical seal (only bacterial system)	Medicinal Glycerine 85 % Quality: PhEur

13.6 Emissions

Description	Value	Units
Noise emission	<70	dB (A)