

Minifors 2

Operating manual



Minifors 2 – Rel. 2.1
Bench-Top Bioreactor
SW: 3.5

Doc-ID: D012, 2, en_GB – Original
Art. 78972

More information about the product is
available online at:
www.infors-ht.com/de/minifors2



INFORS HT
Headoffice, Switzerland
Rittergasse 27
CH-4103 Bottmingen

T +41 (0)61 425 77 00

info@infors-ht.com
service@infors-ht.com

Supplemental directives

About this Manual



This manual enables the safe and efficient handling of the device. All the information and instructions in this operating manual comply with the current standards, legal regulations and the latest technological developments.

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

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

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

Customer Service and Services

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

Declaration of Conformity

The device meets the general requirements of the following standards:

- Machinery Directive 2006/42/EC
- EMC Directive 2014/30/EU

The declaration of conformity in the sense of the Machinery Directive, Annex II 1 A is attached to the operating manual.

Table of contents

Table of contents

1	Safety and Responsibility.....	13
1.1	Explanation of Special Displays.....	13
1.1.1	Warning Messages.....	13
1.1.2	Other Messages.....	13
1.2	Intended Use, Incorrect Use and Misuse.....	14
1.3	Qualified Personnel.....	14
1.3.1	Operator.....	14
1.3.2	Technician.....	15
1.3.3	INFORS HT Service Technician or Licensed Dealer.....	15
1.4	Unauthorized Persons.....	15
1.5	Responsibility of the Provider.....	16
1.6	Residual Risks.....	16
1.7	Warning Symbols on the Device.....	19
1.8	Declaration of Decontamination.....	19
2	Setup and Function.....	20
2.1	Basic Unit.....	20
2.1.1	Overview.....	20
2.1.2	Operating Panel.....	21
2.1.3	Power Switch.....	21
2.1.4	LED Strip – Status Indicator.....	21
2.1.5	Mains Connection.....	22
2.1.6	Water Connections.....	22
2.1.7	Gas Connections.....	23
2.1.8	Signal Connections.....	23
2.1.9	Motor Cable Connection.....	25
2.1.10	Connections for Sensors (Sensor Cables).....	25
2.1.11	Gassing Connection.....	26
2.1.12	Connections Exit Gas Cooler and Valve for Water Flow.....	26
2.1.13	Pumps.....	27
2.1.14	Identification Plate.....	28

Table of contents

2.2	Culture Vessel.....	29
2.2.1	Overview.....	29
2.2.2	Top Plate.....	30
2.2.3	Ports in the Vessel Top Plate.....	31
2.3	Temperature Control System.....	34
2.4	Stirrer.....	35
2.4.1	Overview.....	35
2.4.2	Motor.....	35
2.4.3	Impeller.....	37
2.5	Gassing System.....	38
2.6	pH Control.....	39
2.7	pO ₂ Control.....	41
2.8	Antifoam Control.....	43
3	Options.....	44
3.1	Turbidity Measurement.....	44
3.1.1	Setup and Function.....	44
3.1.2	Mounting the Turbidity Sensor.....	46
3.2	Exit Gas Analysis.....	47
3.2.1	Setup and Function.....	47
3.2.2	Connecting the Gas Sensor.....	47
3.3	Redox Measurement.....	49
3.4	Balances.....	50
4	Accessories.....	51
4.1	Accessories in the Scope of Delivery.....	51
4.2	Cone Plug for Drive Hub.....	52
4.3	Sparger.....	52
4.4	Baffles.....	53
4.5	Blanking Plugs.....	53
4.6	Clamping Adapters and Fastening Screws.....	54
4.7	Sensor Holder.....	55
4.8	Addition Port Adapters and Feed Needles.....	55
4.9	Septum Collar.....	57

Table of contents

4.10	Dip Tubes.....	57
4.11	Immersion Pocket for Temperature Sensor (Pt100).....	58
4.12	Exit Gas Cooler.....	59
4.13	Cold Finger.....	61
4.14	Reagent Bottles.....	62
4.15	Sampling System Super Safe Sampler.....	63
4.16	Pump Heads.....	65
4.17	Vessel Holder.....	66
4.18	Sterile Filters.....	67
4.19	Hoses and Accessories.....	69
4.20	O-Rings and Gaskets.....	70
4.21	Inoculation Accessories and Tools.....	70
4.22	Starter Set.....	71
4.23	Service Sets.....	71
4.24	Auxiliary Supplies.....	71
5	Transport and Storage.....	72
5.1	Transport.....	72
5.2	Storage.....	72
6	Installation and Commissioning.....	73
6.1	Operating Conditions at the Installation Location.....	73
6.2	Minimum Distances to the Device.....	73
6.3	Connecting the Device to On-Site Supply Lines.....	73
6.3.1	Power Supply.....	74
6.3.2	Water Supply and Return.....	74
6.3.3	Gas Supply.....	75
6.3.4	Exit Gas.....	76
6.4	Connecting the Motor Cable.....	76
6.5	Test Run.....	77
7	Before Cultivation.....	82
7.1	Preparing the Culture Vessel.....	82
7.1.1	Checking Gaskets (O-Rings).....	82
7.1.2	Mounting the Impellers.....	83

Table of contents

7.1.3	Mounting Dip Tubes and Spargers.....	84
7.1.4	Inserting the Vessel into the Vessel Holder.....	85
7.1.5	Inserting the Baffles.....	86
7.1.6	Moistening/Filling the Culture Vessel.....	86
7.1.7	Mounting the Top Plate.....	87
7.1.8	Mounting the Blanking Plugs.....	88
7.1.9	Mounting Addition Port Adapters.....	89
7.1.10	Mounting the Feed Needles.....	89
7.1.11	Mounting the Immersion Pocket for Temperature Sensor (Pt100).....	90
7.1.12	Equipping a Port with Septum Collar and Septum for Inoculation.....	90
7.1.13	Preparing the Dip Tube / Addition Port Adapter for Inoculation.....	92
7.1.14	Mounting the Exit Gas Cooler.....	92
7.1.15	Mounting the Cold Finger.....	93
7.1.16	Preparing the Sensors.....	94
7.1.16.1	Calibrating the pH Sensor.....	95
7.1.16.2	Mounting Sensors into 12 mm Ports.....	95
7.1.16.3	Mounting Sensors with Sensor Holder.....	96
7.1.16.4	Mounting the Antifoam Sensor.....	98
7.1.17	Preparing the Sampling System Super Safe Sampler.....	99
7.1.18	Mounting the Sparger Hose and the Inlet Air Filter..	101
7.1.19	Mounting the Hose and Inlet Air Filter for Head Space Gassing.....	102
7.1.20	Preparing the Reagent Bottles, Pumps and Hoses.....	102
7.1.21	Sterile Hose Connections.....	105
7.1.22	Setting the Pumps.....	106
7.1.23	Removing the Pump Heads.....	106
7.1.24	Fitting the Cone Plug for Drive Hub.....	107
7.2	Autoclaving the Culture Vessel.....	108
7.2.1	Checklist Before Autoclaving.....	108
7.2.2	Autoclaving.....	109

Table of contents

7.3	Connecting the Culture Vessel and Preparing the Cultivation.....	111
7.3.1	Hanging the Culture Vessel in Place and Fitting the Pump Heads.....	111
7.3.2	Filling the Reagent Hoses.....	111
7.3.3	Connecting the Gassing.....	112
7.3.4	Connecting the Exit Gas Cooler.....	113
7.3.5	Connecting the Cold Finger.....	113
7.3.6	Coupling the Motor.....	113
7.3.7	Filling the Culture Vessel.....	114
7.3.8	Connecting the Temperature Sensor (Pt100).....	115
7.3.9	Connecting the Antifoam Sensor.....	115
7.3.10	Connecting the pH Sensor.....	116
7.3.11	Connecting the pO ₂ Sensor.....	116
7.3.12	Calibrating the pO ₂ Sensor.....	117
7.3.13	Checking the Hoses and Hose Connections.....	117
8	Cultivation.....	118
8.1	Preparing the Medium.....	118
8.2	Sampling.....	118
8.3	Inoculation.....	122
8.3.1	Inoculation with a Syringe.....	122
8.3.2	Inoculation Using Dip Tube / Addition Port Adapter.....	123
8.4	Harvest.....	123
8.5	Emptying the Culture Vessel.....	124
8.6	Emptying the Reagent Hoses.....	124
8.7	Autoclaving the Culture Vessel After Cultivation.....	125
9	Operation.....	127
9.1	Screen Areas, Menu Navigation and Control Elements.....	127
9.1.1	Overview.....	127
9.1.2	Main Screen.....	128
9.1.3	EDIT VIEW.....	130

Table of contents

9.1.4	START BATCH / INOCULATE / STOP BATCH.....	131
9.1.5	SAMPLE NOW.....	132
9.2	Menus for System Settings.....	134
9.2.1	Overview.....	134
9.2.2	VESSEL TYPE – Selecting a Culture Vessel.....	135
9.2.3	APPEARANCE – Display Settings.....	136
9.2.4	NETWORK SETTINGS.....	138
9.2.5	EVE COMMUNICATION – Communication Settings..	139
9.2.6	USB Data Export and Import from a USB Stick.....	140
9.2.7	SYSTEM INFO – System Information.....	143
9.3	Parameter – Parameter Groups.....	144
9.3.1	Overview.....	144
9.3.2	Parameters – Displays and Functions.....	145
9.3.3	SETPOINT – Setting the Setpoint.....	146
9.3.4	Parameter Alarms.....	147
9.3.5	Cascades.....	149
9.4	MAIN Parameter Group.....	150
9.4.1	Temperature.....	150
9.4.2	Stirrer.....	151
9.4.3	pH.....	151
9.4.4	pO ₂	152
9.4.5	Total Flow.....	155
9.4.6	GasMix.....	155
9.4.7	Foam.....	156
9.5	EXTENDED Parameter Group.....	158
9.5.1	Balance (Optional).....	158
9.5.2	Flow Parameters.....	159
9.5.3	Turbidity (Optional).....	161
9.5.4	Redox (Optional).....	161
9.5.5	Analog IO1 & Analog IO2.....	161

Table of contents

9.6	EXIT GAS Parameter Group.....	163
9.6.1	Exit Gas O ₂	163
9.6.2	Exit Gas CO ₂	163
9.7	PUMPS Parameter Group.....	164
9.7.1	Overview.....	164
9.7.2	Configuring the Pumps.....	165
9.7.3	Pump1.....	167
9.7.4	Pump2.....	167
9.7.5	Pump3.....	167
9.7.6	Pump4.....	168
9.7.7	AUTO FILL/EMPTY – Automatically Filling/Emptying Pump Hoses.....	169
9.8	Calibrating the Sensors.....	171
9.8.1	Calibrating the pH Sensor.....	171
9.8.2	pH Sensor Product Calibration.....	175
9.8.3	Calibrating the pO ₂ Sensor.....	177
9.8.4	Calibrating the Turbidity Sensor.....	180
9.9	PID Controller – Basic Principle.....	182
9.9.1	Table with Settings for the PID Controller.....	182
9.9.2	Tips for Readjusting a PID Controller.....	183
9.9.3	Adjusting PID Settings.....	183
9.10	Alarms – Equipment Alarm Menu.....	184
9.11	Switching off the Device.....	185
10	Cleaning and Maintenance.....	186
10.1	Cleaning Agent and Disinfectant.....	186
10.2	Cleaning the Culture Vessel - Routine Cleaning.....	187
10.3	Removing the Vessel Top Plate and Accessories.....	188
10.3.1	Removing the Exit Gas Cooler.....	188
10.3.2	Removing the Sensors.....	190
10.3.3	Removing Hoses, Filters and Pump Heads.....	190
10.3.4	Removing Blanking Plugs.....	191
10.3.5	Removing the Septum Collar and Septum.....	191

Table of contents

10.3.6	Removing Addition Port Adapters, Feed Needle and Temperature Sensor Immersion Pocket.....	192
10.3.7	Removing the Vessel Top Plate.....	192
10.3.8	Removing the Sparger and the Dip Tube(s).....	193
10.3.9	Removing the Impellers.....	193
10.4	Cleaning and Storing Individual Parts.....	194
10.5	Cleaning the Sensors.....	195
10.6	Cleaning the Hoses and Pump Heads.....	195
10.7	Cleaning the Super Safe Sampler.....	195
10.8	Cleaning the Basic Unit and Operating Panel.....	196
10.9	Maintenance Plan.....	196
10.10	Decalcifying the Device.....	197
11	Rectifying Faults.....	199
11.1	General Faults.....	199
11.2	Faults Drive System.....	200
11.3	Faults Temperature Control System.....	201
11.4	Faults Gassing System.....	202
11.5	Faults pH Control.....	204
11.6	Faults pO ₂ Control.....	206
11.7	Faults Antifoam/Level and Pump.....	207
11.8	Faults Feed and Pump.....	208
11.9	Interferences Turbidity Measurement.....	209
11.10	Replacing Device Fuses.....	210
11.11	Behavior in Case of a Power Interruption.....	210
11.12	Returning for Repair.....	210
12	Disassembly and Disposal.....	211
12.1	Disassembly.....	211
12.2	Disposal.....	211
13	Technical Data.....	213
13.1	Dimensions.....	213
13.2	Weight.....	215

Table of contents

13.3	Connections and Connection Values.....	215
13.3.1	Electrical Connection and Power Values.....	215
13.3.2	Water.....	216
13.3.3	Process Gas.....	217
13.4	Specifications of the Basic Unit.....	217
13.4.1	Operating Panel.....	217
13.4.2	Culture Vessel.....	217
13.4.3	Stirrer.....	219
13.4.4	Temperature Control System.....	222
13.4.5	Gassing System.....	223
13.4.6	pH Control.....	225
13.4.7	pO ₂ Control.....	226
13.4.8	Antifoam Control.....	226
13.4.9	Pumps.....	227
13.5	Specifications of the Options.....	227
13.5.1	Turbidity Measurement.....	227
13.5.2	Exit Gas Analysis.....	228
13.5.3	Redox Measurement.....	228
13.6	Operating Conditions.....	229
13.7	Emissions.....	229
14	EU Declaration of Conformity.....	230

1 Safety and Responsibility

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



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

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

1.1 Explanation of Special Displays

1.1.1 Warning Messages

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



WARNING

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



CAUTION

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



NOTICE

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

1.1.2 Other Messages



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

Safety and Responsibility

1.2 Intended Use, Incorrect Use and Misuse

Intended Use

The bench-top bioreactor Minifors 2 from INFORS HT is designed especially for running bio processes with microorganisms or animal cells for research and development in a biotechnology laboratory.

WARNING

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

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

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

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

Incorrect Use/Misuse

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

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

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

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

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

1.3 Qualified Personnel

1.3.1 Operator

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

Safety and Responsibility

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

To be allowed to operate the device, the operator must have received thorough training and have read and understood the operating manual.

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

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

1.3.2 Technician

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

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

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

1.3.3 INFORS HT Service Technician or Licensed Dealer

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

1.4 Unauthorized Persons

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

Safety and Responsibility

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

1.5 Responsibility of the Provider

Provider

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

Provider Obligations

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

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

1.6 Residual Risks

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

Safety and Responsibility

Electric Current



The device is operated electronically. There is an immediate risk of fatal injury if contact is made with live parts. The following points must be observed in order to avoid the risk of fatal injury:

- In case of damage to insulation, disconnect the device from the power supply immediately and arrange for it to be repaired.
- Disconnect the device from the power supply before commencing any work on the electrical components.
- Always use qualified electricians for any work on the electrical components.
- When replacing fuses, ensure they have the correct number of Amperes.
- If the power cable is defective, replace it with a power cable of the same type.
- Keep moisture away from live parts. It could cause a short circuit.

Hot Surfaces



The culture vessel, the thermal block and adapter as well as the motor (only with the version for microorganisms) can get hot during operation. There is a risk of burns if you come into contact with hot surfaces.

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

Dangerous Gases



The use or production of dangerous – i.e. toxic or asphyxiant – gases entails a significant health risk, especially in small rooms. To prevent high emissions of dangerous gases, the following measures must be taken:

- The gas connections on the device must be checked before any cultivation using dangerous gases are initiated.
- Check the seals on the device at regular intervals and replace them if necessary.
- Check gas-carrying hoses for leaks at regular intervals.
- Safely discharge exit gases.

Flammable or Explosive Substances



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

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

Safety and Responsibility

Corrosive or Toxic Substances



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

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

Bioactive or Pathogenic Organisms



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

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

Overpressure or Vacuum



Glass vessels may break or shatter when subjected to overpressure or vacuums.

Environmental Hazards



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

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

Accessories and Spare Parts



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

1.7 Warning Symbols on the Device

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

Warning symbol	Position	Meaning
	■ Thermal block adapter ■ Motor (version for microorganisms)	Hot surfaces



WARNING

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

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

1.8 Declaration of Decontamination

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

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



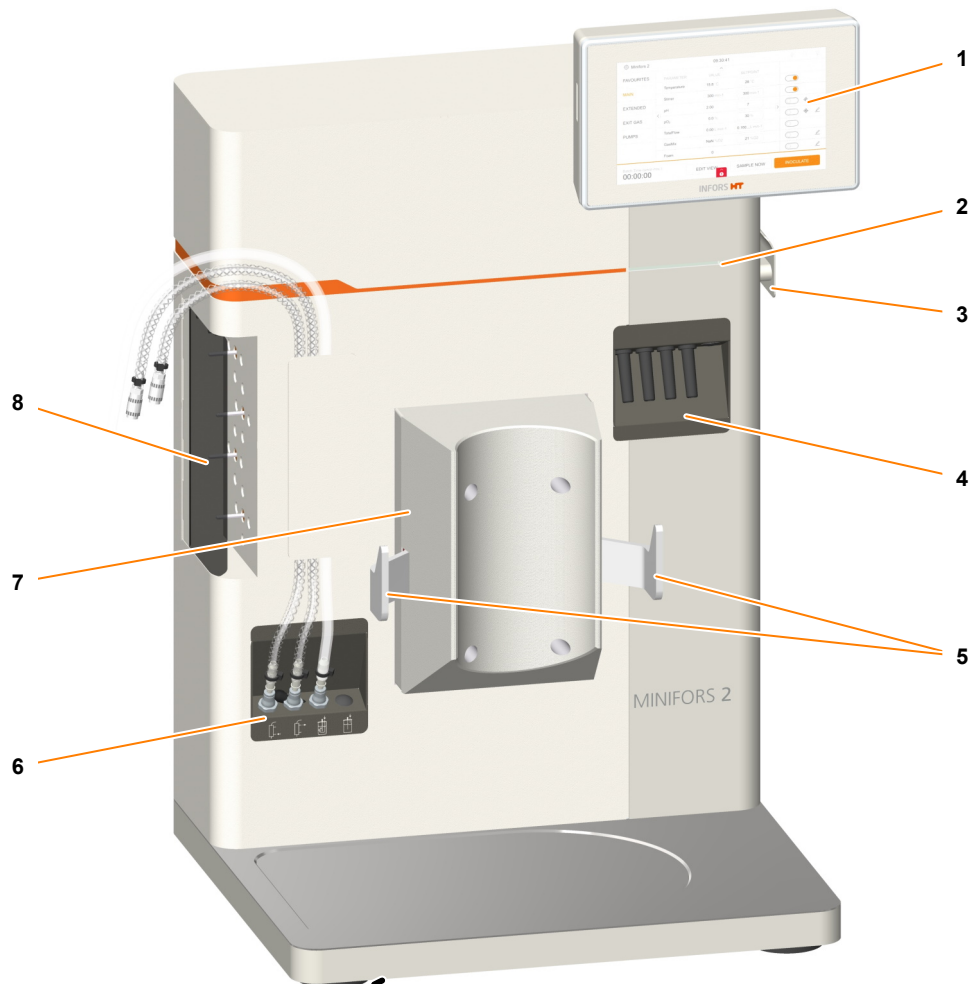
If the return shipment is not accompanied by a signed and complete declaration of decontamination or it is not affixed to the outer packaging, the shipment will be returned unopened to the sender at their expense (see also T&C).

Setup and Function

2 Setup and Function

2.1 Basic Unit

2.1.1 Overview



- | | | | |
|---|-------------------------|---|---|
| 1 | Operating panel | 5 | Hooks for vessel holder |
| 2 | LED signal strip | 6 | Connections for gassing and exit gas cooler |
| 3 | Power switch | 7 | Thermal block and adapter |
| 4 | Connections for sensors | 8 | Pumps |

All of the measurement and control technology is built into the basic unit. The basic unit is equipped as standard with a thermal block plus adapter for regulating the temperature of the culture vessel, four pumps for adding reagents and nutrient solution, and the operating panel.

2.1.2 Operating Panel

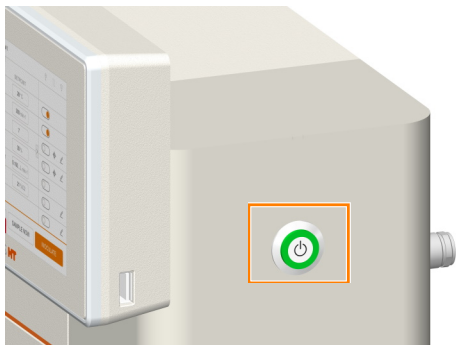


The operating panel on the top right of the basic unit has a 7" TFT touch screen.

- On the right-hand side of the panel is a USB port.
- On the left-hand side is a slot for an SD card (not visible in the figure, without function).

The operating panel switches on via the power switch.

2.1.3 Power Switch



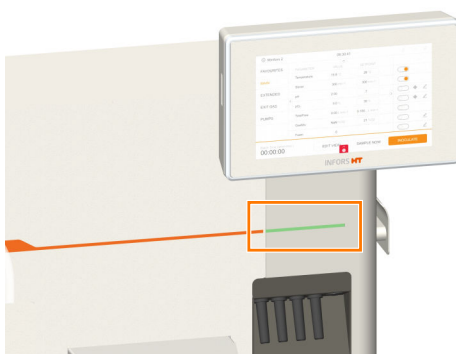
The power switch is located on the right-hand side on the basic unit. In addition to normal switching on and off, the power switch also serves as an emergency switch.

The power switch lights up green as soon as the device is switched on.



In the event of an emergency shutdown via the power switch during a running batch (bioprocess), all settings are saved. After switching on via the power switch, the batch continues with the same settings as before the emergency shutdown. This is also the case if the batch is controlled via eve®, the platform software for bioprocesses.

2.1.4 LED Strip – Status Indicator



The LED strip is located on the front of the basic unit and indicates the following states:

- Green steady light: the device is functioning as normal. The led strip lights up green as soon as the device is switched on.
- Green blinking light: one or several parameter alarm(s) has/have occurred (→ Chapter 9.3.4 'Parameter Alarms' on page 147).
- Red blinking light: one or several device error(s) has/have occurred (→ Chapter 11 'Rectifying Faults' on page 199).

Setup and Function

2.1.5 Mains Connection



The mains connection is located at the bottom left of the back of the basic unit. The device is protected against excessive current consumption by two fuses. The device fuses are located directly above the mains connection. The country-specific power cable required for connection to the power supply is included in the scope of delivery. If the power cable is defective, replace it with a power cable of the same type.

Before connecting the device, make sure that the voltage values of the device correspond to the local mains voltage. The mains connection must be easily accessible at all times so that the device can be disconnected from the power supply quickly in case of an emergency.

2.1.6 Water Connections

The water connections are located on the rear of the basic unit, at the bottom right. They are marked with the following symbols:

Symbol	Designation	Function
	<i>H₂O IN</i>	Water inlet
	<i>H₂O OUT</i>	Water outlet

Setup and Function

2.1.7 Gas Connections

The connections for the gas supply are located on the rear of the basic unit, at the bottom right, above the water connections. They are marked with the following symbols:

Symbol	Designation	Function
	<i>CO₂ IN</i>	Inlet carbon dioxide
	<i>N₂ IN</i>	Inlet nitrogen
	<i>O₂ / GAS 2 IN</i>	Inlet oxygen or 2 nd gas
	<i>AIR IN</i>	Inlet air



The gas supply connections *CO₂ IN* and *N₂ IN* are closed with blanking plugs on the device version for microorganisms. They are used in the device version for cell cultures.

2.1.8 Signal Connections

Overview Signal Connections

The following signal connections with the corresponding symbols and labelling are located on the left rear side of the basic unit:

Symbol	Designation	Function
	<i>ANALOG I/O</i>	Analogue input/output for connection of external devices. It has a connector with PUSH IN spring connection (➔ 'Pis Assignment Plug ANALOG I/O' on page 24).

Setup and Function

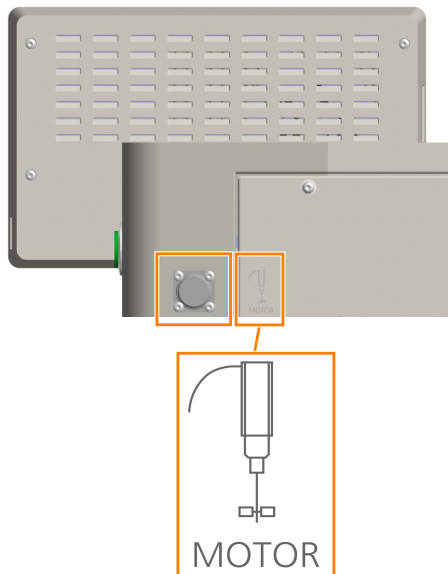
Symbol	Designation	Function
 SERVICE	<i>SERVICE</i>	9-pin RS232 for connecting a diagnostic computer for maintenance.
 BALANCE	<i>BALANCE</i>	9-pin RS232 for connecting a balance.
 LAN	<i>LAN</i>	Port for connecting a network cable.

Pis Assignment Plug ANALOG I/O

1	2
3	4
5	6
7	8

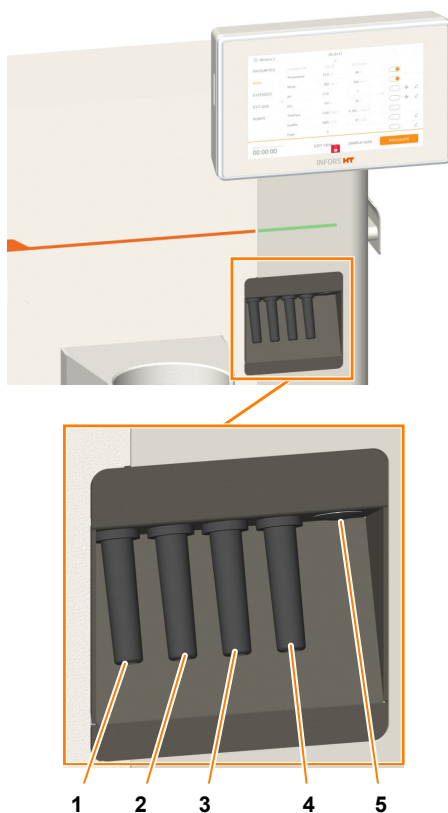
- 1 +Analogue Out A
- 2 GND (Analogue Out A)
- 3 +Analogue Out B
- 4 GND (Analogue Out B)
- 5 Analogue In A (240 Ohm burden)
- 6 GND (Analogue IN A)
- 7 Analogue In B (240 Ohm burden)
- 8 GND (Analogue IN B)

2.1.9 Motor Cable Connection



The connection for the motor cable is located on the rear of the basic unit at the top left, and marked with a corresponding symbol.

2.1.10 Connections for Sensors (Sensor Cables)

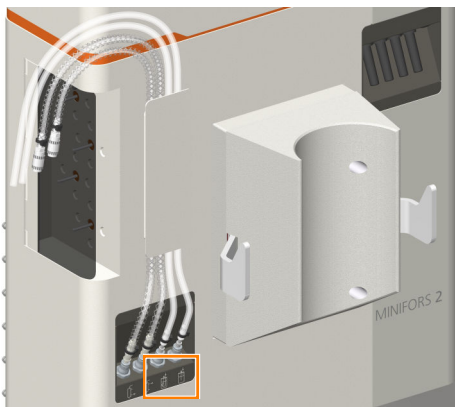


- 1 pO₂
- 2 Temperature (Pt100)
- 3 Antifoam
- 4 pH
- 5 Spare connection for turbidity measurement sensor (option)

The basic unit is equipped and configured by default for measurement of temperature, pH, pO₂ and for foam detection ("antifoam"). This means, the temperature sensor (Pt100) and the cables for connecting the pH, pO₂ and antifoam sensors are always present. The appropriate sensors are included in the standard package.

Setup and Function

2.1.11 Gassing Connection



The connections for gassing are located on the front of the basic unit, at the bottom left. They are marked with a corresponding symbol.

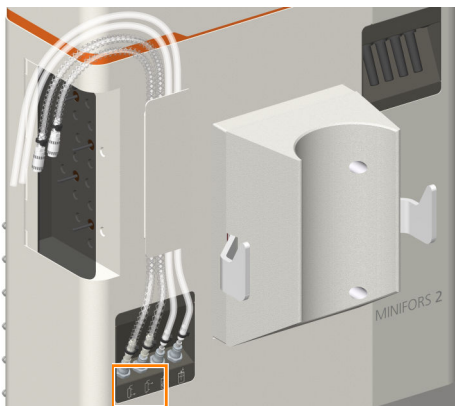
Symbol	Function
	Connection for gassing via sparger.
	Connection for addition port adapter for head space gassing (only version for cell cultures).



The hoses are already connected to the basic unit ex-factory.

2.1.12 Connections Exit Gas Cooler and Valve for Water Flow

Connections Exit Gas Cooler

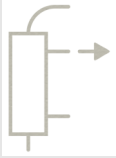


The water connections for the exit gas cooler are located on the front of the basic unit, at the bottom left. The water supply and return hoses for the exit gas cooler are connected to the basic unit ex-factory. The rapid couplings at both ends of the hoses are used to connect them to the exit gas cooler. Due to the different hose lengths, it is not possible to connect them to the exit gas cooler incorrectly.

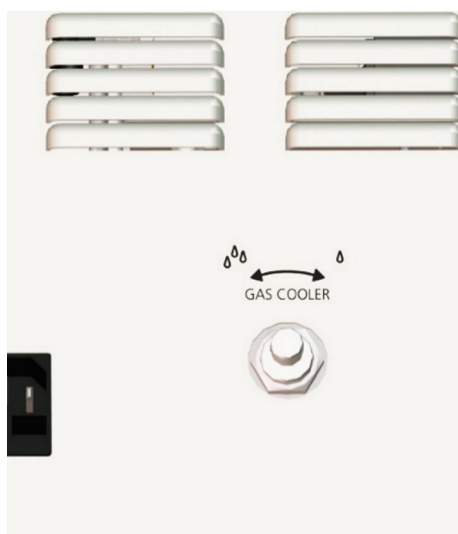
The water connections are marked with the corresponding symbols:

Symbol	Function
	Water inlet exit gas cooler

Setup and Function

Symbol	Function
	Water outlet exit gas cooler

Valve for Water Flow



The manual valve for setting the water flow is located on the rear of the basic unit, labelled with *GAS COOLER* and marked with a corresponding symbol.

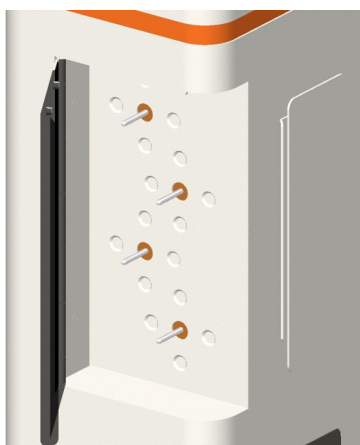
Symbol	Function
	Regulation of water flow exit gas cooler

The valve is set ex-factory. If necessary, the water flow rate can be adjusted using the valve:

- Turn counter-clockwise to increase the water flow rate.
- Turn clockwise to reduce the flow rate.

The valve can be fixed in the required position using a lock nut.

2.1.13 Pumps



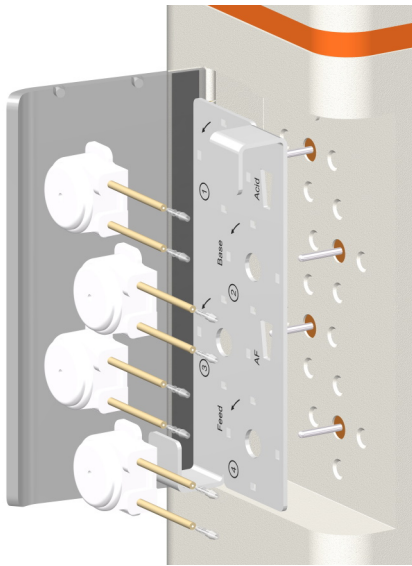
Reagents and nutrient solution (Feed) are supplied via four peristaltic pumps. The pumps are driven by stepper motors. The pump drive shafts are located on the left-hand side of the basic unit. The drive shafts' direction of rotation is set as standard to counter-clockwise for "filling"; see marking on mounting plate.

The pumps can be configured individually using the operating panel, and thus each set to digital or analogue operating mode as required:

- Digital = OFF/ON operation with fixed speed
- Analogue = continuous operation with variable speed

A hinged Plexiglas cover acts as a guard during operation.

Setup and Function



The autoclavable pump heads are plugged into a mounting plate (depicted separately here in order to show the marking under the pumps). The pump heads and the mounting plate can be simply pushed onto or pulled off the drive shafts.

The mounting plate is numbered 1 to 4 from top to bottom, and labelled to indicate the standard factory settings:

- Pump 1: *Acid* (digital)
Alternative setting: *Feed* (analogue)
- Pump 2: *Base* (digital)
Alternative setting: *Feed* (analogue)
- Pump 3: *AF* (antifoam, digital)
Alternative setting: *Level* (digital) or *Feed* (analogue)
- Pump 4: *Feed* (analogue)
Alternative setting: *Balance* or *Dose* (analogue)

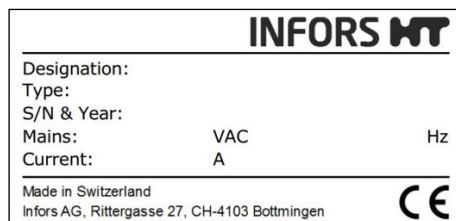
For more information on possible pump settings, see ➔ Chapter 9.7.1 'PUMPS Parameter Group' on page 164.

2.1.14 Identification Plate

Position

The identification plate is located at the side of the basic unit.

Content

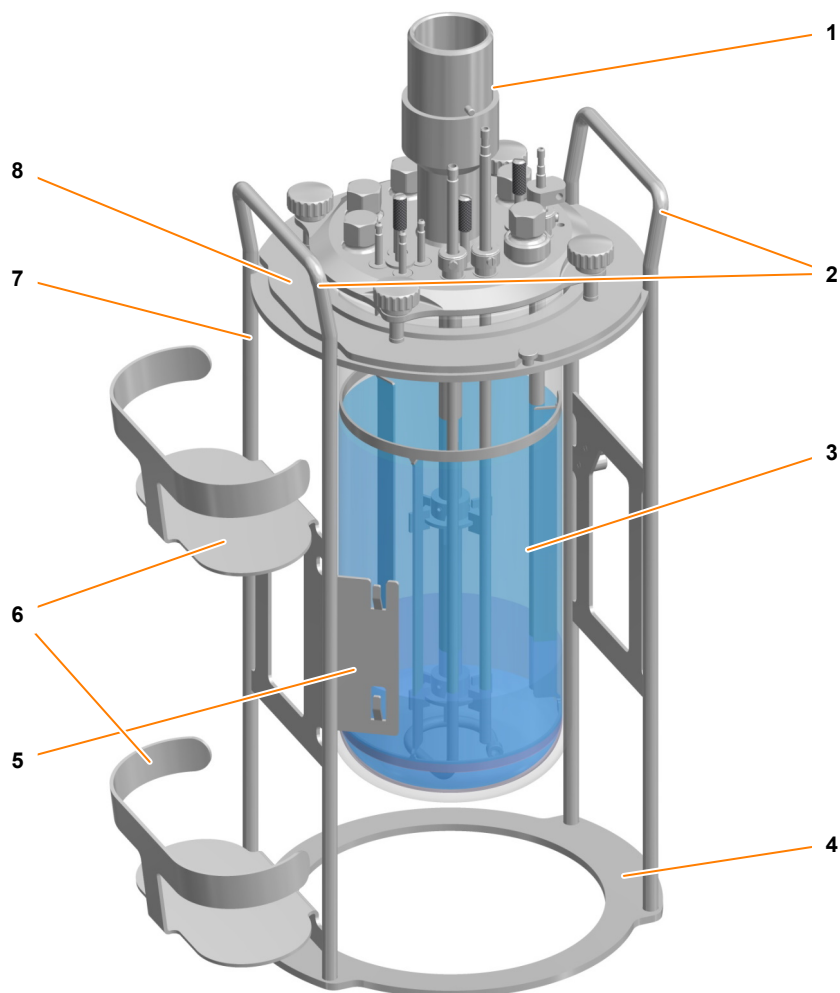


The identification plate is designed to allow clear identification of the device. It contains the following information:

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

2.2 Culture Vessel

2.2.1 Overview



- 1 Motor coupling
- 2 Vessel holder handle
- 3 Glass vessel
- 4 Vessel holder stand

- 5 Pump holder
- 6 Reagent bottle holder
- 7 Vessel holder
- 8 Top plate

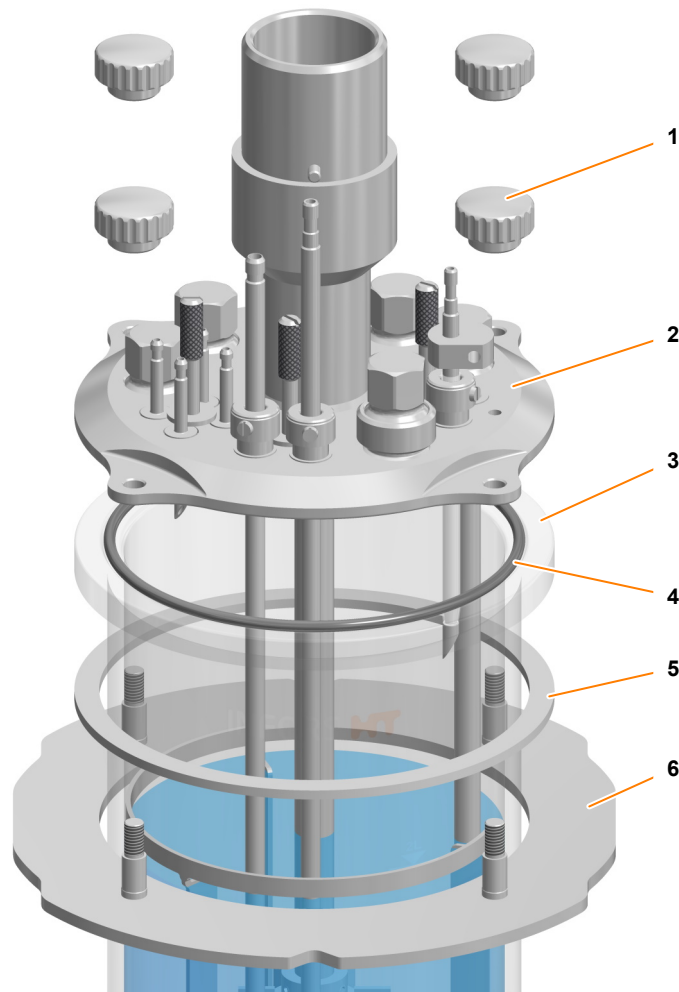
The culture vessel comprises a glass vessel, the top plate with the standard fittings (which vary based on vessel size) and the vessel holder with handles. The vessel is made of borosilicate glass.

The figure shows a culture vessel for microorganisms with a total volume of 1.5 L and a nominal diameter of 90 mm. There are three vessel sizes available, each with a matching top plate.

The vessel holder has two handles on the side, which are used when emptying and cleaning the vessel or transporting it to the autoclave.

Setup and Function

2.2.2 Top Plate



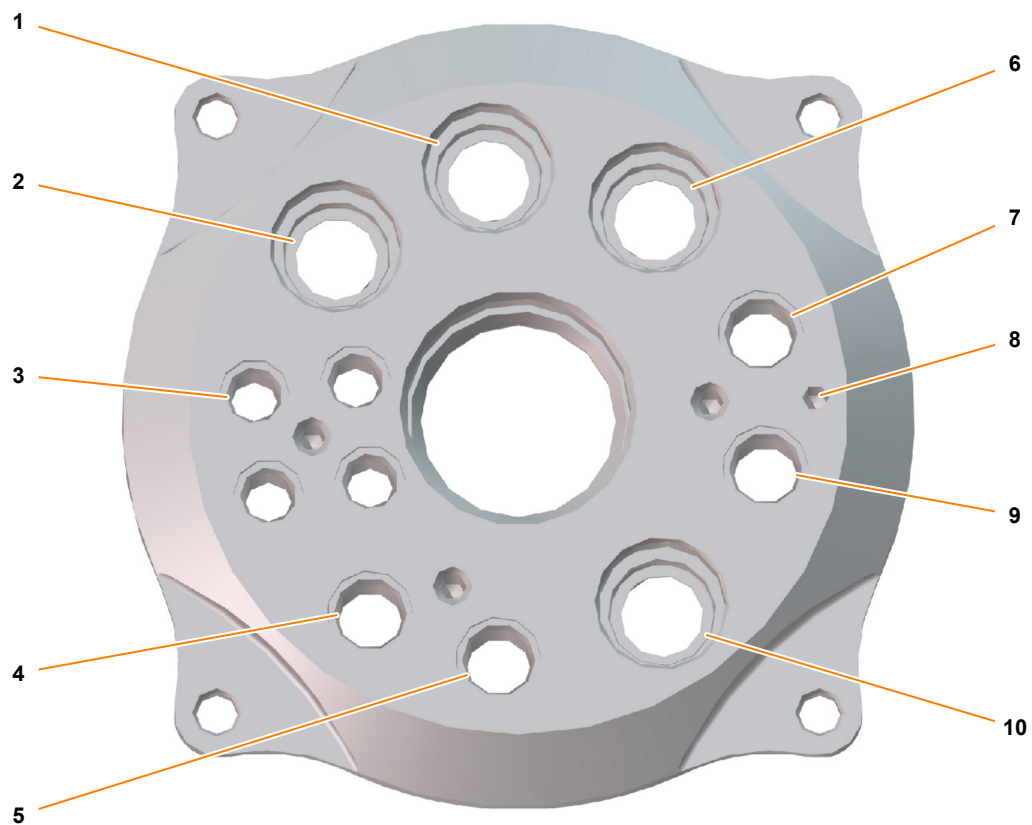
- 1 Knurled nut (4 x)
- 2 Top plate
- 3 Vessel
- 4 O-ring
- 5 Shock-absorbing ring (spacer ring)
- 6 Flange

The top plate is attached to the vessel using four knurled nuts and a flange. The knurled nuts also hold the vessel in place in the vessel holder. An O-ring is used to seal the top plate. A spacer ring is used to prevent the top plate from exerting pressure on the rim of the vessel.

2.2.3 Ports in the Vessel Top Plate

The vessel top plate has different ports of different sizes to mount the different components such as sparger, blanking plugs, sensors etc. The number of ports in the top plate and its configuration depends on the nominal diameter (DN = inner diameter) of the culture vessel.

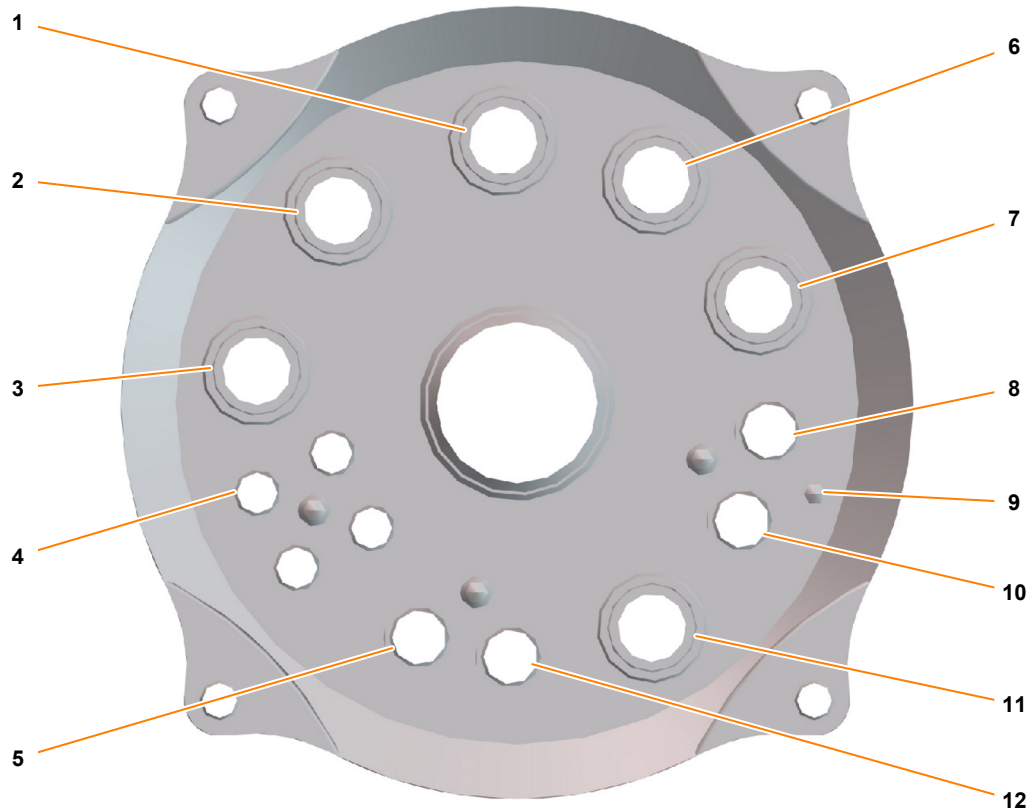
Vessel Top Plate, DN 90



- | | |
|--|--|
| 1 Ø 12 mm Pg13.5: pH sensor | 7 Ø 10 mm: immersion pocket temperature sensor (Pt100) |
| 2 Ø 12 mm Pg13.5: exit gas cooler | 8 Ground connection antifoam sensor |
| 3 Ø 7.5 mm: addition port adapter, 4 x | 9 Ø 10 mm: antifoam sensor |
| 4 Ø 10 mm: sparger | 10 Ø 12 mm Pg13.5: inoculation |
| 5 Ø 10 mm: dip tube sampling | |
| 6 Ø 12 mm Pg13.5: pO ₂ sensor | |

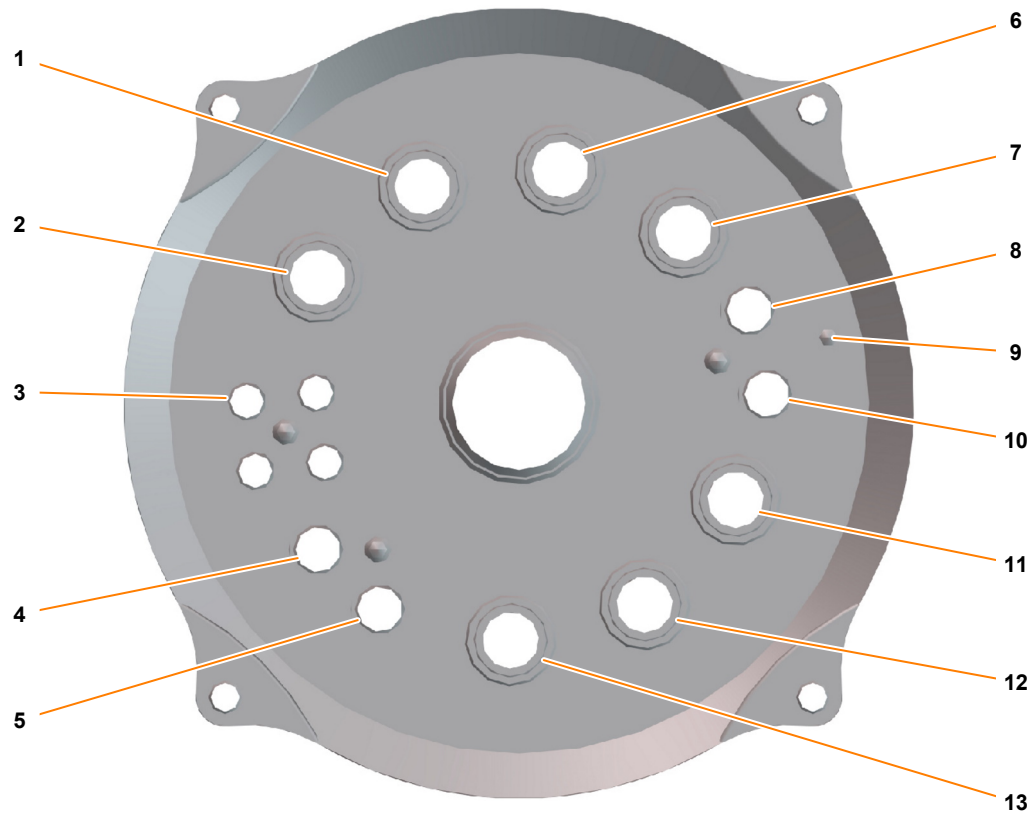
Setup and Function

Vessel Top Plate, DN 115



- 1 Ø 12 mm Pg13.5: pH sensor
- 2 Ø 12 mm Pg13.5: exit gas cooler
- 3 Ø 12 mm Pg13.5: additional sensor
- 4 Ø 7.5 mm: addition port adapter, 4 x
- 5 Ø 10 mm: sparger
- 6 Ø 12 mm Pg13.5: pO₂ sensor
- 7 Ø 12 mm Pg13.5: additional sensor

- 8 Ø 10 mm: immersion pocket temperature sensor (Pt100)
- 9 Ground connection antifoam sensor
- 10 Ø 10 mm: antifoam sensor
- 11 Ø 12 mm Pg13.5: inoculation
- 12 Ø 10 mm: dip tube sampling

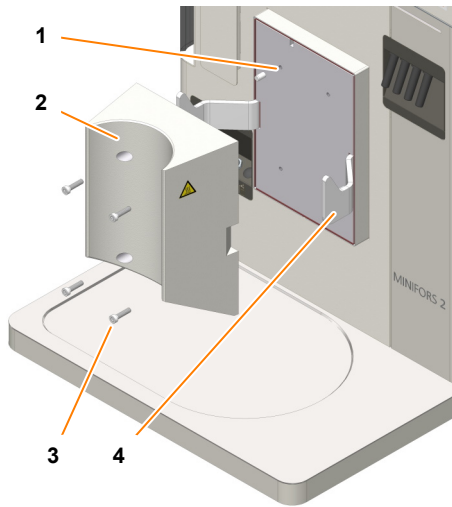
Vessel Top Plate, DN 145


- 1 Ø 12 mm Pg13.5: exit gas cooler
- 2 Ø 12 mm Pg13.5: additional sensor
- 3 Ø 7.5 mm: addition port adapter, 4 x
- 4 Ø 10 mm: sparger
- 5 Ø 10 mm: dip tube sampling
- 6 Ø 12 mm Pg13.5: pH sensor
- 7 Ø 12 mm Pg13.5: pO₂ sensor

- 8 Ø 10 mm: immersion pocket temperature sensor (Pt100)
- 9 Ground connection antifoam sensor
- 10 Ø 10 mm: antifoam sensor
- 11 Ø 12 mm Pg13.5: additional sensor
- 12 Ø 12 mm Pg13.5: additional sensor
- 13 Ø 12 mm Pg13.5: inoculation

Setup and Function

2.3 Temperature Control System



- 1 Thermal block
- 2 Thermal block adapter
- 3 Fastening screw, 4 x
- 4 Hook, 2 x

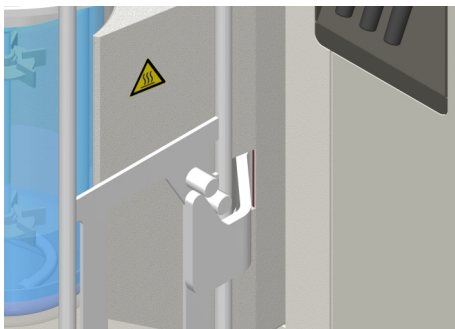
The temperature (heating and cooling) is controlled using a thermal block and its adapter.

There is a thermal block adapter for each vessel size. The thermal block adapters are screwed onto the thermal block.

The temperature in the culture vessel is measured using a platinum resistor temperature sensor (Pt100). The temperature is transmitted from the thermal block to the adapter and from the adapter to the culture vessel by means of heat exchange.

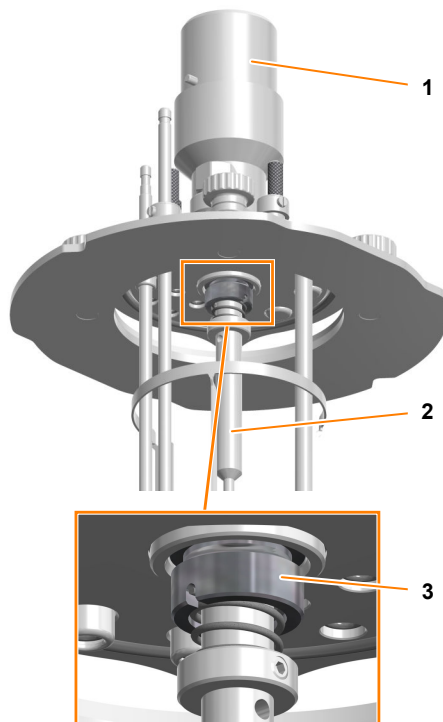
The thermal block is heated electrically using heating cartridges. It is cooled by water flowing through it.

The two hooks on the thermal block hold the culture vessel in place on the basic unit. In order to ensure optimum heat transmission, the two hooks also pull the culture vessel right up against the thermal block.



2.4 Stirrer

2.4.1 Overview



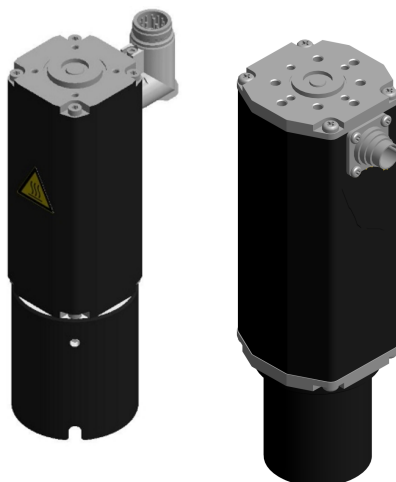
- 1 Drive hub
- 2 Stirrer shaft
- 3 Mechanical seal

The stirrer shaft is driven from above and turns counter-clockwise.

The stirrer shaft is sealed using a mechanical seal.

2.4.2 Motor

Version for Microorganisms



A brushless gear motor with a mechanical coupling is used as standard. Depending on the size of the vessel, two motors with different power levels are used (→ Chapter 13.4.3 'Stirrer' on page 219).

- Left: Small motor for culture vessels DN 90
- Right: Large motor for culture vessels DN 115 and 145

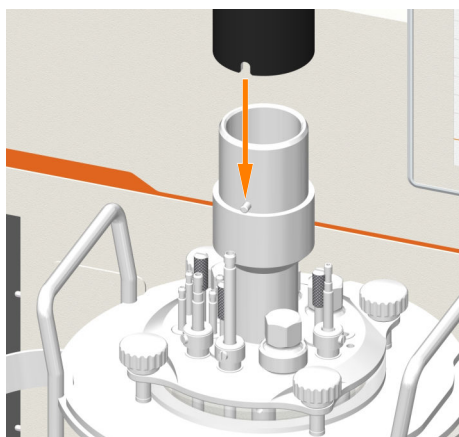
Setup and Function

Version for Cell Cultures



The same brushless gear motor with mechanical coupling is used for all vessel sizes.

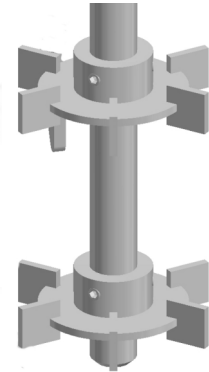
Coupling/Uncoupling the Motor



The motor is connected by pushing it onto the drive hub on the top plate.

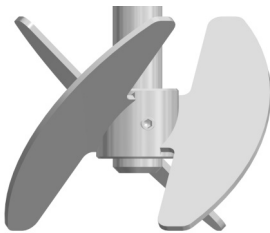
2.4.3 Impeller

Version for Microorganisms



Two Rushton impellers are attached to the stirrer shaft by means of grub screws.

Version for Cell Cultures



One pitched blade impeller is attached to the stirrer shaft by means of grub screws.

Setup and Function

2.5 Gassing System

Gases

The following gases can be used:

Version for microorganisms	■ Air ■ Oxygen (O₂) or Nitrogen (N₂) The basic unit is equipped and configured with two mass flow controllers for controlling the gas flow and, if necessary, the gas mixture. If oxygen or nitrogen are used in addition to air, the gases are mixed before being fed into the culture vessel. Both the gas flow rate(s) and the composition of the gas mixture (where applicable) are set using the operating panel.
Version for cell cultures	■ Air ■ Oxygen (O₂) ■ Nitrogen (N₂) ■ Carbon dioxide (CO₂) The basic unit is equipped and configured with five mass flow controllers for controlling the gas flow and the gas mixture. Air, oxygen and nitrogen are used for sparger gassing. Additionally, air can be used for head space gassing. CO₂ can be used instead of liquid acid for pH control and is either added via sparger or head space. The gases are mixed before being fed into the culture vessel. Both the gas flow rate(s) and the composition of the gas mixture are set using the operating panel.

Gas Entry

Version for microorganisms	A hose line leads the gas or gas mixture from the gassing connection on the basic unit to the culture vessel, via a sterile filter. The gas is fed directly into the medium via the sparger (sparger gassing).
Version for cell cultures	Two hose lines lead the gas or gas mixture from the gassing connections (sparger and head space) on the basic unit to the culture vessel, via sterile filters. Gas or the gas mixture is fed directly into the medium via the sparger. For head space gassing, the gas is led via addition port adapter into the head space of the culture vessel, i.e. above the culture medium.

Setup and Function

Exit Gas

Even without active gassing, any cultivation can increase the pressure inside the vessel through heating or gas production. As such, an exit gas line is essential for each cultivation.

Siphoning off exit gas via the exit gas cooler: the exit gas cooler dries the exit gas through condensation, thus preventing the exit gas filter from becoming clogged with moisture. At the same time, it also prevents liquid loss in the culture medium



If heavy foaming is expected, a bottle of antifoam agent can be installed upstream of the exit gas filter as a foam trap.

The exit gas cooler is included in the standard package (→ Chapter 4.12 'Exit Gas Cooler' on page 59).

2.6 pH Control

Function

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

The reagents are kept in reagent bottles that are connected to the culture vessel via hoses with addition port adapters in the vessel top plate and the two pumps.

Version for cell cultures: here, CO₂ can be used for pH control instead of liquid acid and added either via the sparger or into the head space.

Measurement System

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



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

Measurement system	Properties
METTLER digital	- Conventional pH sensor (potential measurement against reference) with built-in electronics - Type: InPro 3253i, ISM
HAMILTON digital	- Conventional pH sensor (potential measurement against reference) with built-in electronics - Type: Easyferm Plus ARC

Setup and Function

Calibration

Generally speaking, the following applies: the calibration of a pH sensor is always performed BEFORE the autoclaving (➔ Chapter 7.1.16.1 'Calibrating the pH Sensor' on page 95).



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

Mounting

For culture vessels with nominal widths of 90 and 145, pH sensors can be mounted directly into 12 mm/Pg13.5 ports. For culture vessels with a nominal width of 115, a sensor holder is used. For details on the sensor holder, see ➔ Chapter 4.7 'Sensor Holder' on page 55.

2.7 pO₂ Control

Function

The oxygen saturation in the (culture) medium is measured by the pO₂ sensor and can be adjusted as follows:

pO₂ increase	The concentration of oxygen dissolved in the medium (pO₂) can be increased using the following methods: ■ Increasing the rotation speed of the stirrer ■ Increasing the gas volume flow rate (air and/or oxygen) ■ Increasing the oxygen content in the Gasmix These approaches can also be combined.
pO₂ reduction	In anaerobic processes, the vessel can be gassed using nitrogen. This displaces the oxygen dissolved in the medium.

Measurement System

Depending on the variant selected, the measurement system for pO₂ is equipped for digital sensors manufactured by METTLER or HAMILTON.



Digital pO₂ sensors have been preconfigured by the INFORS HT device manufacturer. Replacement sensors must be configured before use.

Measurement system	Properties
METTLER digital	■ pO₂ sensor with integrated opto electronics ■ Type: InPro6860i, ISM, selection: – Traditional , with straight opto cap – HD, with angled opto cap, with noise-free measurement signal with anti-bubble technology
HAMILTON digital	■ pO₂ sensor with integrated opto electronics ■ Type: VisiPerm DO ARC / VisiPerm RS485-ECS, selection: – ODO-Cap H0 ¹⁾ / H3, straight, standard applications – ODO-Cap H2 ¹⁾ / H4, convex, more robust, slightly longer response time ¹⁾ Only VisiPerm DO ARC

Setup and Function

Measurement und Calibration

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



Depending on the specifications defined by the user, the pO₂ sensor is calibrated either before the vessel is filled with medium or afterwards, in the prepared medium.

Mounting

For culture vessels with nominal widths of 90 and 145, pO₂ sensors can be mounted directly into 12 mm/Pg13.5 ports. For culture vessels with a nominal width of 115, a sensor holder is used. For details on the sensor holder, see ➔ Chapter 4.7 'Sensor Holder' on page 55.

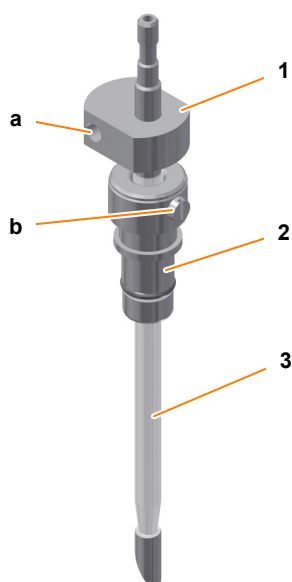
2.8 Antifoam Control

Function

Foam hinders the exchange of gas between the medium and the gas phase in the head space. The exit gas filter can become clogged with foam, which causes a pressure build-up in the vessel. This can be prevented by adding antifoam agent.

The antifoam agent is kept in a reagent bottle that is connected to the antifoam sensor and the antifoam pump via a hose. The sensor also acts as a dosing needle. When the sensor comes in contact with foam, the antifoam pump is activated and antifoam agent is fed into the vessel via the dosing needle.

Antifoam sensor



- 1 Sensor head with port for banana connector (a)
- 2 Clamping adapter with slotted screw (b)
- 3 Needle with transparent insulation

Data	Value	Unit
Inside-Ø	2	mm
Outside-Ø hose connection	4	mm

A clamping adapter is used to mount the sensor in the 10 mm port in the vessel top plate.

The antifoam sensor is equipped with two NON-autoclavable protective caps.

Options

3 Options

3.1 Turbidity Measurement

3.1.1 Setup and Function

Turbidity measurement can be used to draw conclusions regarding the biomass concentration in the culture. To determine the turbidity in the culture two measurement systems are available:

Variant ASD12-N

The measurement system ASD12-N consists of a sensor (single channel light absorption) with integrated transmitter.

The ASD12-N sensors supply a non-linearised turbidity measurement for the culture. This can be linearised manually using the soft sensor in eve®, for example, to determine correlation with factors such as the biomass concentration or optical density. The following path lengths are available:

- Version for microorganisms: OPL05 for higher cell densities
- Version for cell cultures: OPL10 for lower cell densities



If the temperature of the sensor rises above 50 °C during operation in the medium, an automatic switch-off takes place. After the medium has cooled down, the measurement continues automatically.

Variant CGQ BioR

The CGQ BioR sensors non-invasively measure the scattered light of the culture. This is proportional to the biomass concentration in the bioreactor, but can also be processed, e.g. by a soft sensor in eve®, to obtain e.g. a correlation with the optical density

The sensor has two LEDs/measurement modes:

- Infrared: (940 nm) for high cell densities
- Green: (521 nm) for low cell densities

**CAUTION**

The light emitted by the LEDs on the sensor plate is highly sensitive and can damage the iris or retina. The CGQ BioR sensor plate contains an infrared LED that emits high energy radiation in the invisible range. Sensor plates with this LED carry the warning symbol shown here.

- Wear safety goggles and avoid direct contact of LEDs with eyes or skin.
- Always keep a safety distance of >1 m from active sensor plates.
- Pause or stop running measurements before all work within the safety distance.



CGQ BioR sensors are optimised for microbial bioprocesses. The sensors may be used in temperatures from 15 to 50 °C.

Calibration

ASD12-N sensors are pre-calibrated ex-factory. Inserts are available for reference measurement. Due to the different light absorption of different media, zero point calibration should be performed before each cultivation process. This can be done on the operating panel, either before or after autoclaving, depending on the application in question (→ Chapter 9.8.4 'Calibrating the Turbidity Sensor' on page 180).

CGQ BioR sensors are pre-calibrated ex-factory. A new calibration is not necessary.

Options

3.1.2 Mounting the Turbidity Sensor

Variant ASD12-N

For culture vessels DN 90 and DN 145, ASD12-N sensors can be mounted directly into 12 mm/Pg13.5 ports. For culture vessels with DN 115, a sensor holder is used. For more details on the sensor holder, see ➔ Chapter 4.7 'Sensor Holder' on page 55.

Note the following points for mounting:

- Ensure that the sensor is fitted with an O-ring; fit an O-ring if necessary.
- Mount the sensor by hand – do not use any tools!
- If the mounting depth of the sensor is adjustable (mounting with sensor holder), make sure the mounting depth is set correctly prior to autoclaving, as later adjustment represents a contamination risk.
- Mount the sensor in such a way that it cannot come in contact with other components or the glass vessel.
- Mount the sensor in such a way that it has good access to the flow and there is no risk of bubbles collecting in the measurement gap.

Variant CGQ BioR

CGQ BioR sensors are always attached to the culture vessel with the strap attached to the sensor. For this purpose, the sensor with the measuring window is pressed against the glass vessel and fixed with the strap. Depending on the culture vessel, different positions of the sensor or attaching methods may be necessary. For mounting details, see separate documentation of the sensor manufacturer.

Note the following points for mounting:

- Ensure that the sensor is not attached to markings or stickers on the glass vessel, this may affect the measurement.
- Mount the sensor so that it is not in front of or in the direct vicinity of reflective steel parts (< 20 mm).
- Ensure that the sensor is positioned in such a way that liquid is in front of the measurement window during the entire bioprocess
- Foam, high gas hold-ups and the use of antifoam agents can (significantly) interfere with the light scattering of growing cells.

3.2 Exit Gas Analysis

3.2.1 Setup and Function

Setup and Function

To allow the user to draw conclusions regarding the status of the culture while the bioprocess is still underway, the CO₂ and O₂ measurements are often taken and analyzed in the exit gas flow of the bioreactor.

For exit gas analysis, combined CO₂ and O₂ sensors of the type BlueInOne Firm or Cell as well as BlueVary by the manufacturer BlueSens are available.

3 m of pressure hose, D = 8 x 14.5mm and a clamp are included for establishing the hose line between the gas sensor and the culture vessel (exit gas filter).

Calibration

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

Replacing the BlueVary Gas Sensor Cartridge

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

3.2.2 Connecting the Gas Sensor

To view measurements on the operating panel, the gas sensor must be connected to the sensor cable, and the exit gas from the bioreactor must be led through the gas sensor using a hose. The cable is usually connected once during commissioning and can remain untouched thereafter. The connection to the exit gas line must be re-established before each cultivation process

The ideal connection conditions are detailed in the separate documentation provided by the manufacturer.

Connecting the Sensor Cable

The sensor cable is pre-installed on the rear of the device ex-factory. The cable has an 8-pin round plug connector. To connect the sensor, the plug connector is plugged into the socket marked Port A on the gas sensor.

Due to the length of the sensor cable, the gas sensor can be positioned in a large number of possible locations.

Options

Establishing the Hose Connection

The hose connection between the culture vessel (exit gas filter) and the gas sensor must be designed in line with the direction in which the gas flows through the gas sensor:

1. ➔ Cut as short a piece as possible off the supplied pressure hose.
2. ➔ Push one end of the hose onto the hose nozzle (observe direction of flow) on the gas sensor's flow adapter and fasten in place with the clamp.
3. ➔ Push the open end of the hose onto the exit gas filter on the exit gas cooler.



Do NOT use a clamp here, as the hose must be easy to disconnect at this point, e.g. for autoclaving the culture vessel.

3.3 Redox Measurement

For measurement of the reduction/oxidation potential (redox) in the medium, a redox sensor can be connected instead of the pO₂ sensor. The prerequisite for this is that the device is equipped for HAMILTON sensors

Measurement System

- Classic combined sensor (oxidation reduction potential measurement against a reference) with integrated electronics
- Type: Easyferm Plus ORP ARC

Mounting

The redox sensor is mounted in the same way as a pH sensor.

Calibration

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

Options

3.4 Balances

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

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

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

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

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

4 Accessories

4.1 Accessories in the Scope of Delivery

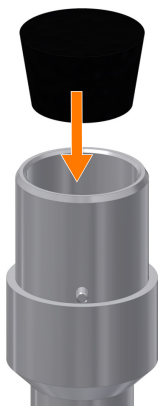
The table below lists all the accessories included in the standard package, divided according to vessel size (TV = total volume) and nominal diameter (DN), inside diameter) as well as version of the device. M = version for microorganisms, C = version for cell cultures.

Accessories	1.5 l TV / DN 90		3.0 l TV / DN 115		6.0 l TV / DN 145	
	M	C	M	C	M	C
Impeller, Rushton	2	--	2	--	2	--
Impeller, pitched bladed, downward flow	--	1	--	1	--	1
Baffles	1	--	1	--	1	--
Sparger, ring-shaped	1	1	1	1	1	1
Immersion pocket for temperature sensor in 10 mm port	1	1	1	1	1	1
Dip tube, straight, Ø 6 mm for 10 mm port	1	1	1	1	1	1
Addition port adapter, for 7.5 mm port	4	4	4	4	4	4
Clamping adapter for 10 mm port	3	3	3	3	3	3
Antifoam sensor for 10 mm port	1	1	1	1	1	1
Blanking plug for 12 mm/Pg13.5 port	4	4	6	6	7	7
Blanking plug for 10 mm port (in starter set)	2	2	2	2	2	2
Exit gas cooler for 12 mm/Pg13.5 port	1	1	1	1	1	1
Reagent bottle, 250 mL	4	4	4	4	4	4
Pump heads with hoses inside diameter: 1.0 mm/wall thickness: 1.1 mm	4	4	4	4	4	4
pO ₂ sensor (sensor type according to existing measurement system)	1	1	1	1	1	1
pH sensor (sensor type according to existing measurement system)	1	1	1	1	1	1
Sensor holder for 12 mm/Pg13.5 port (in starter set)	--	--	2	2	--	--

Accessories

Accessories	1.5 l TV / DN 90		3.0 l TV / DN 115		6.0 l TV / DN 145	
	M	C	M	C	M	C
Starter kit	1	1	1	1	1	1
Cone plug for drive hub (in starter set)	1	1	1	1	1	1

4.2 Cone Plug for Drive Hub



The cone plug (EPDM) provided in the starter set protects the drive hub from penetration of condensate water during sterilisation in the autoclave.

It must be plugged into the opening of the drive hub for autoclaving of the culture vessel!

4.3 Sparger

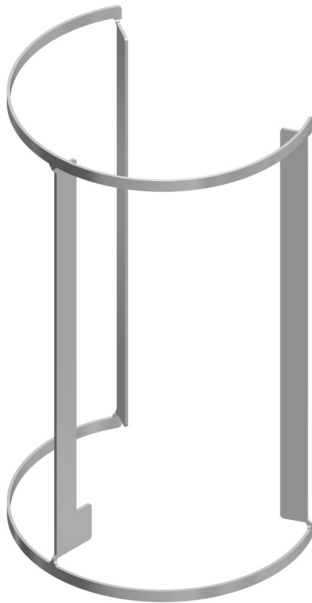


The gas is fed directly into the medium via a ring sparger (Ø 6 mm) with evenly distributed holes on the bottom side of the ring through which the air/gas bubbles into the culture medium.

Data	Value	Unit
Inside diameter	4.0	mm
Hose connection outside diameter	6.0	mm

The sparger is mounted in a 10 mm port in the vessel top plate with a clamping adapter and connected to the gas supply on the basic unit via a silicone hose with sterile filter.

4.4 Baffles



The baffles are used to mix the culture in culture vessels for microorganisms. They are simply inserted into the glass vessel.

4.5 Blanking Plugs

Blanking plugs are used to seal open ports. There are different blanking plugs for the different types of port.

Blanking plug, Ø 10 mm



- With O-ring
- A fastening screw is used to fasten it in the 10 mm vessel top plate port (➔ Chapter 4.6 'Clamping Adapters and Fastening Screws' on page 54).

Blanking plug, Ø 12 mm



- Must be fitted with an O-ring before being mounted in the 12 mm/Pg13.5 port.
- Mounted using a thread.

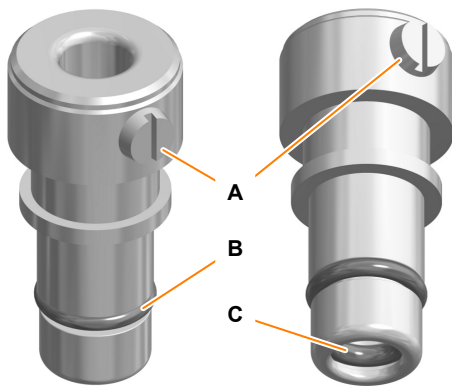
Accessories

4.6 Clamping Adapters and Fastening Screws

Clamping adapters are used when mounting the sparger, the various dip tubes and the antifoam/level sensors. The clamping adapter fixes the built-in-part in place and can be used to adjust its mounting depth.

The clamping adapter must match the outside diameter of the built-in-part being installed and the size of the port in the vessel top plate.

Clamping Adapter Ø 6 / 10 mm



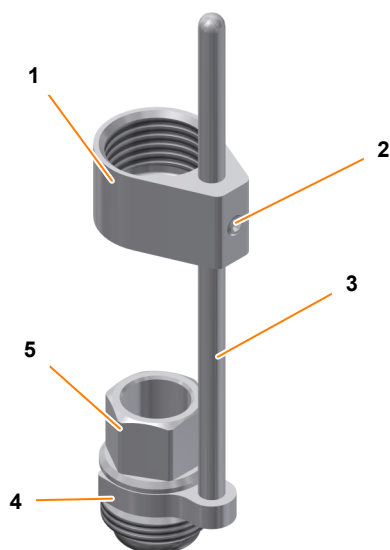
- Fitted with two O-rings (B & C)
- When the slotted screw is loosened, the component with a diameter of 6 mm can be inserted in or removed from the clamping adapter. When the slotted screw is tightened, the built-in-part is clamped in the clamping adapter.

Fastening Screw M5



- The fastening screws are used to hold built-in-parts in place in the Ø 10 mm and Ø 7.5 mm ports in the vessel top plate.

4.7 Sensor Holder



- 1 Sheath
- 2 Grub screw
- 3 Guide bar
- 4 Fork
- 5 Hollow screw

Sensor holders are used to adjust the mounting depth of sensors (pH, pO₂, etc.) in 12 mm/Pg 13.5 ports. The sensor holder, respectively the sensor must be fitted with an O-ring for mounting.

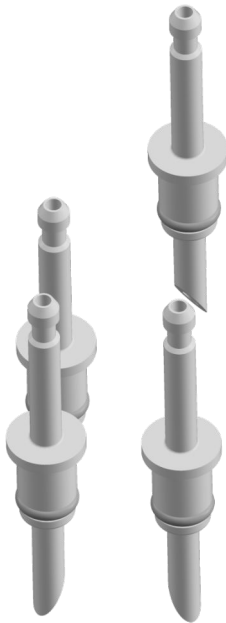
The sensor holder comprises a sheath with a grub screw, a guide bar with a fork, and a hollow screw. The wrench for the grub screw is also included in the scope of supply.

4.8 Addition Port Adapters and Feed Needles

Addition port adapters and feed needles are used to feed liquid into the culture vessel or are used for head space gassing (version for cell cultures), too. They each come with a hose connection, are fitted with an O-ring and are mounted into the four 7.5 mm ports in the vessel top plate. A single fastening screw is used to fasten all four addition port adapters and/or feed needle(s) in place.

Accessories

Addition Port Adapter Ø 7.5 mm



Data	Value	Unit
Inside diameter	2	mm
Hose connection outside diameter	4	mm
Mounting depth	17	mm

- Addition port adapters protrude as far as the head space of the vessel, and have very sharp ends with slanted points.
- Each culture vessel comes with four addition port adapters as standard.

Feed Needle Ø 7.5 mm



Data	Value	Unit
Inside diameter	2	mm
Hose connection outside diameter	4	mm

- Feed needles protrude to below the minimum fill level (= min. working volume) of the culture vessel.
- This method of adding liquid allows more precise and regular dosing even when handling small volumes as, unlike the port adapter, the feed needle does not drip.



The figure does not show the whole length of the feed needle.

4.9 Septum Collar



The septum collar with inside thread is used to inoculate the culture in combination with the syringe, injection needle and septum (→ Chapter 4.21 'Inoculation Accessories and Tools' on page 70). The septum collar is used to hold the septum in place in the 12 mm/Pg13.5 port.

4.10 Dip Tubes

Dip tubes are open at both ends and are mounted in a vessel top plate port with a clamping adapter.

Dip tubes are used for a variety of purposes:

- For filling the culture vessel after autoclaving. Using a dip tube prevents foaming.
- For adding inoculum.
- For sampling. The aseptic Super Safe Sampler system can be used for sampling.
- For harvesting.
- For siphoning off medium during continuous cultivation.
- For draining the culture vessel.

Depending on the purpose, silicone hoses are connected to the dip tube via other vessels, sampling systems or, if necessary, hose networks.

Multiple dip tubes can be used at any one time, providing that enough vessel top plate ports are available.

Accessories

Dip Tube, Straight, Ø 6 mm



Data	Value	Unit
Inside diameter	3	mm
Hose connection outside diameter	4	mm

The dip tube does not reach as far as the bottom of the vessel.



The illustration on the left shows only the upper section of the dip tube.

4.11 Immersion Pocket for Temperature Sensor (Pt100)

The immersion pocket is a tube with a sealed bottom end, and is used to insert the temperature sensor.

Immersion Pocket Ø 10 mm



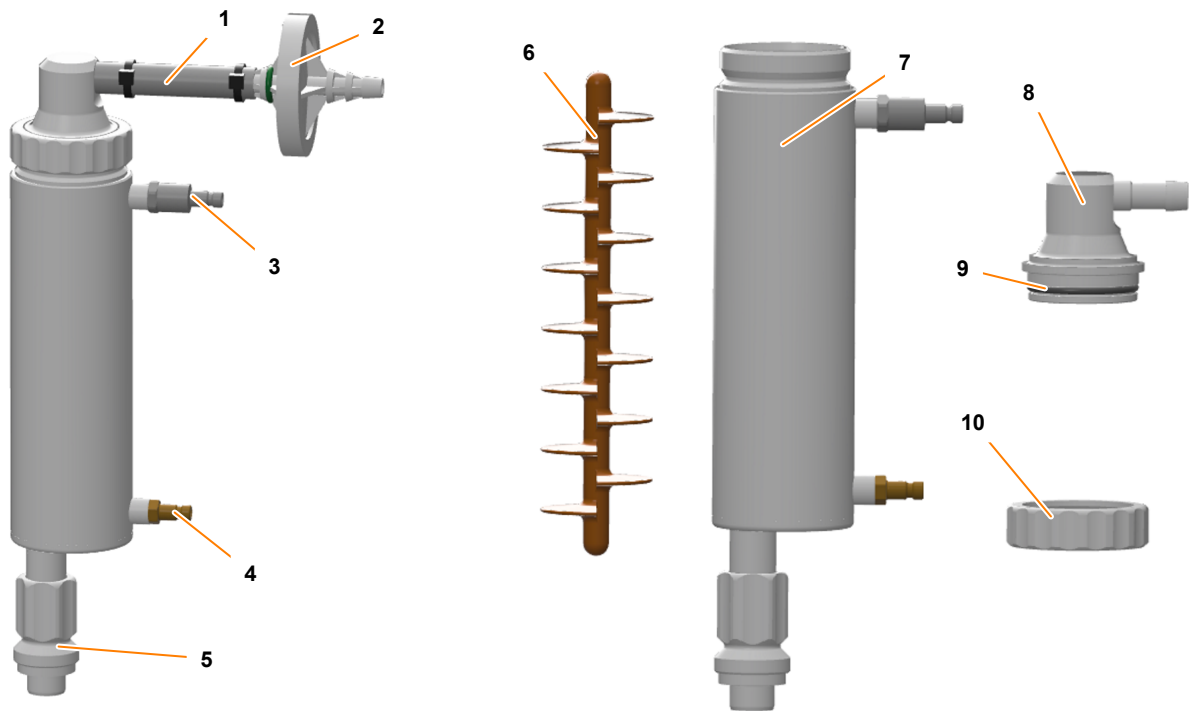
- With O-ring.
- A fastening screw is used to fasten it in the 10 mm vessel top plate port.



The figure on the left does not show the full length of the immersion pocket.

4.12 Exit Gas Cooler

Overview



- 1 Pressure hose
- 2 Exit gas filter
- 3 Hose connection water outlet
- 4 Hose connection water inlet
- 5 Screw thread

- 6 Baffle (silicone)
- 7 Cooling pipe with jacket
- 8 Lid
- 9 O-ring
- 10 Coupling nut

The exit gas cooler is equipped with a piece of pressure hose and exit gas filter. The hose and filter are secured with cable ties. The hoses for the water inlet and outlet are connected to the basic unit ex-factory. They are connected to the exit gas cooler via rapid couplings. Different hose lengths prevent incorrect connection.

Accessories

Function

The exit gas cooler dries the exit gas through condensation, thus preventing the exit gas filter from becoming clogged with moisture. At the same time, it also prevents liquid loss in the culture medium. The exit gas is passed through the cooling pipe of the exit gas cooler. The cooling is done by water, which is led through the jacket of the cooling pipe. A baffle in the cooling pipe serves to extend the residence time of the exit gas in the cooling pipe. The water supply to the exit gas cooler is provided by the basic unit. The water flow rate can be adjusted using the control valve on the basic unit.

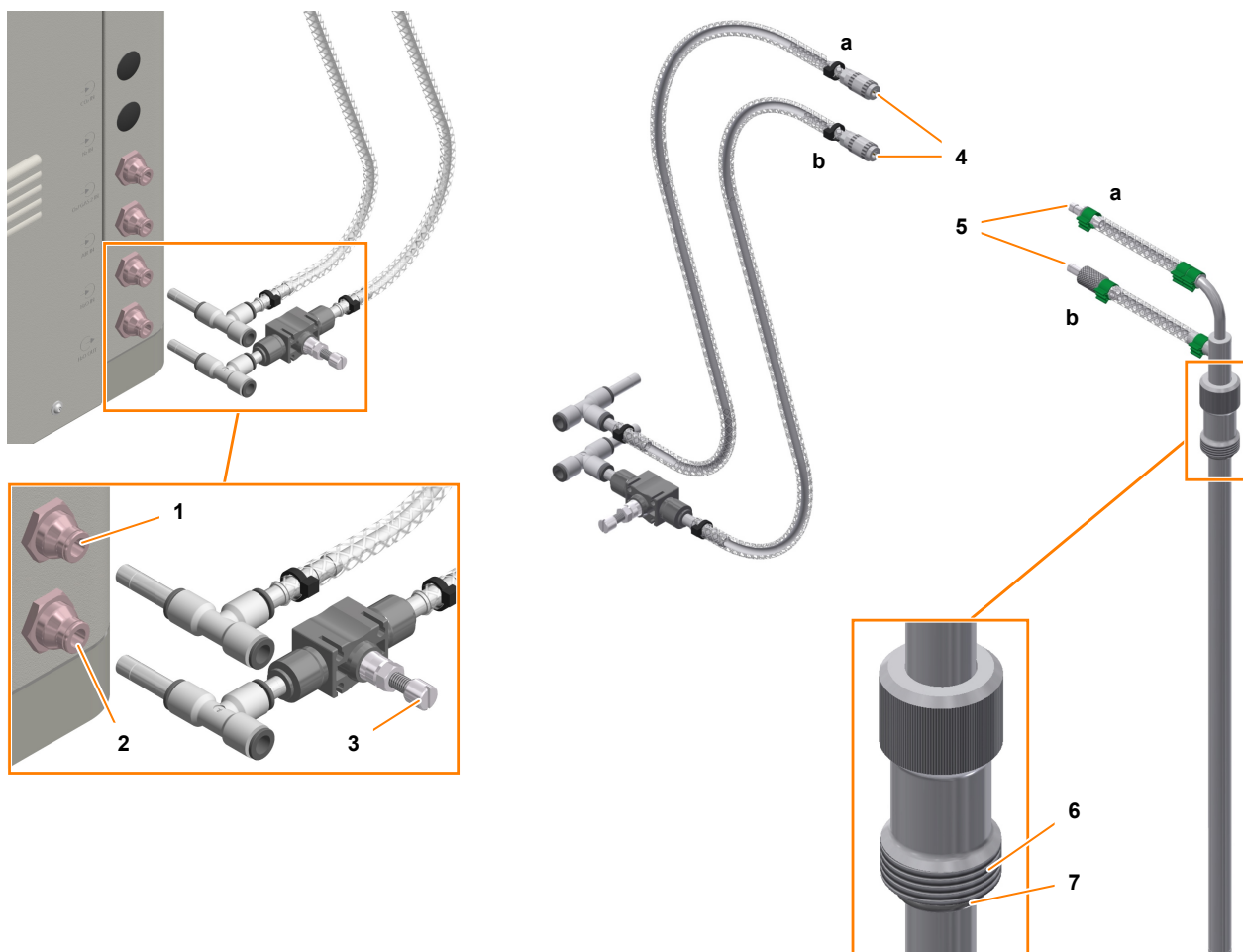
Observe the following points:

- The exit gas cooler only works when the temperature control system is switched on.
- The exit gas filter must be replaced with a new filter after each cultivation.

Mounting

The exit gas cooler must be equipped with an O-ring before mounting. A screw thread is used to mount it in the 12 mm/Pg13.5 vessel top plate port.

4.13 Cold Finger



- 1 Connection *H2O IN*: water inlet
- 2 Connection *H2O OUT*: water outlet
- 3 Manual valve for water flow
- 4 Rapid coupling DN6, water inlet (a) and water return (b)

- 5 Plug nipple, water inlet (a) and water return (b)
- 6 Screw thread
- 7 O-ring

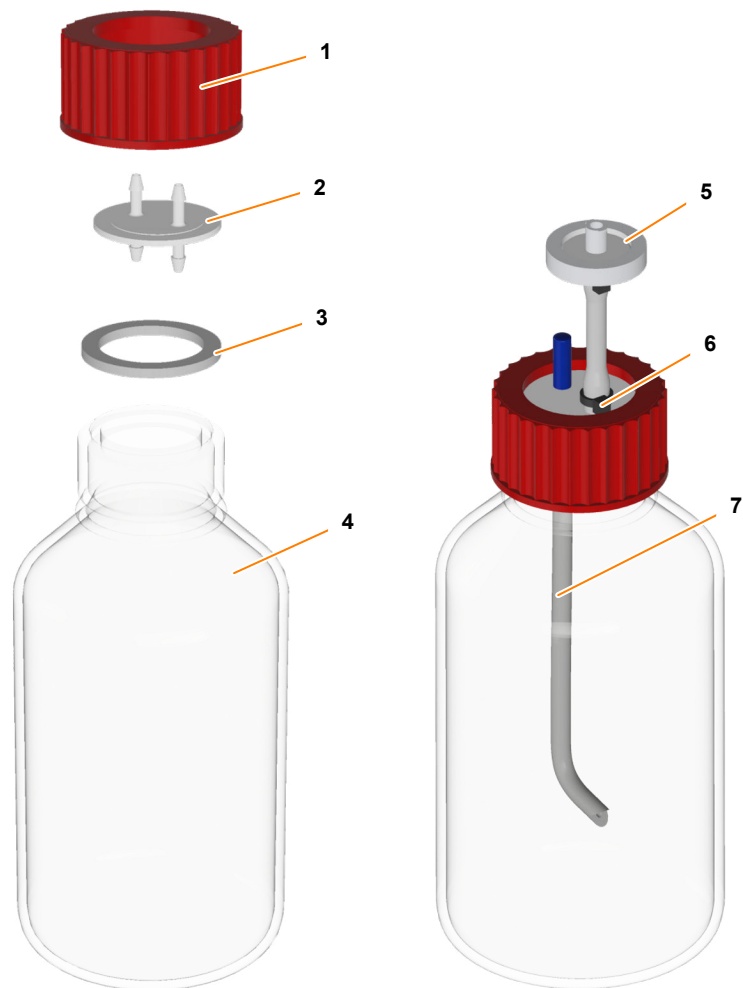
For microbial bioprocesses with very high waste heat, a cold finger can be used to increase the cooling capacity. The cold finger is connected directly to the water supply of the device. The flow rate is adjusted manually via a valve. The valve must always be closed during the heating phase!

The cold finger is supplied ready for use. For mounting in the 12 mm / Pg13.5 port a screw thread is used.

The two hoses for water inlet and return are two-part. They are connected to each other for operation via rapid couplings and separated there for autoclaving the culture vessel. The T-connectors at the hose ends also serve as coupling pieces for the connection of the pressure hoses for water supply and return of the device.

Accessories

4.14 Reagent Bottles



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

Reagent bottles made of borosilicate are used as containers for reagents and nutrient solution. 250 mL reagent bottles are supplied as standard in the device package. These fit in the reagent bottle holder that is built into the vessel holder. 500 mL reagent bottles are optionally available.

A 2 m piece of hose is included in the scope of supply for connecting the reagent bottle to the addition port adapter in the culture vessel and to a pump head.

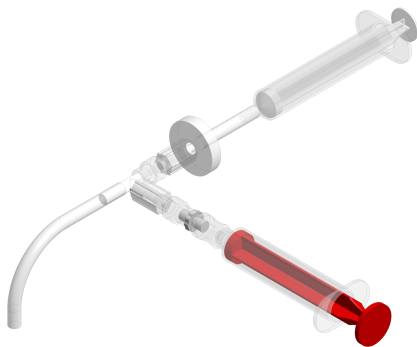
4.15 Sampling System Super Safe Sampler

Basically different systems and also individual components are available for sampling. This operating manual describes the operation and handling of the aseptic sampling system Super Safe Sampler combined with a dip tube.

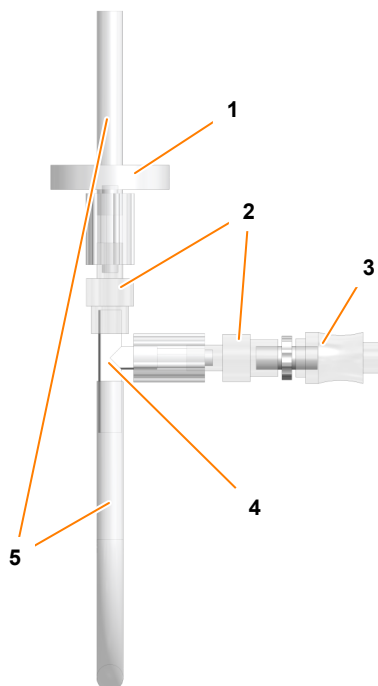
The use of the Super Safe Sampler prevents the culture vessel from contamination when sampling.

Content of the Set

The set consists of a completely pre-assembled group of valves with hoses and two syringes. It is connected via silicone hose with a dip tube.



Valve Assembly

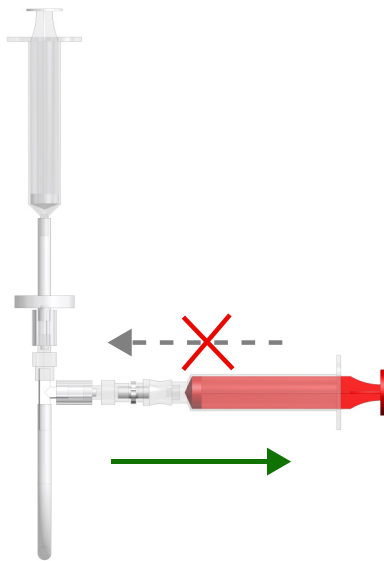


- 1 Sterile filter
- 2 Check valve
- 3 Sample valve
- 4 T-piece
- 5 Silicone hose

The valve assembly consists of a T-piece, two check valves, a Luer-activated automatic sample valve, a sterile filter, a length of hose as an adapter for the syringe and another hose to connect to the dip tube for connection to the culture vessel.

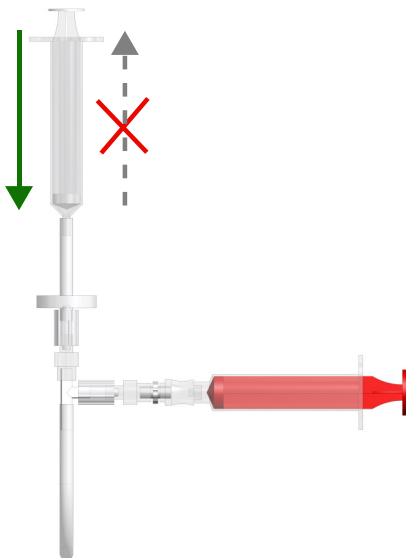
Accessories

Principle of Function



The sample valve on the side arm of the T-piece opens by putting the Luer connector of the syringe into the valve and closes by removing the syringe. No further handling is necessary.

Unintentional re-introduction of the sample material once it has been withdrawn is prevented by a check valve. Thus, contamination of the culture vessel is impossible.



After sampling, the second syringe is used to push air through the sterile filter to displace culture solution from the sampling hose and the dip tube of the culture vessel. Removing and discarding of culture solution for rinsing the sampling hose and the dip tube is not necessary. This saves culture volume, which is particularly important for small culture vessels and/or frequent sampling.

The dead volume of the culture remaining in the valve assembly after flushing with sterile air amounts to a few μl and is negligibly small. If the withdrawal of a very small sample volume is required, with minimum possibility of falsification, a small quantity of culture solution (e.g. 1 ml) can be introduced and rejected before the actual sample is taken.

Designated Use

The Super Safe Sampler is designed for aseptic sampling of completely liquid samples. Solid parts in the sample may lead to clogging of the valves. Therefore, employing the Super Safe Sampler for solid media is not recommended.

The Super Safe Sampler is autoclavable (not the syringes) and for this reason reusable.

Practical Tips for the Use of the Super Safe Sampler

Sterility of the culture vessel is ensured at all times without the possible measures mentioned below. The use of a sterile syringe and sterile caps is only necessary if the sample has to be processed under sterile conditions. For sampling, the same non-sterile syringe can be used repeatedly, without fear of contamination of the culture vessel.

Aseptic Sampling

For each sample, use a new, sterile syringe with Luer Lock fitting, in order to ensure the sterility of the sample. Sterile syringes are consumables and therefore not included in the set.



The use of another syringe is also possible. But a syringe with Luer lock prevents unwanted movement of the syringe.

- Before fitting the syringe for sampling, disinfect the sample valve. For this, spray a commercially available disinfectant onto the valve.
- After spraying and after each sampling, close the sample valve with a sterile Luer-Lock cap (Dead End Cap) to keep the valve and sample sterile.

The caps are not included in the kit. Very convenient to use are so-called combi-caps that fit on male and female connectors alike. Caps that are vented and made of steam sterilisable material can also be fitted during autoclaving.

4.16 Pump Heads



The autoclavable pump heads are fitted with PharMed pump hoses prior to delivery. Three different hose diameters are available for different delivery rates:

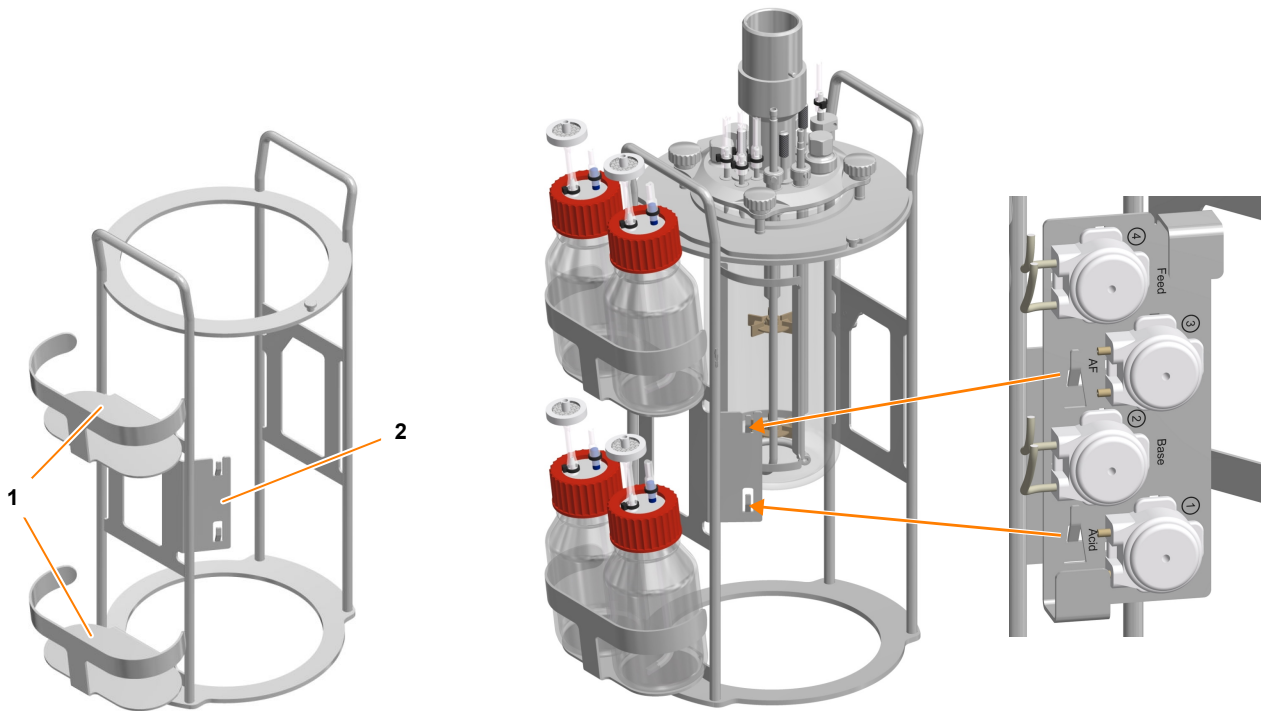
- 1.0 mm (standard)
- 0.5 mm
- 2.5 mm

For more detailed information about pumps and hoses, see ➔ Chapter 2.13 'Pumps' on page 27.

Accessories

4.17 Vessel Holder

Standard



- 1 Reagent bottle holder
- 2 Pump holder

The vessel holder for all vessel sizes has two holding devices for a total of four reagent bottles and one holder for the four pump heads. The reagent bottles are placed in the two holders, and the mounting plate with the pump heads is simply pushed onto the pump holder. The culture vessel can this be transported and autoclaved as a single unit together with the reagent bottles and pump heads.

Option



For vessels with nominal diameters (DN) 90 mm and 115 mm, a smaller compact model ¹⁾ is available in addition to the standard vessel holder. This vessel holder has one holding device for two reagent bottles and the same pump holder as the standard model.

¹⁾ Figure shows vessel holder DN 90 mm

4.18 Sterile Filters

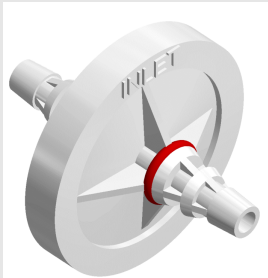
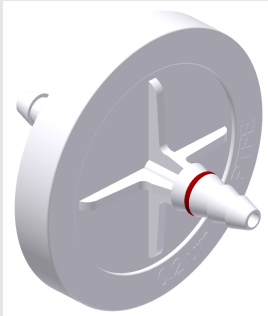
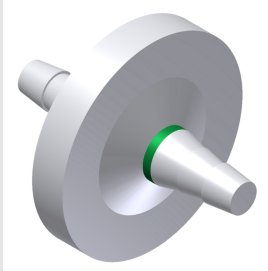
Sterile filters are used to protect against contamination in both the gassing line and the exit gas line ¹⁾. All the sterile filters in the scope of supply are autoclavable, disposable filters with PTFE diaphragms.

¹⁾ *Exception: Version for microorganisms, here an autoclavable depth filter is used in the exit gas line.*

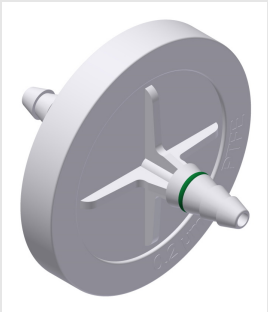
Reagent bottles are fitted with a short piece of hose with an autoclavable depth filter to equalise the pressure.



Sterile filters must be clean and dry at all times, and should thus ideally be replaced after each use.

Figure	Diameter	Marking	Retention rate	Application
	37 mm	red	0.2 µm	- Version for cell cultures: sparger & head space gassing all vessel sizes - Version for microorganisms: sparger gassing 1.5 L culture vessels
	50 mm	red	0.2 µm	Version for microorganisms: sparger gassing, 3.0 & 6.0 L culture vessels
	37 mm	green	0.3/1 µm	Version for microorganisms: exit gas

Accessories

Figure	Diameter	Marking	Reten- tion rate	Application
	50 mm	green	0.2 µm	Version for cell cultures: exit gas
	25 mm	without	0.2 µm	Super Safe Sampler
	25 mm	without	0.45 µm	Reagent bottles (pressure equalisation)

4.19 Hoses and Accessories

Hose type	Ø mm	Application
Pressure hose, fibreglass-woven	6 x 11.9	Water and gas connections (on-site)
Pressure hose, fibreglass-woven	6 x 10	Exit gas filter attachment (on exit gas cooler)
Pressure hose, transparent	5 x 10	Inlet air filter attachment on sparger for 3.0 and 6.0 L culture vessels for microorganisms
Silicone hose	5 x 8	Hose line from basic unit to inlet air filters for all culture vessels Inlet air filter attachment on sparger ¹⁾
Silicone hose	3 x 6	Inlet air filter attachment for head space gassing (version for cell cultures)
Pressure hose, transparent	4 x 8	Water supply and return, exit gas cooler
Silicone hose, transparent	2 x 6	Reagent bottles

¹⁾ Version for microorganisms: 1.5 L culture vessel, version for cell cultures: all vessel sizes.

Attachments	Application
Hose clamp, screw with screwdriver slot, 14 mm, INOX	Water and gas connections (on-site)
Hoffmann pinchcock, 12 mm, nickel-plated brass	To clamp off hose lines, e.g. unused addition port adaptors/feed needles, sparger hose line, etc.
Cable tie, 2.4 x 85, polyamide	Hoses for reagent bottles and pumps, inlet air filter, sparger, water supply and return for exit gas cooler and exit gas filter attachment, sampling system dip tube
Hose connector, 3/32" x 1/16", PVDF	Pump heads with hoses to reagent bottles

Accessories

4.20 O-Rings and Gaskets

Designation	Ø mm	Application
O-ring, EPDM	3.53 x 94.84	Top plate gasket, culture vessel, DN 90
O-ring, EPDM	3.53 x 120.24	Top plate gasket, culture vessel, DN 115
O-ring, EPDM	3.53 x 148.8	Top plate gasket, culture vessel, DN 145
O-ring, EPDM	2.62 x 10.77	Gasket, port size 12 mm/Pg13.5
O-ring, EPDM	1.5 x 7.5	Gasket, port size 10 mm
O-ring, EPDM	1.5 x 5.0	Gasket, port size 7 mm
O-ring, EPDM	1.78 x 5.28	Inner gasket for clamping adapter for 10 mm ports
O-ring, EPDM	2.0 x 26	Lid gasket for exit gas cooler
PTFE ring	120 x 105	Damping ring between glass vessel and vessel holder, DN 90
PTFE ring	145 x 130	Damping ring between glass vessel and vessel holder, DN 115
PTFE ring	175 x 160	Damping ring between glass vessel and vessel holder, DN 145
Flat gasket, silicone	32 x 42 x 2	Gasket for reagent bottle lid (all sizes)

4.21 Inoculation Accessories and Tools

Accessories for inoculation

Septum, Ø = 16 mm MVQ silicone, transparent, for 12 mm/Pg13.5 ports

Sterile disposable syringe, Luer, 10 mL, inside Ø 14.35 mm

Sterile hollow needle, 20G, L = 40 mm/Ø = 0.9 mm

Tool	Application
Hex key, WAF 2, DIN911	Grub screws impellers 3.0 and 6.0 L culture vessels
Hex key, WAF 1.27	Grub screws impellers 1.5 L culture vessels
Hexagon socket spanner, WAF 17	Blanking plugs 12 mm/Pg13.5 ports
Torx screwdriver, TX25	Screws thermal block adapter

4.22 Starter Set

Each device package comes with a starter kit with a variety of hoses, attachments, inoculation accessories and tools. A detailed contents list is included in each starter kit.

4.23 Service Sets

Service sets with O-rings, gaskets, sterile filters, hoses, etc. to fit each vessel size are available separately. A detailed contents list is included in the service set.

4.24 Auxiliary Supplies

The term “auxiliary supplies” covers all the substances and materials required for operation and/or maintenance that cannot be considered part of the device or the system.

pH Buffers

pH buffers are used to calibrate the pH sensors. 250 mL bags are available for the following buffers:

- pH 4.04
- pH 7.01

Transport and Storage

5 Transport and Storage

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

5.1 Transport



WARNING

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

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

- Always work in pairs and use suitable auxiliary equipment when transporting the device.
- The entire device (basic unit and culture vessel) contains delicate glass parts.
- Especially when using auxiliary tools, it is important to observe that the device's centre of gravity is not in the middle.



WARNING

The entire device (basic unit and culture vessel) is too heavy to be carried by one person alone.

Even the basic unit on its own exceeds the weight that should be carried by one person alone.

5.2 Storage

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

6 Installation and Commissioning



WARNING

Faulty installation may lead to dangerous situations or severe loss of property.

Follow the installation and commissioning instructions in this operating manual precisely.

6.1 Operating Conditions at the Installation Location

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

- The figures and ranges specified in the technical data must be observed (➔ Chapter 13.3.1 'Connections and Connection Values' on page 215 and ➔ Chapter 13.6 'Operating Conditions' on page 229).
- The device must only be installed inside a laboratory or a laboratory-like environment.
- The installation surface must be level, sufficiently stable and load-bearing.
- There must not be any sources of electrical interference in the vicinity.
- The working environment is equipped with a sufficient ventilation system, depending on the application.

6.2 Minimum Distances to the Device

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

6.3 Connecting the Device to On-Site Supply Lines

The following chapters describe which connection requirements must be fulfilled on site and how the device is connected to on-site supply lines.

Installation and Commissioning

6.3.1 Power Supply

Connection Conditions

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

- Constant power supply

In addition to that, ensure the following:

- The voltage values of the device match those of the local mains voltage. Note the information on the identification plate.
- Use the power cable provided. If the power cable becomes defective, replace it with a power cable of the same type.
- The mains connection can be accessed at all times.

Refer to the technical data for the electric connection values.

Connection

To connect the device to the in-house power supply, proceed as follows:

1. ➞ Insert the power cable supplied into the connector socket on the device.
2. ➞ Insert the cable into the in-house power supply.

6.3.2 Water Supply and Return

Connection Conditions

! NOTICE

Not observing the water quality requirements may lead to damage or failure of the device.

The in-house water supply to the device, as well as the drainage of the water, must meet the following requirements:

- Water quality: CaCO_3 concentration 0 mmol L⁻¹ to 1.5 mmol L⁻¹
- Min. flow temperature: 10 °C
- Constant water supply at a pressure of 2 ± 1 bar
- Manometer to check the primary pressure available
- The drain is heat-resistant and without backpressure

Installation and Commissioning

Connection

To connect the device to the in-house water supply and drainage, proceed as follows:

1. ➤ Cut the required quantity of the supplied pressure hose ($\varnothing = 6 \times 11.9$ mm).
2. ➤ Position the pressure hoses on the appropriately marked hose nozzles on the device.
3. ➤ Connect the hoses to the in-house water supply and drainage.
4. ➤ Secure the hoses with hose clamps to prevent slipping.
5. ➤ Check to ensure that the hoses neither have kinks nor are able to kink and that connections and hoses do not have any leaks.

6.3.3 Gas Supply

Connection Conditions

NOTICE

The use of impure gases can lead to blockage of the sterile filter and damage the mass flow controller.

Only use dry, clean and oil-free gases.

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

- Constant gas supply at a pressure of 2 ± 0.5 bar.
- Gas(es) is/are dry, clean and free of oil and dust.
- Recommended compressed-air quality as per DIN ISO 8573-1: Class 1,2,3,4.

Connection

WARNING

The use of inappropriate or damaged hoses and/or inappropriate fixing may lead to leakage of gases. Depending on the gas in question, there may be a danger of gas explosion and/or danger of suffocation as well as a hazard for the health of the operator.

Always close the gas supply before a hose is removed and when the device is not in use.

To connect the device to the in-house gas supply, proceed as follows:

1. ➤ Cut the required quantity of the supplied pressure hose ($\varnothing = 6 \times 11.9$ mm).

Only use hoses supplied by the manufacturer.

Installation and Commissioning

2. ➤ Position the pressure hoses on the appropriately marked hose nozzles on the basic unit.
3. ➤ Connect the hoses to the in-house gas supply.
4. ➤ Secure hoses with hose clamps to prevent slipping.
5. ➤ Check to ensure that hoses neither have kinks nor are able to kink and that connections and hoses do not have any leaks.

6.3.4 Exit Gas

Ensure the following on the building side:

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

6.4 Connecting the Motor Cable

The motor is controlled directly by the basic unit and is connected to it via the motor cable.

For routine operation, it is not necessary to plug in and unplug the motor cable. The connected motor is only coupled before cultivation (➔ Chapter 7.3.6 'Coupling the Motor' on page 113).

To connect the motor cable, proceed as follows:

1. ➤

! NOTICE

If the motor cable is connected to or disconnected from the motor while the device is switched on, there is a risk of a short circuit that could damage the control electronics.

Ensure the device is switched off.

2. ➤ Insert the (angled) plug of the motor cable into the socket on the rear of the basic unit and tighten the coupling nut by hand.
3. ➤ Insert the other plug into the socket on the motor and tighten the coupling nut by hand.

6.5 Test Run

To become familiar with the basic functions of the device before the first cultivation, a short test run can be executed. The test run comprises:

- Temperature control (cooling/heating)
- Stirring
- Gassing

Compressed air of the stated quality is used for gassing (→ Chapter 6.3.3 'Gas Supply' on page 75).

To avoid calcium deposits, demineralised water is recommended for filling the vessel.

The following description of the test run does not detail handling of individual components. Detailed descriptions of their handling are given in → Chapter 7 'Before Cultivation' on page 82.

For details on operation, see → Chapter 9 'Operation' on page 127.

Preparing the Test Run

Before starting the test run, check and ensure the following:

- The device is correctly connected to the water, power and gas supply and is operational.
- The motor cable is connected to the basic unit and the motor.

The following work is to be executed before the test run:

1. →

NOTICE

If the vessel top plate presses against long components such as the stirrer shaft etc., they could bend because of the weight of the top plate.

Always position the vessel top plate so that it does not lie on top of components.

Remove the vessel top plate and put it aside carefully.

2. →

Fill the culture vessel with water – preferably demineralised – to the working level.

3. →

Ensure that the impeller, sparger, and one addition port adapter, if applicable, are mounted; if necessary, mount them.

4. →

Fit the top plate and secure it.

Installation and Commissioning

- 5.** ➤ Screw the exit gas cooler into the port on the vessel top plate port.



The exit gas cooler is equipped with a new exit gas filter ex-factory.

- 6.** ➤ Connect the exit gas cooler to pre-fitted hoses on the basic unit; to this end, follow the symbols on the basic unit:
- Water inlet on bottom of exit gas cooler
 - Water outlet at top of exit gas cooler
- 7.** ➤ Close all remaining open ports with blanking plugs.
- 8.** ➤ Hang the culture vessel on the basic unit.
- 9.** ➤ Connect the gassing (compressed air) to the sparger and, if applicable, to the addition port adapter, by connecting the gassing hose(s) on the basic unit to the nozzle(s) on the inlet air filter(s).



The sparger is equipped with a hose and the inlet air filter ex-factory. The version for cell cultures additionally has an addition port adapter equipped with a hose and the inlet air filter for head space gassing.

The gassing hose(s) is/are attached to the basic unit ex-factory.

- 10.** ➤ Insert the temperature sensor as far as it will go into the immersion pocket in the top plate.
- 11.** ➤ Couple the motor.
- 12.** ➤ Switch on the device at the power switch and wait until the system has started up.

Installation and Commissioning

Cooling

To activate the cooling system, proceed as follows:

1. ➤ On the operating panel, set a low setpoint for the *Temperature* parameter, e.g. 10 °C, to activate the water supply to the temperature control system.
2. ➤ Start the batch (bioprocess) using **Start Batch** and switch on the *Temperature* parameter.
3. ➤ All parameters except for *Temperature* remain switched off; switch them off if necessary.
 - ➔ You should now hear water flowing into the temperature control system.
 - ➔ The water supply to the exit gas cooler should be activated, too now.
4. ➤ Use your hands to check whether the exit gas cooler and thermal block and/or adapter are beginning to cool down.
 - ➔ As soon as the temperature control circuit is full, water will flow out of the water outlet (*H2O OUT*) of the basic unit.

Stirring

Precondition: batch is running with temperature control switched on.

To test the stirrer, proceed as follows:

1. ➤ On the operating panel for the *Stirrer* parameter, set a low setpoint, e.g. 200 min⁻¹.



CAUTION

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

2. ➤ Switch on the *Stirrer* parameter.

Installation and Commissioning

Heating and Adjusting Temperature

Precondition: batch is running with temperature control switched on and stirrer running.

To test the heating and adjust the temperature, proceed as follows:

1. **CAUTION**

Risk of minor burns if the heated thermal block and thermal block adapter are touched!

On the operating panel, set a high setpoint for the *Temperature* parameter, e.g. 45 °C.

➡ The water supply for cooling is stopped; the system heats up.

2. ➡ Wait until the temperature has adjusted to the setpoint.

Gassing (Sparger Gassing)

Precondition: batch is running with temperature control switched on and stirrer running.

To test the gassing via sparger, proceed as follows:

1. ➡ On the operating panel for the *Total Flow* parameter, set a low setpoint, e.g.:

- Version for microorganisms: 1.0 L min⁻¹
- Version for cell cultures: 100 mL min⁻¹

2. ➡ Select *OnlyAir* setting for parameter *GasMix*, so that its setpoint is preset to 21 %.

➡ If the gassing is working, air bubbles now form in the water in the culture vessel.

Gassing (Head Space Gassing, Version for Cell Cultures)

Precondition: batch is running with temperature control switched on and stirrer running.

To test the gassing via head space, proceed as follows:

1. ➡ On the operating panel for the *Air Headspace* parameter, set a setpoint, e.g. 1000 mL min⁻¹.

2. ➡ Remove the gassing hose from inlet air filter on the addition port adapter in the vessel top plate and hold the hose end on e.g. the back of the hand or on a finger, to feel the air flow.



If the hose line is blocked for too long, the overpressure sensor may trigger an overpressure alarm *Gas pressure high* and switch off the gas supply for 10 seconds.

Installation and Commissioning

End of Test

After all parameter setpoints have been reached, the test can end here. The inoculation that now takes place during normal operation is not relevant to the test run. Proceed as follows:

1. ➤ On the operating panel, press **Inoculate** and then **Stop Batch** to stop the batch (bioprocess).
2. ➤ Switch off the device at the power switch.
3. ➤ Shut off the supply lines.

4. ➤



CAUTION

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

Let the motor cool down (motor for device version for microorganisms).

5. ➤ Uncouple the motor from the vessel and place it on a clean and dry work surface.
6. ➤ Empty the culture vessel.

Before Cultivation

7 Before Cultivation

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

- Preparing the culture vessel:
 - Checking the gaskets (O-rings) on accessories and on the culture vessel
 - Mounting built-in-parts/accessories
 - Filling or moistening the culture vessel
 - Preparing sensors and accessories
- Autoclaving the culture vessel
- Connecting the culture vessel and preparing for cultivation:
 - Hanging the culture vessel into place on the basic unit and connecting cables and hoses between the culture vessel and the device
 - Filling the vessel if necessary
 - Preparing sensors and accessories

7.1 Preparing the Culture Vessel

All accessories required for later cultivation must be prepared and mounted accordingly and autoclaved together with the culture vessel.

7.1.1 Checking Gaskets (O-Rings)

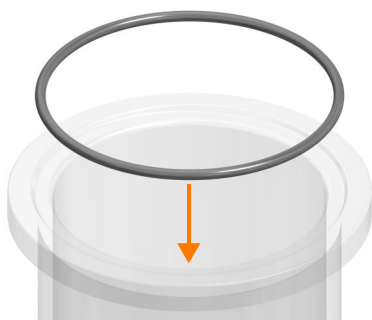
O-rings are used to seal all openings on the vessel and top plate. The top plate, its ports and all accessories are thus equipped with O-rings. Before every use, the O-rings must be checked that they are present, undamaged and correctly seated. Damaged O-rings must be replaced.



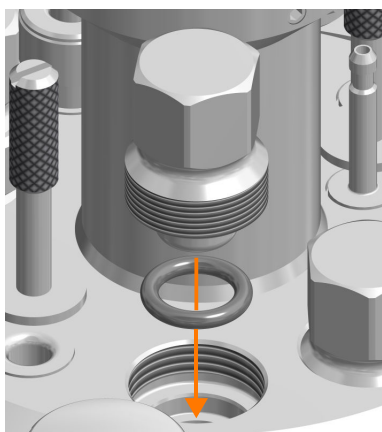
Wet the O-rings with 70 % alcohol or a little water to facilitate removing and replacing O-rings or accessories with O-rings. Do not use silicone grease; this can affect sterilisation results.

To check the gaskets, proceed as follows:

Before Cultivation



1. ➤ Check the O-ring for sealing the top plate for damage and to ensure that it is positioned correctly in the groove on the vessel flange.



2. ➤ Ensure that every built-in-part is equipped with an intact O- ring:
Check that the O-rings are correctly positioned and are undamaged. If necessary, reposition or replace. If built-in-parts are fitted into other component parts (clamping adapter), there must also be an O-ring between them.



Septum collars are sealed with a septum. No O-ring is used!

7.1.2 Mounting the Impellers

To mount the impellers to the stirrer shaft, proceed as follows:

1. ➤ Slide the impellers onto the stirrer shaft.
2. ➤ Set the desired height.



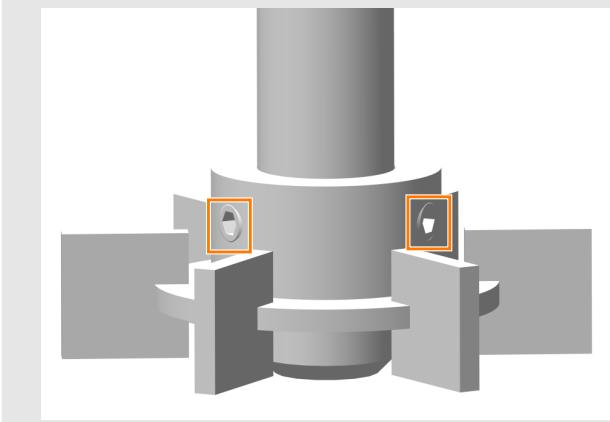
To avoid unnecessary foam formation, do not fit the impellers at the same height as the surface of the medium.

The ideal mounting heights of both impeller types (Rushton and pitched blade) are defined ex-factory for each vessel size and can be found in the technical data (➔ 'Impeller Mounting Heights ex-factory' on page 222).

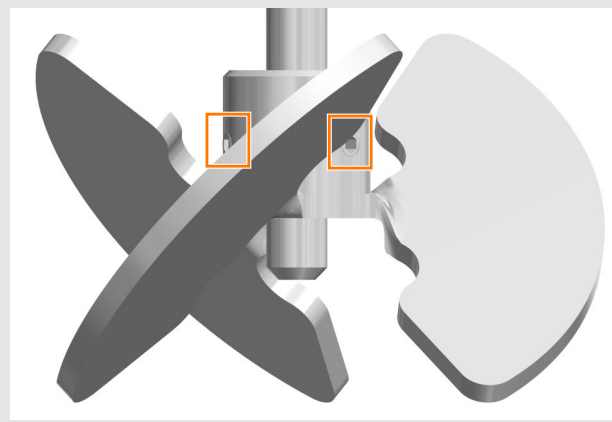
3. ➤ Tighten the grub screws on the impellers with the hex key.

Before Cultivation

Rushton impeller (version for microorganisms)



Pitched blade impeller (version for cell cultures)



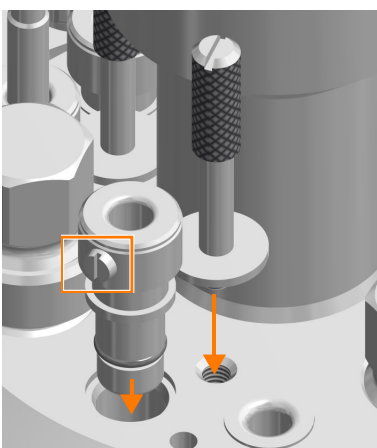
7.1.3 Mounting Dip Tubes and Spargers

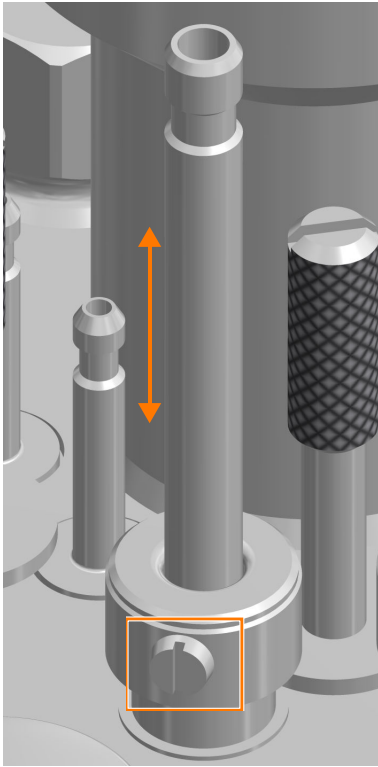
Straight spargers and dip tubes can be mounted from the outside in the vessel top plate. Curved spargers and dip tubes can only be mounted from the inside to the vessel top plate. Since this device uses curved spargers and straight dip tubes, mounting from the inside to the vessel top plate is described here. This means that the vessel top plate is still removed.

During mounting, ensure that the sparger or the dip tube does not come into contact with other built-in-parts (stirrer). The sparger is positioned below the stirrer shaft.

To mount dip tubes and spargers, proceed as follows:

1. ➤ Ensure that the clamping adapter is equipped with an interior and exterior O-ring; if necessary, attach O-ring(s).
2. ➤ Insert the clamping adapter into the intended port and fix it with a fastening screw.
3. ➤ Loosen the slotted screw at the clamping adapter.
4. ➤ Insert the sparger/dip tube into the clamping adapter from below.

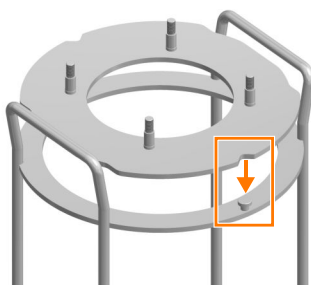




5. ➤ Set the desired mounting depth, align the sparger.
6. ➤ Tighten the slotted screw.

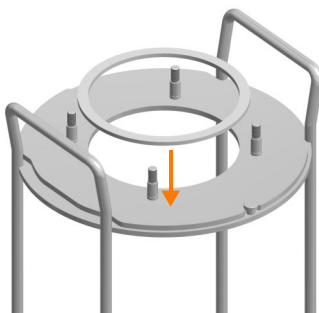
7.1.4 Inserting the Vessel into the Vessel Holder

To insert the glass vessel into the vessel holder, proceed as follows:



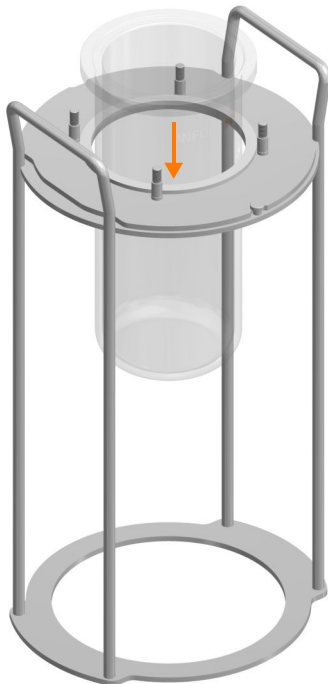
1. ➤ Place the flange onto the ring of the vessel holder:

The two opposing recesses on the flange fit with the bolt on the ring.



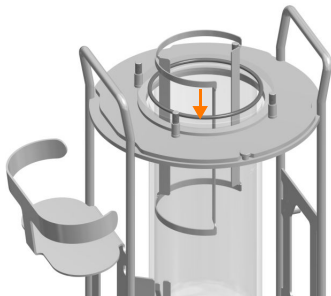
2. ➤ Place the damping ring onto the flange.

Before Cultivation



3. → Insert the vessel carefully.

7.1.5 Inserting the Baffles



→ Culture vessels for microorganisms are provided with baffles. To insert them into the glass vessel, proceed with caution.

7.1.6 Moistening/Filling the Culture Vessel

If the culture vessel is to be autoclaved with the medium, the vessel can be filled before the top plate is put in position and the additional built-in-parts are mounted.

Note the following about filling the culture vessel before autoclaving:

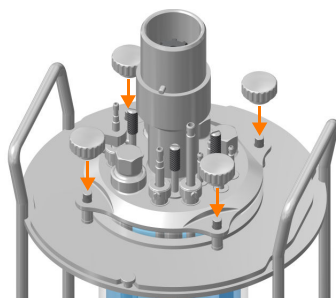
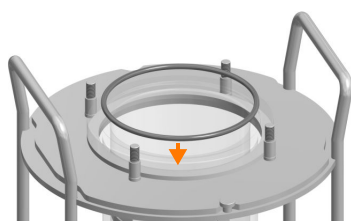
- Only top up with heat-resistant media.
- During autoclaving, evaporation may result in a loss of volume and thus to increased salt concentration in the medium. If necessary, top up with sterile water.



Development of steam is not possible when autoclaving an empty and dry culture vessel. Successful sterilisation is not guaranteed.

Ensure that there is liquid in the culture vessel (approx. 10 mL of water per litre of total volume).

7.1.7 Mounting the Top Plate



Proceed as follows to fit and fix the vessel top plate:

1. ➔ Fit the O-ring for the top plate gasket into the groove on the edge of the vessel.
2. ➔ Place the top plate carefully and with the correct alignment into position.

For culture vessels for microorganisms: ensure that built-in-parts do not touch the baffles.

3. ➔ Tighten the knurled nuts on the top plate by hand (no tool) crossways.

! NOTICE

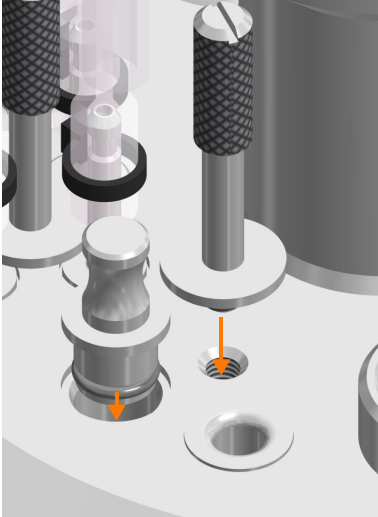
If the knurled nuts are tightened too much, components may be damaged, which can result in failure of the device. The knurled nuts may not be tightened with a tool under any circumstances.

This applies to all screw connections where the instructions specify that they must be tightened by hand!

Before Cultivation

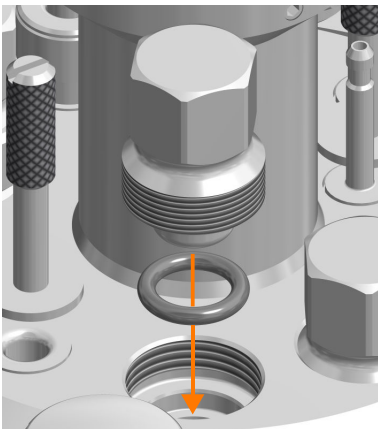
7.1.8 Mounting the Blanking Plugs

Ø 10 mm Ports



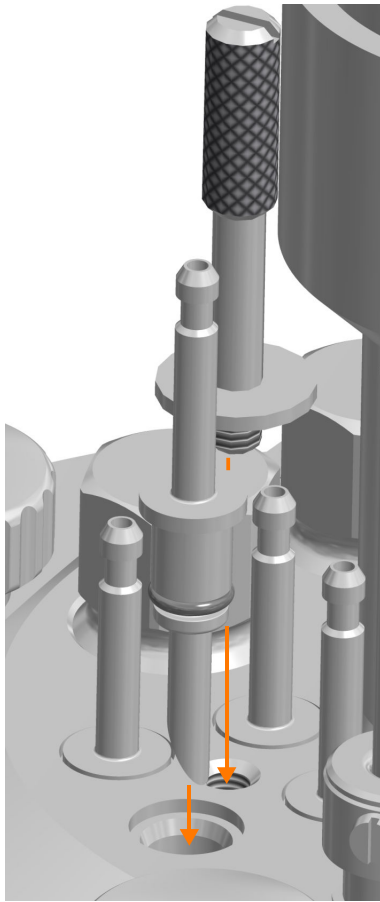
1. ➤ Insert the blanking plug with O-ring into all unused ports.
2. ➤ Fix with a fastening screw.

Ø 12 mm / Pg13.5 Ports



1. ➤ Insert the O-ring and blanking plug into all unused ports.
2. ➤ Tighten by hand.
3. ➤ Use the hexagon socket spanner to make it hand-tight.

7.1.9 Mounting Addition Port Adapters



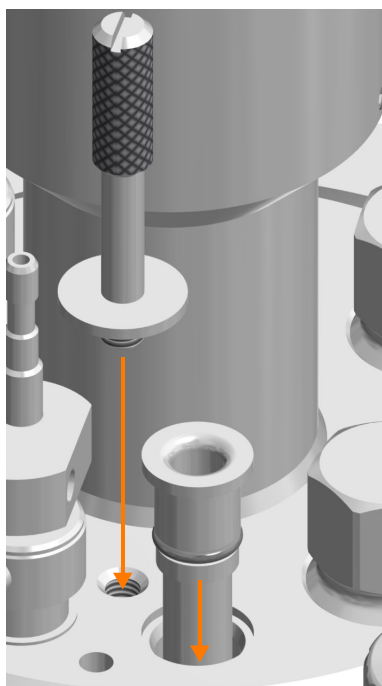
1. ➔ Insert the addition port adapters with O-rings into the four 7.5 mm ports.
2. ➔ Fix them with the fastening screw.

7.1.10 Mounting the Feed Needles

The procedure for mounting one or more feed needles instead of addition port adapters is the same as for the mounting of the addition port adapters (➔ Chapter 7.1.9 'Mounting Addition Port Adapters' on page 89).

Before Cultivation

7.1.11 Mounting the Immersion Pocket for Temperature Sensor (Pt100)



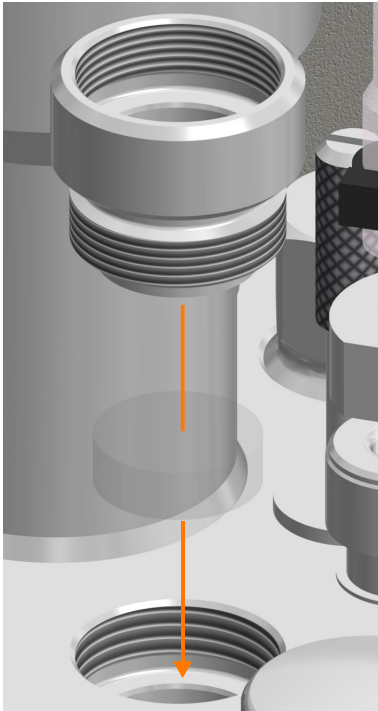
1. ➤ Insert the immersion pocket with the O-ring into the 10 mm port.
2. ➤ Fix it with the fastening screw.

7.1.12 Equipping a Port with Septum Collar and Septum for Inoculation

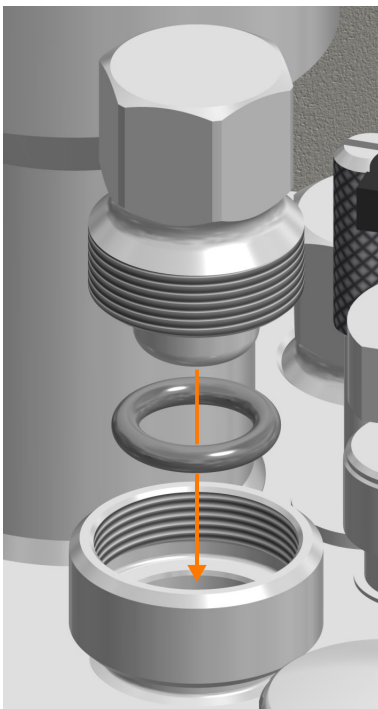
For later inoculation with a syringe, the 12 mm/Pg13.5 port in the top plate must be prepared as follows:

1. ➤ Ensure that there is no O-ring in the port; if there is, remove it.

Before Cultivation



- 2.** ➤ Insert the septum into the port.
- 3.** ➤ Screw the septum collar into the port by hand.



- 4.** ➤ Insert the blanking plug equipped with an O-ring into the septum collar and screw it tight by hand.
If necessary, use the hexagon socket spanner to make it hand-tight.

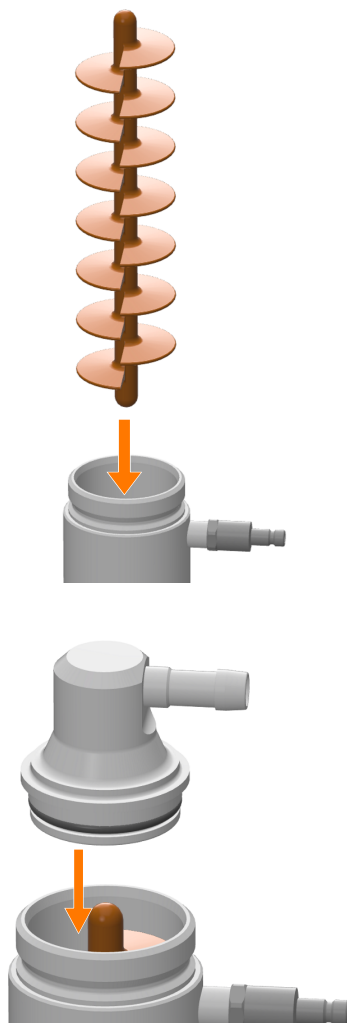
Before Cultivation

7.1.13 Preparing the Dip Tube / Addition Port Adapter for Inoculation

If later inoculation is to be carried out by means of a dip tube or addition port adapter, proceed as follows:

1. ➤ Mount the dip tube with the clamping adapter or addition port adapter in the port.
2. ➤ Place a piece of silicon hose onto the dip tube/addition port adapter.
3. ➤ Equip the hose for a sterile hose connection (depending on the application: rapid coupling, sterile connector or weldable hose with sterile filter).
4. ➤ Secure the hose transition points with cable ties.

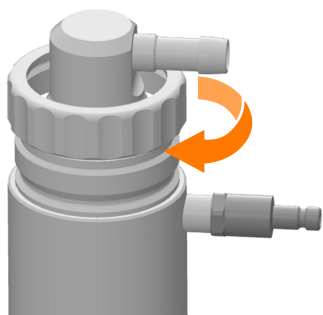
7.1.14 Mounting the Exit Gas Cooler



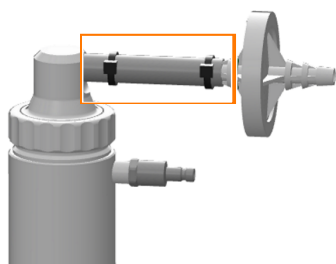
1. ➤ Insert the silicone baffle into the exit gas cooler.

2. ➤ Place the lid with intact O-ring vertically onto the exit gas cooler by hand.
 - Align the exit gas pipe as far as possible on the same side as the hose connections.
 - The lid must sit straight and tight. If necessary, wet the O-ring on the lid lightly with water to facilitate putting it on.

Before Cultivation



3. ➤ Attach the coupling nut and tighten it by hand in clockwise direction.



4. ➤ Equip the exit gas pipe with a piece of pressure hose (D = 6 x 10 mm) and a clean, dry exit gas filter. To do this, plug the inlet side (INLET) with the green marking in the piece of hose.
5. ➤ Secure the hose and exit gas filter with cable ties.
6. ➤ Attach the O-ring to the thread of the exit gas cooler.
7. ➤ Screw the exit gas cooler into the 12 mm/Pg13.5 port by hand.
8. ➤ Align the exit gas cooler to ensure that handling of other built-in-parts is impaired as little as possible.
9. ➤ Cap the exit gas filter loosely with a little aluminium foil.



A humidifier bottle with antifoam reagent can be installed between exit gas cooler and the exit gas filter if significant foam formation is expected.

Take the following into account for autoclaving:

- Only use a new, clean and dry exit gas filter and fix it in such a way that it cannot slip.
- ALWAYS keep the exit gas line - hose at the exit gas cooler with secured exit gas filter - open.



CAUTION

If pressure equalisation does not take place via a top plate opening or the mounted exit gas cooler, overpressure or vacuum in the culture vessel may occur during autoclaving.

7.1.15 Mounting the Cold Finger

When using the optional cold finger, ensure it is fitted with the O-Ring, then screw it into the 12 mm / Pg13.5 port by hand, just like the exit gas cooler. For details, see ➔ Chapter 4.13 'Cold Finger' on page 61.

Before Cultivation

7.1.16 Preparing the Sensors

All sensors that come into contact with the medium are mounted before autoclaving and are autoclaved together with the culture vessel.

Note the following about all sensors:

- Mount all sensors by hand – do not use any tools!
- Mount the sensors in such a way that they cannot come in contact with other built-in-parts or the glass vessel.
- If the mounting depth is adjustable (mounting with sensor holder/clamping adapter), make sure the mounting depth is set correctly prior to autoclaving, as later adjustment represents a contamination risk.
- For all sensors that are mounted in a 12 mm/Pg13.5 port, only use the O-ring of the vessel top plate port. Always remove the sensor's own O-rings and support rings.

Note the following about the pH and pO₂ sensors:

- For vessels with a nominal width of 90 and 145, the pH and pO₂ sensors are screwed directly into a 12 mm/Pg13.5 port. For vessels with a nominal width of 115, the sensors are mounted with a sensor holder.
- Calibrate the pH sensor before mounting and autoclaving.
- Mount the pO₂ sensor in such a way that it has good access to the flow and there is no risk of bubbles collecting.

! NOTICE

Risk of damage to the pH and pO₂ sensors (as well as to the optional Redox sensor).

Covering the sensor heads with aluminium foil during autoclaving may lead to water gathering under the film, thus damage the contacts on the sensor head.

Do not cover the sensor heads with aluminium foil during autoclaving!

7.1.16.1 Calibrating the pH Sensor

Calibration of a pH sensor must always be carried out before autoclaving. Proceed as follows:

- 1.** ➤ Connect the sensor cable (➔ Chapter 7.3.10 'Connecting the pH Sensor' on page 116).
- 2.** ➤ Switch on the device at the power switch.
 - ➔ The operating panel is switched on automatically and the system is started.
- 3.** ➤ Calibrate the pH sensor (➔ Chapter 9.8.1 'Calibrating the pH Sensor' on page 171).



If the pH sensor has already been calibrated before connection to the system, the bioreactor will use this data and calibration using the operating panel is no longer necessary.

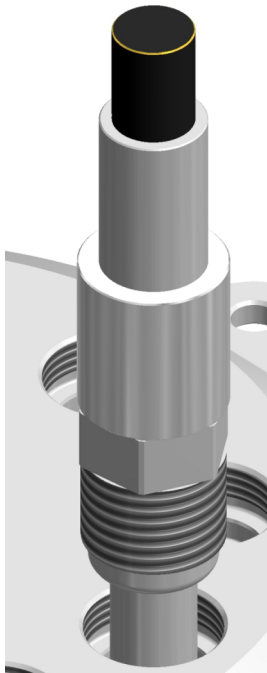
7.1.16.2 Mounting Sensors into 12 mm Ports

For culture vessels with nominal widths of 90 and 145, sensors can be screwed directly into 12 mm/Pg13.5 ports. To do so, proceed as follows:

- 1.** ➤ Slide the O-ring onto the sensor.



Only use the O-ring of the vessel top plate port. Always remove the sensor's own O-rings and support rings.

Before Cultivation

2. ➤ Insert the sensor into the port.
3. ➤ Screw the sensor on its thread into the port by hand.

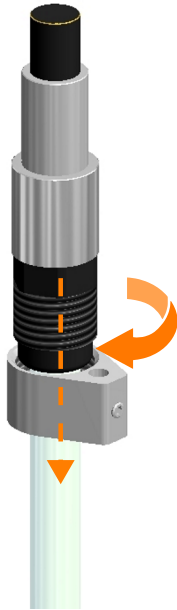
7.1.16.3 Mounting Sensors with Sensor Holder

For the mounting of a sensor in a 12 mm/Pg13.5 port for culture vessels with a nominal width of 115, a sensor holder must be used. To do so, proceed as follows:

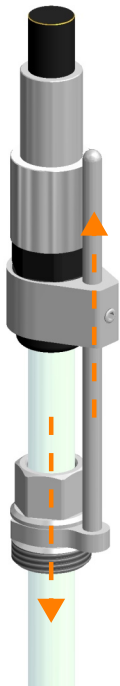
1. ➤ Lightly loosen the grub screw in the support guide with the key and pull the support guide from the guide bar.



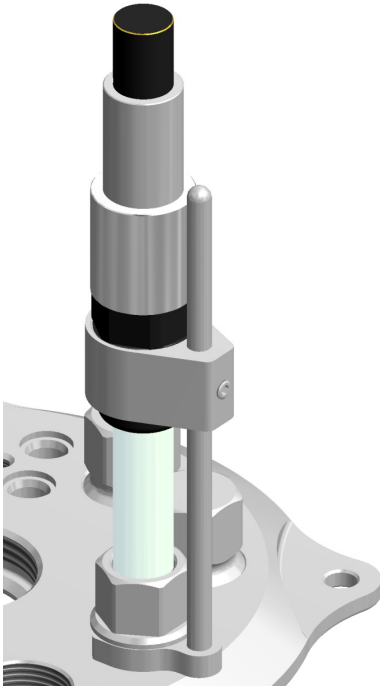
- 2.** ➔ Insert the sensor into the support guide and tighten it.



- 3.** ➔ Insert the sensor into the hollow screw with the thread pointing in the downward direction.
- 4.** ➔ Fit the fork of the guide bar into the groove of the hollow screw.
- 5.** ➔ Push the hollow screw and the guide bar together upwards and insert the guide bar into the hole of the support guide.



Before Cultivation



- 6.** → Slide the O-ring onto the sensor and insert the sensor into the port.



Only use the O-ring of the vessel top plate port. Always remove the sensor's own O-rings and support rings.

- 7.** → Adjust the sensor to the desired mounting depth.
- 8.** → Screw the sensor on the hollow screw into the port and tighten it
- 9.** → Tighten the grub screw in the support guide with the key.

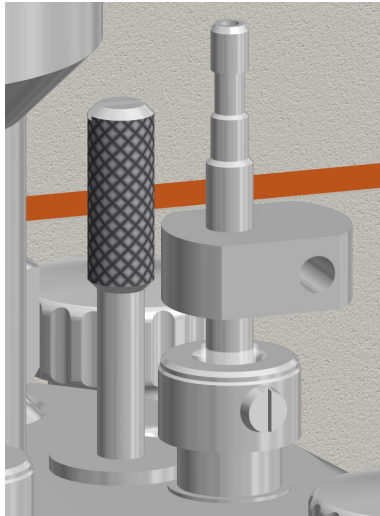
7.1.16.4 Mounting the Antifoam Sensor

Please note the following points for mounting:

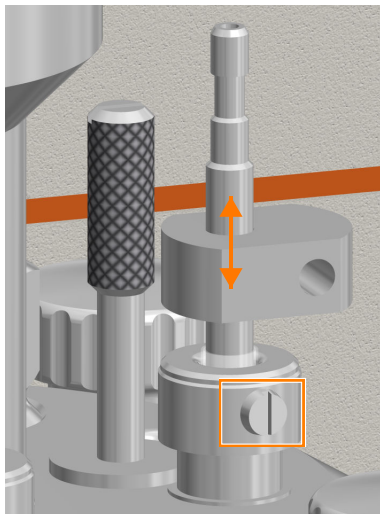
- The antifoam sensor is equipped with transparent insulation that must be intact, as otherwise a continuous signal "Foam/liquid detected" may be generated.
- The sensor head must not touch the clamping adapter, otherwise a continuous short-circuit is generated, indicating "Foam/liquid detected".
- The clamping adapter on the sensor must be equipped with an intact O-ring.

To mount the antifoam sensor, proceed as follows:

- 1.** → Remove the protective cap from the sensor.
- 2.** → Insert the sensor into the port.



3. ➔ Fix the clamping adapter with the fastening screw.



4. ➔ Loosen the slotted screw at the clamping adapter.
5. ➔ Set the desired mounting depth of the sensor carefully.
6. ➔ Tighten the slotted screw carefully.

! NOTICE

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

7.1.17 Preparing the Sampling System Super Safe Sampler



The following figures are for general purposes of comprehension.

To prepare the sampling system Super Safe Sampler for autoclaving, proceed as follows:

Before Cultivation



1. ➤ Attach the hose of the valve assembly to the dip tube.

2. ➤ Secure the hose with a cable tie.



3. ➤ Tighten the sample valve carefully by hand in clockwise direction.

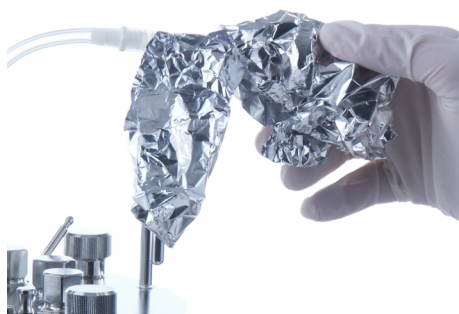
➡ This ensures that the non-return valve/sample valve screw connection is tight.



4. ➤ Turn the sterile filter carefully by hand in clockwise direction.

➡ This ensures that the non-return valve/sterile filter screw connection is tight.

Before Cultivation



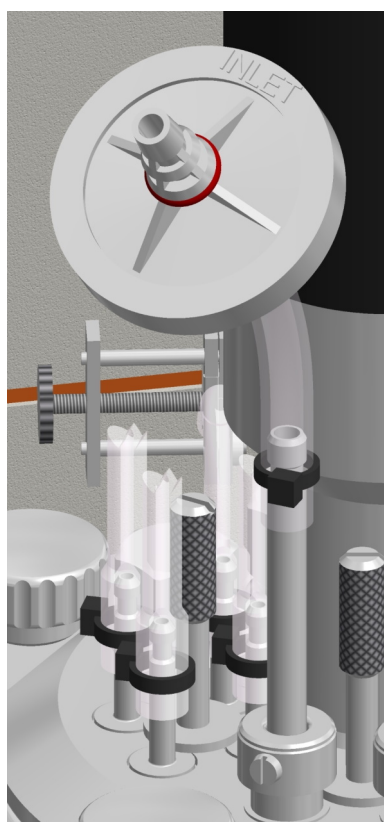
5. ➤ Cover the valve assembly loosely with aluminium foil.
6. ➤ Clamp off the hose on the dip tube.

7.1.18 Mounting the Sparger Hose and the Inlet Air Filter

The sparger must be equipped with the hose and inlet air filter before autoclaving. To do so, proceed as follows:

1. ➤ Cut a short piece of hose:
 - Silicone hose $\varnothing = 5 \times 8$ mm: 1.5 L culture vessel for microorganisms and all vessel sizes for cell cultures.
 - Pressure hose transparent, $\varnothing = 5 \times 10$ mm: 3.0 L and 6.0 L culture vessels for microorganisms.
2. ➤ Fit the inlet air filter to the hose piece, fit it in the direction of the air flow to the hose end; the nozzle with the red marking remains exposed:
 - Filter $\varnothing = 37$ mm: 1.5 L culture vessel for microorganisms and all vessel sizes for cell cultures.
 - Filter $\varnothing = 50$ mm: 3.0 L and 6.0 L culture vessels for microorganisms.
3. ➤ Fit the hose to the sparger.

The figure to the left shows an inlet air filter for 1.5 L culture vessels for microorganisms as an example.
4. ➤ Secure the ends of the hose with the cable tie.
5. ➤ Clamp off the hose with a clamp.
6. ➤ Lightly cap the inlet air filter with aluminium foil.



Before Cultivation

7.1.19 Mounting the Hose and Inlet Air Filter for Head Space Gassing

An addition port adapter in the vessel top plate must be equipped with a hose and an inlet air filter for head space gassing before autoclaving. To do so, proceed as follows:

1. ➤ Cut a short piece of silicone hose ($\varnothing = 3 \times 6$ mm).
2. ➤ Place the inlet air filter, marked in red, $\varnothing = 37$ mm, onto the hose end in the direction of the air flow.

The nozzle with the red *INLET* marking remains exposed.

3. ➤ Place the silicone hose onto the addition port adapter.
4. ➤ Secure the ends of the hoses with cable ties.

If applicable, close unused inlets on the addition port adapter with hose pieces and cable ties.

5. ➤ Clamp off the silicone hose with a clamp.
6. ➤ Lightly cap the inlet air filter with aluminium foil.

7.1.20 Preparing the Reagent Bottles, Pumps and Hoses

When delivered with the device, the reagent bottles are connected to the pump heads. They are equipped with filters for pressure equalization and with hoses of the correct length.

! NOTICE

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

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

The following describes how to prepare unequipped reagent bottles and connect them to the pump and the culture vessel.

Equipping Reagent Bottles

1. ➤ Unscrew the screw cap together with the hose connector plate.

Before Cultivation

- 2.** ➤ Fit a piece of silicone hose onto one hose connector on the inside of the plate.

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



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

- 3.** ➤ Secure the hose connection with a cable tie.
- 4.** ➤ Fit a short piece of silicone hose on the (non-equal-sided) connection on the outside of the hose connection plate.
- 5.** ➤ Fit the filter for pressure equalisation on the short hose piece.
- 6.** ➤ Secure the hose connections with cable ties.
- 7.** ➤ Label the reagent bottles according to its content.
- 8.** ➤ Depending on the application: fill the reagent bottle and reclose it.

! NOTICE

Use of highly corrosive reagents, such as hydrochloric acid HCl, leads to damage to components made of stainless steel such as e.g. built-in-parts or the top plate.

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



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

- 9.** ➤ Place the reagent bottle in the reagent bottle and pump holder.
- 10.** ➤ Repeat the same procedure with each reagent bottle.

Before Cultivation

Preparing the Hose Lines



1. ➔ Cut two long silicone hoses ($\varnothing = 2 \times 6 \text{ mm}$) per pump/reagent bottle.



The length of the silicone hoses must be selected so the hose connections between the reagent bottles and culture vessel do not have any tensions or kinks.

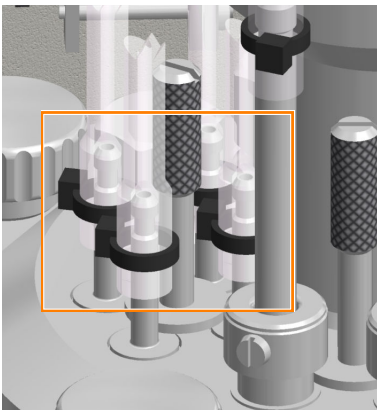
2. ➔ Thoroughly rinse the silicone hoses with distilled water.
3. ➔ Connect the silicone hoses and pump hoses of the pump heads with hose connectors.

For filling (via **FILL**):

- Right-hand side = suction side = hose line to reagent bottle.
 - Left-hand side = pumping side = hose line to culture vessel.
- See arrow for direction of rotation.

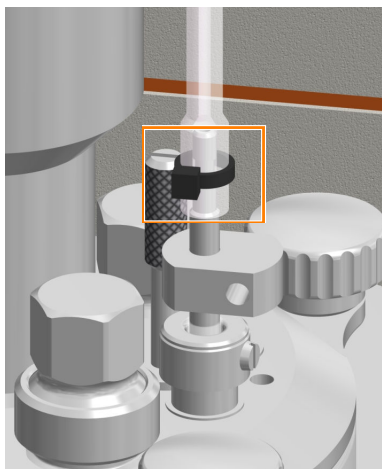
4. ➔ Secure with cable ties.

Connection between Pump and Culture Vessel



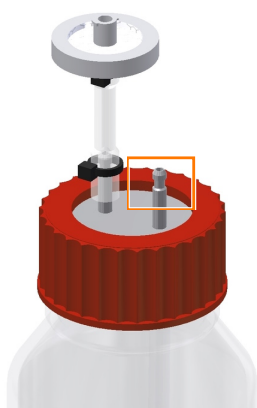
1. ➔ Fit silicone hoses for base, acid and feed to addition port adapters and/or feed needles and secure them with cable ties

Before Cultivation



2. → Attach the silicone hose of the antifoam pump to the mounted antifoam sensor in the culture vessel and secure it with a cable tie.

Connection between Reagent Bottle and Pump



1. → Attach the appropriate silicone hoses to the free-standing hose connections of each of each reagent bottle and secure with cable ties.
2. → Close the silicone hoses with clamps as close as possible to the hose connections of the reagent bottles so that no corrective agent can flow into the culture vessel.
3. → Ensure the following:
 - Each reagent bottle is connected with the appropriate pump according to its contents, base to base pump, etc.
 - Filters are clean and dry; short hose line is open.
4. → Cap the filter loosely with aluminium foil.

7.1.21 Sterile Hose Connections

If additional vessels are needed and these can only be connected to the culture vessel after autoclaving, such as vessels for the inoculum or bottles for sampling etc., rapid couplings (male/female), sterile connectors or – if weldable hoses are used – a hose welding device can be used to form a sterile connection.

The connection pieces must be fitted to the appropriate hoses before autoclaving. Rapid couplings are connected after autoclaving in a sterile workbench. Sterile connectors and hose welding devices allow sterile connecting without a clean bench.

Before Cultivation

7.1.22 Setting the Pumps

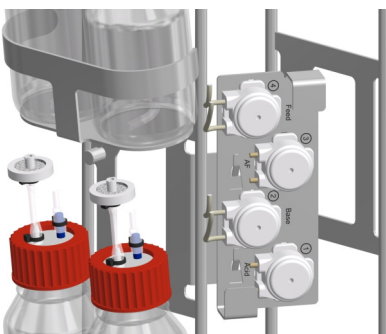
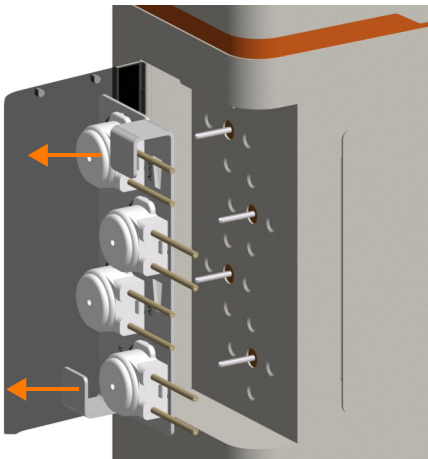
If the pumps are not used with the default settings, we recommend that the appropriate settings are now made on the operating panel. It is possible, for example, to estimate and display the volume (in mL) that has been pumped since the batch (process) started. To this end, the diameter of the hose used must be selected.

For details on the pumps and the setting options, see ➔ Chapter 9.7.1 'PUMPS Parameter Group' on page 164.

7.1.23 Removing the Pump Heads

To remove the pump heads from the basic unit, proceed as follows:

1. ➔ Swing open the pump cover.
2. ➔ Remove the mounting plate with the pump heads from the drive shafts by holding the two handles.
3. ➔ Place the mounting plate with the pump heads onto the pump holder on the vessel holder.



7.1.24 Fitting the Cone Plug for Drive Hub

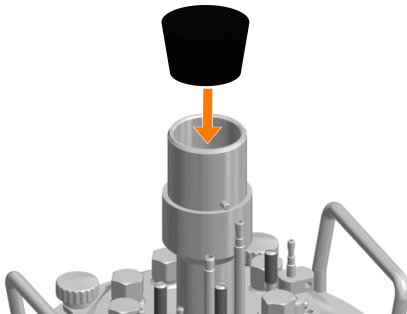
To prevent the penetration of condensation water into the drive hub during autoclaving, the cone plug provided in the starter set must be fitted.

! NOTICE

Risk of loss of property due penetration of condensation water into the drive hub!

Always autoclave the culture vessel with the cone plug fitted to the drive hub!

➔ Plug the cone plug into the opening of the drive hub.



Before Cultivation

7.2 Autoclaving the Culture Vessel

7.2.1 Checklist Before Autoclaving

Check and ensure the following items before autoclaving:

Culture Vessel

Nr.	Task	Further information	☒
1	All necessary O-rings are fitted.	↪ Kapitel 7.1.1, Seite 82	☐
2	All unused ports are closed with blanking plugs.	↪ Kapitel 7.1.8, Seite 88	☐
3	Connection for inoculation is equipped with septum, septum collar and blanking plug.	↪ Kapitel 7.1.12, Seite 90	☐
4	Drive hub is equipped with cone plug.	↪ Kapitel 7.1.24, Seite 107	☐
5	There is liquid in the culture vessel (autoclavable medium or approx. 10 mL water per litre working volume).	↪ Kapitel 7.1.6, Seite 86	☐

Reagent Bottles, Hoses and Pumps

Nr.	Task	Further information	☒
1	Reagent bottles are exclusively filled with autoclavable reagents, correctly labelled and connected with the culture vessel and the pump heads via hoses.	↪ Kapitel 7.1.20, Seite 102	☐
2	Reagent bottles are equipped with filters for pressure equalisation.		☐
3	Reagent bottles are placed in reagent bottle holders and pump heads are placed on the pump holder by means of the mounting plate.	↪ Kapitel 7.1.23, Seite 106	☐

Sampling System Super Safe Sampler

Nr.	Task	Further information	☒
1	The valve assembly is connected to the dip tube in the culture vessel by means of a hose.	↪ Kapitel 7.1.17, Seite 99	☐
2	The valve assembly is lightly capped with aluminium foil.		☐

Before Cultivation

Sparger, Head Space Gassing, Exit Gas Cooler

Nr.	Task	Further information	☒
1	The sparger is equipped with a hose and an inlet air filter.	➔ Kapitel 7.1.18, Seite 101	☐
2	Version for cell cultures: addition port adapter for head space gassing is equipped with hose and inlet air filter.	➔ Kapitel 7.1.19, Seite 102	☐
3	The exit gas cooler is equipped with a new securely fastened exit gas filter.	➔ Kapitel 7.1.14, Seite 92	☐

Filters & Hoses

Nr.	Task	☒
1	All filters are clean, dry and lightly capped with aluminium foil.	☐
2	There are no open hose ends.	☐
3	All hose transition points are secured with an autoclavable cable tie or hose clamp to prevent them from slipping.	☐
4	Hoses on the reagent bottles, for sampling and the gassing system are clamped off with clamps.	☐
5	The exit gas hose is NOT clamped off.	☐
6	The hoses are undamaged; the hose lines show no kinks and are not able to kink.	☐

Sensors

Nr.	Task	Further information	☒
1	All sensors required are mounted and, if necessary, calibrated.	➔ Kapitel 7.1.16, Seite 94	☐
2	The antifoam sensor is mounted, set for the correct mounting depth, and connected to the correct reagent bottle.	➔ Kapitel 7.1.16.4, Seite 98 ➔ Kapitel 7.1.20, Seite 102	☐
3	pH and pO ₂ sensors or optional redox sensor are NOT covered with aluminium foil.		☐

7.2.2 Autoclaving

Before cultivation starts, the culture vessel is autoclaved in accordance with the application in question. The culture vessel can be autoclaved with or without medium.

Before Cultivation

Adhere to the following:

- Never autoclave the culture vessel dry (→ Chapter 7.1.6 'Moistening/Filling the Culture Vessel' on page 86).
- If necessary, pump off any remaining water after autoclaving by means of the dip tube.
- Sterilise all liquid, heat-instable components separately and add them after autoclaving.
- If the medium is autoclaved in the culture vessel, you may then need to add sterile water to make up the volume.



Development of steam is not possible when autoclaving a completely empty and dry culture vessel. Successful sterilisation is not guaranteed. Ensure that there is liquid in the culture vessel, approx. 10 mL of water per litre of total volume.

When transporting the culture vessel to/from the autoclave, note the following:

- Always transport the culture vessel in the vessel holder.
- Always transport the culture vessel to/from the autoclave in pairs and use suitable auxiliary equipment when transporting the culture vessel.



WARNING

Depending on the design, accessories and fill level, the culture vessel may be too heavy to be carried by one person alone.

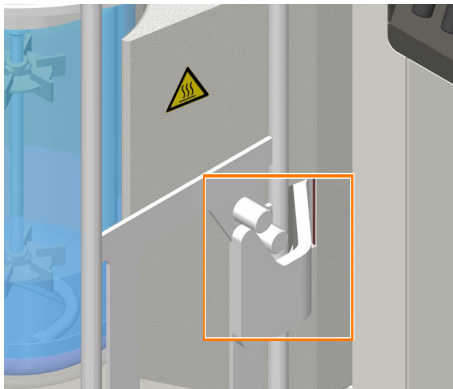
Proceed as follows to autoclave the culture vessel:

1. Place the culture vessel into the autoclave.
2. Ensure that the culture vessel and the accessories do not touch the inner wall of the autoclave.
3. Ensure that the exit gas filter is open.
4. Insert the temperature sensor of the autoclave into the immersion pocket for the temperature sensor.
5. Select the program for liquids.
6. Autoclave the culture vessel in accordance with the operating manual of the autoclave manufacturer.

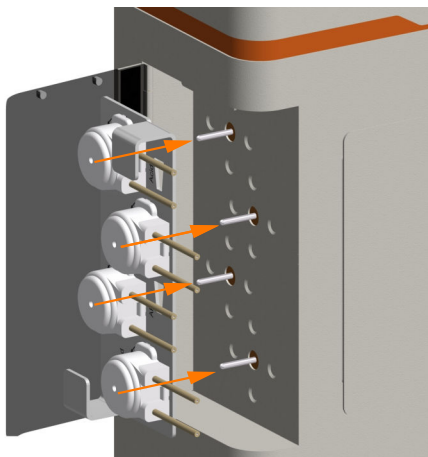
7.3 Connecting the Culture Vessel and Preparing the Cultivation

As soon as the culture vessel with the accessories has cooled sufficiently, it can be hung up within the basic unit and the various cable and hose connections between the basic unit and the culture vessel can be established.

7.3.1 Hanging the Culture Vessel in Place and Fitting the Pump Heads



1. ➤ Hang the vessel holder into place on the two hooks on the thermal block adapter.
2. ➤ Pull off the mounting plate with the pump heads from the pump holder.



3. ➤ If necessary, flip up the pump cover plate.
4. ➤ Plug the mounting plate with the pump heads onto the pump motor drive shafts and close the cover plate.

7.3.2 Filling the Reagent Hoses

To prepare the reagent hoses for operation, they must be filled via the corresponding pump. This is done on the control panel using the **Fill** function.

Before filling, remove the clamps from the reagent hoses.

Before Cultivation

WARNING

When using heavily corrosive reagents (acids and bases), it is particularly important only to use suitable and undamaged hoses. They must also be securely fastened.

Furthermore, the exit gas filter must not be blocked. This ensures that no pressure builds up and no reagent escapes due to burst hoses.

When filling, ensure that no reagent escapes into the culture vessel, if possible.

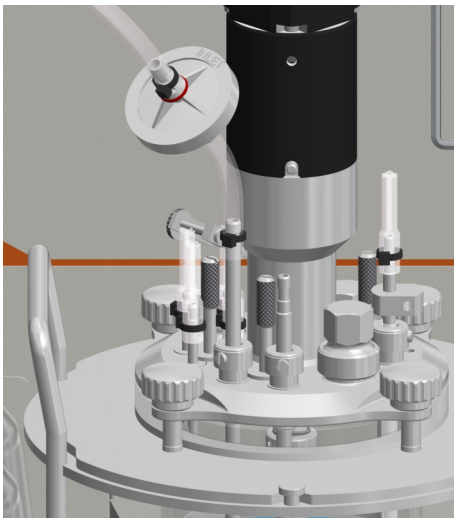
For details on filling, see ➔ Chapter 9.7.1 'PUMPS Parameter Group' on page 164.

7.3.3 Connecting the Gassing

To connect the sparger and the addition port adapter (head space gassing, version for cell cultures) to the gassing, proceed as follows:

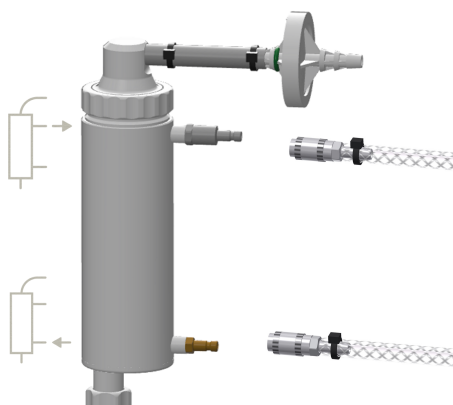
1. ➔ Remove the aluminium foil from the inlet air filter.
2. ➔ Insert the gassing hose of the basic unit to the inlet air filter of the sparger and secure it in place with a cable tie.

The figure to the left shows an inlet air filter for 1.5 L culture vessels for microorganisms as an example.
3. ➔ Remove the clamp.
4. ➔ Head space gassing: connect the gassing hose from the basic unit to the inlet air filter on the addition port adapter and secure it with a cable tie.
5. ➔ Remove the clamp.



7.3.4 Connecting the Exit Gas Cooler

To connect the exit gas cooler to the basic unit, proceed as follows:



1. ➤ Remove the aluminium foil from the exit gas filter.
2. ➤ Connect the hoses according to the symbols on the basic unit:
 - Insert the rapid coupling of the water outlet hose onto the upper connection nozzle on the exit gas cooler.
 - Insert the rapid coupling of the water inlet hose onto the lower connection nozzle on the exit gas cooler.

7.3.5 Connecting the Cold Finger

To connect the optional cold finger to the basic unit, connect the hoses for water inlet and return via the rapid couplings, taking the water flow direction into account.

For details on the cold finger, see ➔ Chapter 4.13 'Cold Finger' on page 61.

7.3.6 Coupling the Motor

For routine operation, it is not necessary to plug in and unplug the motor cable. The motor connected during installation is only coupled before cultivation.

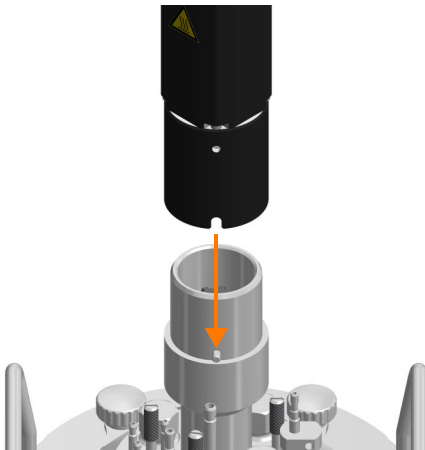
! NOTICE

If the motor cable is connected to or disconnected from the motor while the device is switched on, there is a risk of a short circuit that could damage the control electronics.

For details about connecting the motor cable, see ➔ Chapter 6.4 'Connecting the Motor Cable' on page 76.

To couple the motor, proceed as follows:

Before Cultivation



- ➔ Place the motor onto the drive hub with the groove aligned with the pin on the drive hub.
- ➡ The motor is held in its position.

7.3.7 Filling the Culture Vessel

Depending on the application, the vessel can be filled after auto-claving. To prevent foam formation during filling, add the medium via a dip tube. To do so, proceed as follows:

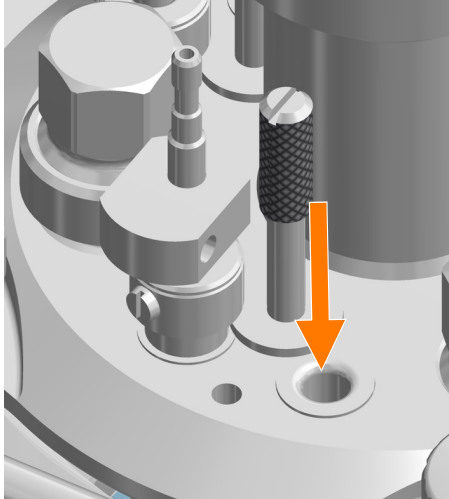
- 1.** ➔ Sterilise the medium separately.
- 2.** ➔ If necessary, pump off any water that remains in the culture vessel.
- 3.** ➔ Establish a sterile hose connection between the culture vessel and the medium container.
- 4.** ➔ Pump the desired quantity of medium into the culture vessel.
- 5.** ➔ Clamp off the medium hose; if necessary, apply a welded seal.
- 6.** ➔ Disconnect the medium container from the culture vessel; if necessary, retain it as a harvest or waste container.



If the impeller is turning on the surface of the medium, foam will be formed. For this reason, only switch on the stirrer if the impeller is fully covered by medium.

7.3.8 Connecting the Temperature Sensor (Pt100)

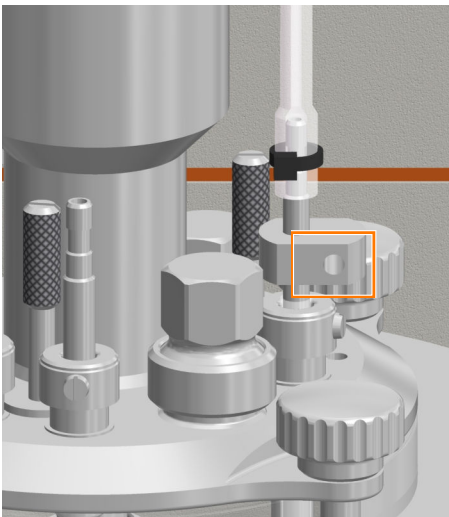
The temperature sensor is not in direct contact with the medium.



- ➔ Insert the sensor into the immersion pocket in the vessel top plate as far as it will go.

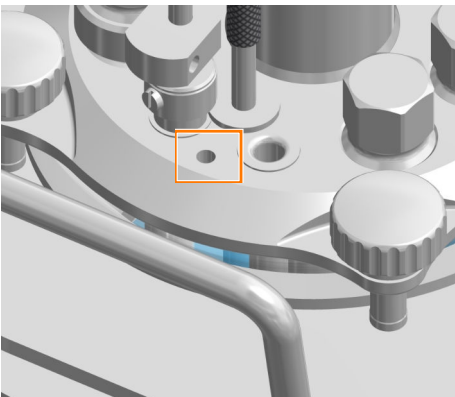
7.3.9 Connecting the Antifoam Sensor

To connect the antifoam sensor, the two banana connectors of the sensor cable must be inserted as follows:



1. ➔ Insert the red banana plug into the connector on the sensor head.

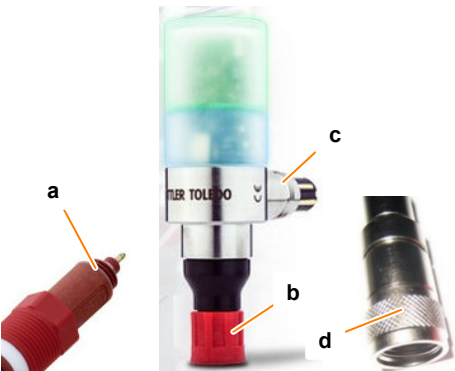
Before Cultivation



2. ➔ Insert the black banana plug into the ground connection in the top plate.

7.3.10 Connecting the pH Sensor

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



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



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

7.3.11 Connecting the pO₂ Sensor

The sensor and cable connections of the pO₂ sensors differ depending on the pO₂ measurement system used.

Before Cultivation



METTLER digital, type InPro6860i

Sensor head connection (a)	VP8
Cable socket (b)	VP8

HAMILTON digital, type VisiForm DO ARC / RS485-ECS

Sensor head connection (a)	VP8
Cable socket (b)	VP8

7.3.12 Calibrating the pO₂ Sensor

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

For more details on the calibration, see ➔ Chapter 9.8.3 'Calibrating the pO₂ Sensor' on page 177.

7.3.13 Checking the Hoses and Hose Connections

Check and ensure the following items before each cultivation:

- Hoses show no kinks and are not able to kink.
- Hoses are undamaged and show no weaknesses.
- Gas hoses and connections do not show any leaks.
- Hose lines are as short as possible.
- Hoses are secured with cable ties and/or hose clamps.
- Only the pressure hoses supplied by the device manufacturer are connected as supply lines (water, gas) between the in-house connections and the device.

Cultivation

8 Cultivation

The following sections describe the work typically performed during a cultivation. This essentially comprises:

- Preparing the medium (starting a batch)
- Sampling
- Inoculation
- Harvest
- (Stopping the batch), if necessary emptying the vessel
- Autoclaving the culture vessel and accessories

The requirement for the first item is that the culture vessel and accessories are autoclaved, cooled and connected to the basic unit. All cable and hose connections between the device and the culture vessel, including the reagent bottles, are present, pump heads are mounted and the reagent hoses are filled. Depending on the user specifications, the pO₂ sensor is already calibrated.

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 pO₂ concentration and the pH are set. The time required for this depends on the working volume. Set and activate the desired setpoint of the parameter in question on the operating panel, and start the batch (bioprocess). Depending on the specifications defined by the user, the pO₂ sensor is calibrated either before the vessel is filled with medium or afterwards, in the prepared medium (→ Chapter 9.8.3 'Calibrating the pO₂ Sensor' on page 177).

CAUTION

If pressure equalisation does not take place via a top plate opening or the mounted exit gas cooler, overpressure in the culture vessel may occur during cultivation as a result of warming, gassing or fermentation processes.

- Exit gas line - hose at the exit gas cooler with secured exit gas filter - ALWAYS keep open.
- Only use clean and dry exit gas filters.

8.2 Sampling

Samples are taken from the culture vessel to gain material for offline analysis.



Using **SAMPLE NOW** on the operating panel, the sampling can be logged in the electronic logbook and assigned a sample ID (➔ Chapter 9.1.5 'SAMPLE NOW' on page 132).

The method of sampling can vary due to the different analyses carried out by the operator.

The sampling procedure using the standard sampling system, Super Safe Sampler, is described in the following.

Before starting, observe the following:



WARNING

Culture solution could emerge from the vessel if the sample valve mechanically fails. This could lead to serious health risks in the event of applications with pathogenic organisms.

- When working with pathogenic organisms, always additionally clamp off the sampling hose with a metal clamp.
- Only remove the clamp when sampling.
- Reattach the clamp before removing the syringe from the sample valve.



WARNING

Loose screws at components could lead to the penetration of unsterile air or contamination of the environment.

Before and after autoclaving: Check that all screws are tightly screwed in and, if necessary, tighten them manually.

If the sample is to be further aseptically processed, use a sterile syringe and sterile closing caps.

For details, see ➔ Chapter 4.15 'Sampling System Super Safe Sampler' on page 63.

Taking Sample

- 1.** ➔ Check that all screw connections of the valve assembly are tightly screwed in. If necessary, gently tighten the screw connections with two fingers.
- 2.** ➔ Remove the clamp from the sampling hose.
- 3.** ➔ If present: remove the closing cap.
- 4.** ➔ If desired: disinfect the sample valve.

Cultivation



5. ➤ Screw open the Luer-Lock syringe on the sample valve.



6. ➤ Pull back the syringe plunger to remove the desired sampling volume.

7. ➤ If the dip tube was rinsed with air, air is sucked in first. Remove it as follows:

- Unscrew the syringe from the valve assembly.
- Hold the syringe with the plunger downwards so that the medium remains in the syringe.
- Push the air out of the syringe.
- Screw the syringe onto the sample valve.
- Draw in again.

8. ➤ Attach the clamp to the sampling hose.

Rinsing the Dip Tube with Sterile Air

The dip tube and its sampling hose can be filled with sterile air after taking a sample.



Only use a clean and dry syringe to avoid blocking the sterile filter. This syringe can be reused as often as desired, since air is provided via a sterile filter.



- 1.** Insert the syringe onto the hose at the sterile filter and push air through.
The remaining liquid in the hose and in the dip tube is pushed back into the vessel.
- 2.** Remove the syringe from the sterile filter to fill it with air again.
- 3.** Repeat steps 1 and 2 as many times as necessary until bubbles rise out of the dip tube.

Removing Residual Fluid



- 1.** Hold the syringe with sample downwards, pull back the plunger.
This removes all but a few μL of the residual fluid.



- 2.** Hold the sample valve with one hand; unscrew the syringe with the other.
- 3.** If desired: Place the closing caps on the sample valve and on the syringe with the sample.

Cultivation

8.3 Inoculation

Requirements

Check and ensure the following before inoculation:

- Medium has been filled.
- Heat-labile, separately sterilized substances have been added.
- The reagent bottles are connected with the pumps and the culture vessel, and are filled with a sufficient amount of reagent and nutrient solution for the duration of the cultivation.
- The hoses of the reagent bottles are filled.
- The correct operating temperature has been reached.
- The required stirring speed is set.
- The sensors are calibrated and the control is correct (or not yet activated).
- Utensils for the inoculation and vessels with inoculum are ready.
- All clamps have been removed (except for sampling system).

Methods

There are a number of ways to add medium or inoculum before and during cultivation:

- In a small volume, with the syringe via the septum
- Via the addition port adapter from the reagent bottle. A sterile hose connection is required for this method.
- Via the dip tube from the reagent bottle. A sterile hose connection is required for this method.

These methods are described in the following.

The implements for inoculation with a syringe are standard accessories for the device. This inoculation method is particularly suitable for all vessel sizes of the device.

8.3.1 Inoculation with a Syringe

1. ➤ Fill the syringe with the required amount of inoculum.
2. ➤ Unscrew the blanking plug from the septum collar.

As a possible additional protection against contamination:
Before piercing, drop a few drops of ethanol (70 %) on the septum.
3. ➤ Pierce the septum and inject the inoculum.
4. ➤ Remove the needle from the septum and close the septum collar with a blanking plug.

8.3.2 Inoculation Using Dip Tube / Addition Port Adapter

1. ➤ Fill the inoculum under sterile conditions into the prepared container.
2. ➤ Create a sterile hose connection with the dip tube/addition port adapter.
3. ➤ Transfer the desired volume of inoculum into the culture vessel. Pump it, if necessary.
4. ➤ Clamp off the hose by means of a clamp, weld it if necessary.

8.4 Harvest

The culture can be harvested at the end of the cultivation.

To prevent possible sedimentation from the culture, the stirrer can be switched on during harvesting. If necessary, activate gassing for sensitive cultures. However, all other parameters should be switched off, provided there are no other specifications for the user.

The following possibilities exist for the harvest:

- Transfer to another vessel: transfer the contents of the vessel to another container in a laminar flow cabinet.
- Pump-down via a sterile hose connection: to do so, proceed as follows:
 1. ➤ Make a sterile connection between the hose at the dip tube for harvest and the new vessel.
 2. ➤ Connect the hose to one of the pumps on the device or to an external pump.
 3. ➤ Pump the desired amount of culture into the new vessel.



Only switch on the stirrer if it is fully covered by medium, as foam otherwise forms.

Cultivation

4. ➔ Switch off all parameters at the operating panel and stop the batch (bioprocess) at the operating panel.



Always stop the running batch on the operating panel. If it is stopped by pressing the power switch, it is akin to a power interruption. This means that when it is switched on again, the previous settings are adopted and the batch continues running where it was interrupted. This also applies, if the batch is controlled via eve®, the platform software for bioprocesses.

8.5 Emptying the Culture Vessel

For emptying the culture vessel, the same options as for harvesting are available (➔ Chapter 8.4 'Harvest' on page 123).

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

If the culture vessel is to be autoclaved before cleaning, it is recommended to autoclave the culture vessel filled with water to facilitate subsequent cleaning.

8.6 Emptying the Reagent Hoses

Before autoclaving the culture vessel with accessories, all reagent hoses must be completely emptied using the corresponding pump. This can either be done manually or time-controlled at the operating panel.

! NOTICE

Residues of acids and bases in the reagent hoses during autoclaving can damage the pump heads.

- Completely empty all reagent hoses before autoclaving.
- Thoroughly rinse the reagent hoses with water after emptying.



If feed needle(s) are used instead of addition port adapters, the vessel contents are simultaneously pumped back into the reagent bottle while emptying the hoses, if the vessel has not been previously emptied.

8.7 Autoclaving the Culture Vessel After Cultivation

Depending on internal regulations, the culture vessel is autoclaved with all accessories after emptying and before cleaning. In this case, observe and comply with the same safety instructions as for autoclaving before cultivation.

Before starting, ensure the following:

- There is liquid in the culture vessel (autoclavable medium or approx. 10 mL water per litre working volume).
- Reagents and nutrient solution have been pumped back out of the hoses.
- The device is switched off.
- The motor has cooled down (version for microorganisms).

Proceed as follows:

- 1.** ➤ Clamp off the hoses of the reagent bottles.
- 2.** ➤ Clamp off the hose of the sparger, and where applicable, the hose for head space gassing.
- 3.** ➤ Remove all cable and hose connections between the basic unit and the culture vessel:
 - Uncouple the motor and place it to the side.
 - Unplug the sensor cables.
 - Pull the temperature sensor out of the immersion pocket.
 - Disconnect the water inlet and water outlet hoses from the exit gas cooler.
 - Remove the gassing hose (emerging from basic unit) from the inlet air filter on the sparger and from the inlet air filter on addition port adapter (head space gassing for cell cultures).
- 4.** ➤ Lightly cover all filters with aluminium foil.

! NOTICE

Risk of damage to the pH and pO₂ sensors (as well as to the optional Redox sensor).

Covering the sensor heads with aluminium foil during autoclaving may lead to water gathering under the film, thus damage the contacts on the sensor head.

Do not cover the sensor heads with aluminium foil during autoclaving!

Cultivation

5. ➤ Fit the cone plug into the opening of the drive hub.

! NOTICE

Risk of loss of property due penetration of condensation water into the drive hub!

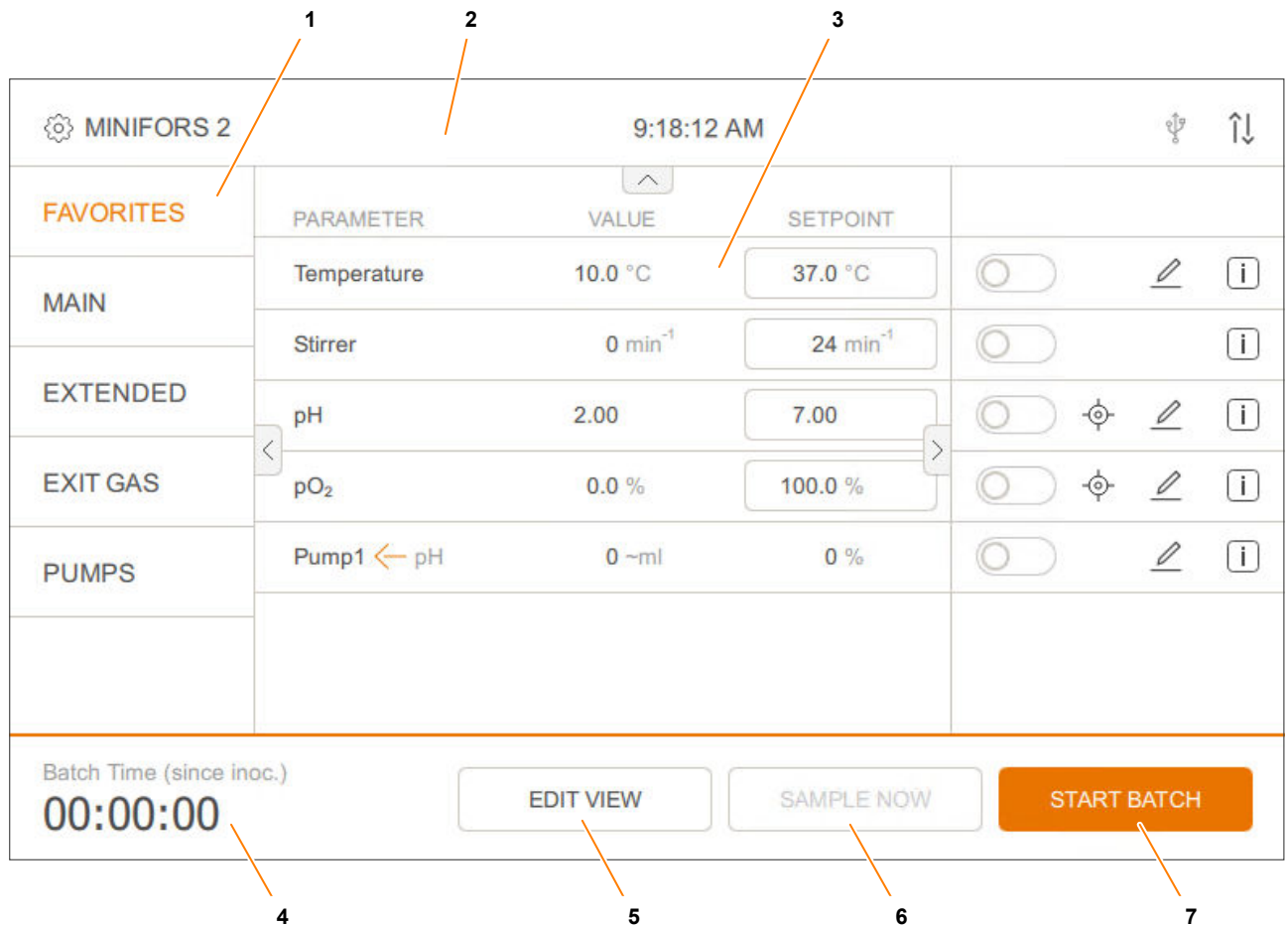
Always autoclave the culture vessel with the cone plug fitted to the drive hub!

6. ➤ Open the pump cover.
7. ➤ Remove the mounting plate with pump heads from the drive shafts on the basic unit and place on the pump holder.
8. ➤ Check and ensure that the exit gas filter is free and dry and the exit gas hose is OPEN.
9. ➤ Insert the temperature sensor of the autoclave into the immersion pocket on the culture vessel and autoclave the culture vessel.

9 Operation

9.1 Screen Areas, Menu Navigation and Control Elements

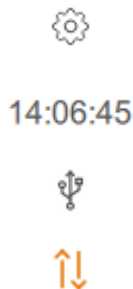
9.1.1 Overview



- | | |
|--|---|
| 1 Left side with selection menus for system settings or parameter groups | 5 Button for the selection of the parameter display |
| 2 Header with status displays | 6 Button for time stamp for sampling |
| 3 Main screen | 7 Buttons with changing function for Batch start, inoculation time stamp and Batch stop |
| 4 Display of the Batch time (since inoculation) and possible alarms | |

Operation

Header Status Display



The following symbols and displays are in the header:

- *Settings* symbol: to switch between menu selection for system settings and parameter groups
- Display of the current time
- Display for connected USB stick
- Display for an active connection to SCADA software

Alarm Display



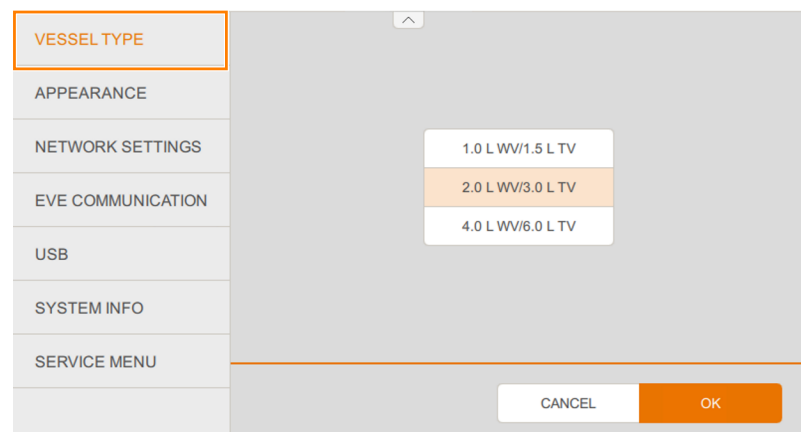
If alarms occur (equipment (device) alarm or parameter alarm), they are signalled by a red exclamation mark highlighted in white on a red background. Pressing the symbol or swiping upwards opens the alarm menu (→ Chapter 9.10 'Alarms – Equipment Alarm Menu' on page 184).

9.1.2 Main Screen

Depending on the menu selected on the left side of the screen, the main screen displays different information.

Menus for System Settings

Example: menu *VESSEL TYPE* for setting the vessel size.



Depending on the menu selected, the **CANCEL** and **OK** buttons, or only the **OK** button, are available in the menu footer:

- **OK** saves the changes and closes the menu.
- **CANCEL** closes the menu without making any changes

Operation

Parameter Groups

Example: parameter group *MAIN* with actual values in the *VALUE* column and input fields for setpoints in the *SETPOINT* column.

MINIFORS 2

13:54:47

FAVORITES

MAIN

EXTENDED

EXIT GAS

PUMPS

PARAMETER

VALUE

SETPOINT

Temperature

10.0 °C

37.0 °C

Stirrer

0 min⁻¹

55 min⁻¹

pH

2.00

7.00

pO₂

0.0 %

21.0 %

TotalFlow

0.000 L min⁻¹

0.000 L min⁻¹

GasMix

NaN %O₂

21 %O₂

Foam

0

Active Menus/Parameter Group(s)



All menus and parameter groups can be selected by pressing them. The selected menu or parameter group is highlighted with a change of colour in the menu/group text from black to orange.

Example to the left: *MAIN* parameter group

Expand and Collapse Section

The arrow buttons at the edge of the main screen can be used to show or hide parts of the menu and display.

The figure below shows the example of the menu with parameter options, which becomes visible after pressing the arrow button on the right-hand edge of the screen (figure above).

Operation

PARAMETER	VALUE	SETPOINT
Temperature	10.0 °C	37.0 °C
Stirrer	0 min ⁻¹	55 min ⁻¹
pH	2.00	7.00
pO ₂	0.0 %	21.0 %
TotalFlow	0.000 L min ⁻¹	0.000 L min ⁻¹
GasMix	NaN %O ₂	21 %O ₂
Foam	0	



Instead of using the arrow buttons, swiping movements to the left, right, upwards or downwards on the screen can also change the display.

9.1.3 EDIT VIEW

EDIT VIEW

EDIT VIEW opens a menu with all available parameters. Here, up to 8 parameters can be selected to appear in the *FAVORITES* parameter group by checking the check boxes.

☆ SELECT YOUR FAVORITES		
☒ Temperature	☒ AirFlow	☐ Pump4
☒ Stirrer	☐ 2nd Gas Flow	
☒ pH	☐ Exit Gas O2	
☒ pO2	☐ Exit Gas CO2	
☒ TotalFlow	☐ Turbidity	
☒ GasMix	☐ Pump1	
☒ Foam	☐ Pump2	
☐ Balance	☐ Pump3	

CANCEL OK

- **OK** confirms the selection and closes the menu.
- **CANCEL** closes the menu without making any changes.

9.1.4 START BATCH / INOCULATE / STOP BATCH

START BATCH

Pressing the **START BATCH** button starts the preparation phase for the batch (bioprocess). The controller is activated. The current parameter settings are simultaneously logged in a log file, and recording of the actual values begins.



Log files can be exported on a USB stick.

INOCULATE

The button now changes function to **INOCULATE**. In this process phase, the parameters can be activated manually and individually.

When all preparations are finished, inoculation can take place. After pressing **INOCULATE**, a dialogue appears asking for confirmation that inoculation takes place.

INOCULATION

Do you really want to inoculate the Batch?

CANCEL

OK

- **CANCEL** cancels the inoculation process without making any changes.
- **OK** starts the batch. After confirming via **OK**, the Batch-Time is started.

Operation

STOP BATCH

The button now changes function to **STOP BATCH**.

After pressing **STOP BATCH**, a dialogue appears asking for confirmation that the batch is to be stopped, as well as the notice that doing so switches all parameters off.

STOP BATCH

Do you really want to stop the Batch? This will switch off all parameters.

CANCEL OK

- **CANCEL** cancels the stop procedure without making any changes.
- **OK** finishes the batch, all parameters are deactivated and the controller is deactivated. Recording of actual values is ended, the button changes function back to **START BATCH**.



Batch Time remains visible until a new batch is started or the device is switched off using the power switch.

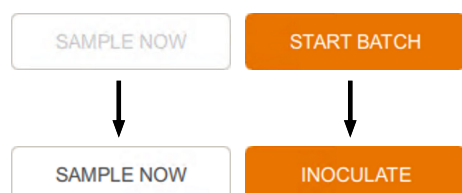
9.1.5 SAMPLE NOW

SAMPLE NOW

If a sample is removed from the culture vessel by hand, this can be signalled to the bioreactor by pressing **SAMPLE NOW**. This logs the sampling, and is visible in the log files for the batch (→ Chapter 9.2.6 'USB Data Export and Import from a USB Stick' on page 140).

If the bioreactor is connected with the bioprocess platform software eve[®], an *offline sample* is automatically created there.

For details on the procedure for process-suitable sampling, see → Chapter 8.2 'Sampling' on page 118.



The **SAMPLE NOW** button only becomes functional after pressing **START BATCH**. This means that it can only be used during a batch.

SAMPLE INFORMATION
Sample Number: 1 Batch Time: 00:04:34
OK

SAMPLE NOW generates consecutive numbers for all samples and logs them with the batch time since inoculation as the time stamp. This means that an information dialogue appears and displays how long the batch has been running since inoculation (*Batch Time...*), and how many samples have been taken (*Sample Number...*), or how many times **SAMPLE NOW** has been pressed since **START BATCH** was pressed.

SAMPLE INFORMATION
Sample Number: 0 Current Time: 15:28:55
OK



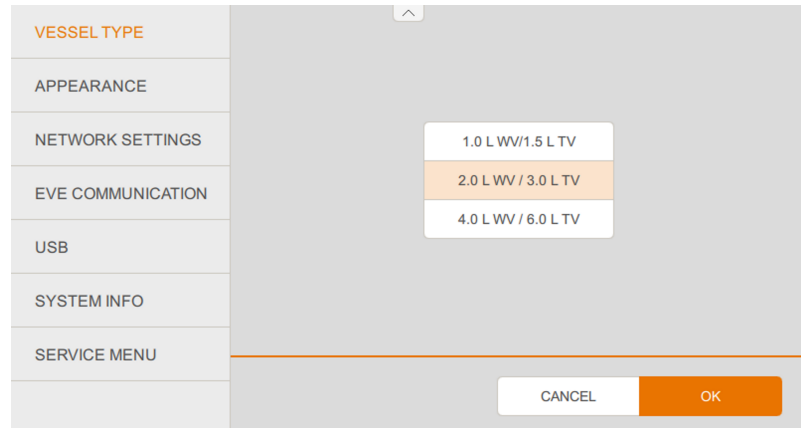
If sampling takes place before inoculation, the current time is logged instead of the batch time since inoculation. There is no numbering of the samples taken before inoculation.

Operation

9.2 Menus for System Settings

9.2.1 Overview

There are seven menus for system settings, of which five are available for the operator.



- **VESSEL TYPE:** selection of the culture vessel used
- **APPEARANCE:** display settings, including language and date/time
- **NETWORK SETTINGS:** network configuration
- **EVE COMMUNICATION:** configuration of the OPC UA server for communication with the bioprocess platform software eve® by the device manufacturer
- **USB:** to export files on a USB stick or load updates and additional packages from a USB stick
- **SYSTEM INFO:** information such as e.g. system and controller version, system uptime etc.
- **SERVICE MENU:** functions for authorised service partners of the device manufacturer, only accessible with the relevant password



Depending on the menu selected, the **CANCEL** (leave the menu without changes) and **OK** (save changes and leave the menu) buttons, or only the **OK** button, are available in the menu footer.

9.2.2 VESSEL TYPE – Selecting a Culture Vessel

The culture vessel used is set in the *VESSEL TYPE* menu. There are three culture vessel sizes.

VESSEL TYPE	1.0 L WW/1.5 L TV 2.0 L WW / 3.0 L TV 4.0 L WW / 6.0 L TV
APPEARANCE	
NETWORK SETTINGS	
EVE COMMUNICATION	
USB	
SYSTEM INFO	
SERVICE MENU	
CANCEL OK	

! NOTICE

With the selection of the culture vessel used, the permitted limit values and control settings for the corresponding vessel size are configured in the background. If the vessel size is set incorrectly, it could cause undesired behaviour from the control.

Operation

9.2.3 APPEARANCE – Display Settings

A variety of display settings can be made in the *APPEARANCE* menu.

VESSEL TYPE	
APPEARANCE	
NETWORK SETTINGS	
EVE COMMUNICATION	
USB	
SYSTEM INFO	
SERVICE MENU	

^

LANGUAGE

English

▼

DISPLAY INFO
BUTTONS

NO ☒ YES

SYNC DATE AND TIME
VIA NTP

NO ☐ YES

SET DATE AND TIME

25

.

11

.

2022

:

10

:

33

Europe

▼

Berlin

▼

TIME FORMAT

24 h ☐ 12 h

CANCEL

OK

LANGUAGE

To select the display language.
The desired display language can be selected using the drop-down list. The languages in the drop-down list are always displayed in English.

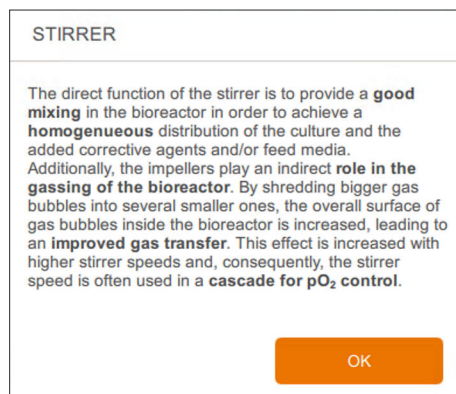
DISPLAY INFO BUTTONS

To swich the on-screen help off or on.
This display of the info buttons for the on-screen help for the various parameters is switched on (*YES*) or off (*NO*) using the switch.

NO ☒ YES

☐			
☐			
☐			

If the display is switched on, the info buttons also appear in the main screen, in the parameter options menu display, see figure to the left illustrating an extract of the menu display.



After pressing an info button, a dialogue appears containing basic information on the selected parameter, example to the left: parameter *STIRRER*.

SYNC DATE AND TIME VIA NTP

If this function is activated, the touchscreen synchronizes its date and time with a network time server (NTP) present and configured in the network.



In this case, the date and the time of the bioreactor cannot be set manually (*SET DATE AND TIME*).

SET DATE AND TIME

To enter the date and time. Can only be done provided *SYNC DATE AND TIME VIA NTP* is not switched on.

TIME FORMAT

To switch between 12 h and 24 h time formats.

Operation

9.2.4 NETWORK SETTINGS

The network connection of the bioreactor is configured in the *NETWORK SETTINGS* menu.

VESSEL TYPE				
APPEARANCE				
NETWORK SETTINGS	CONFIGURATIONS	Auto (DHCP) Manual		
EVE COMMUNICATION	IP ADDRESS	192	168	12
USB	SUBNET MASK	255	255	0
SYSTEM INFO				
SERVICE MENU				
	OK			



If the bioreactor is to be integrated into an existing network, the network specifications are to be followed and the corresponding settings are to be used. Please consult your network administrator.

CONFIGURATIONS

Determine whether the network connection is to be automatically configured (**Auto (DHCP)**) or needs to be set up manually (**Manual**).

A DHCP server is required in the network for automatic configuration with the DHCP protocol. Please consult your network administrator.

IP ADDRESS

Displays the allocated IP address during automatic configuration (*Auto (DHCP)*), or can be used to enter the IP address for manual configuration (*Manual*).

SUBNET MASK

Displays the subnet mask address during automatic configuration (*Auto (DHCP)*), or can be used to enter the subnet mask for manual configuration (*Manual*).



The network connection can be used to connect the device with the bioprocess platform software eve®.

9.2.5 EVE COMMUNICATION – Communication Settings

In the *EVE COMMUNICATION* menu, permissions for server access as well as their security settings for communication with the bioprocess platform software eve® are set.

VESSEL TYPE	INFORMATION Device Name Minifors 2 URL opc.tcp://169.254.44.146:48010 opc.tcp://192.168.1.185:48010 SERVER ACCESS Hidden Read-Only Read/Write
APPEARANCE	
NETWORK SETTINGS	
EVE COMMUNICATION	
USB	
SYSTEM INFO	
SERVICE MENU	
CANCEL OK	

INFORMATION

Display of the device name (*Device Name*) and its network address (*IP*, configuration under *NETWORK SETTINGS*). This information is required for configuration of the connection in eve® (device manufacturer's bioprocess platform software).

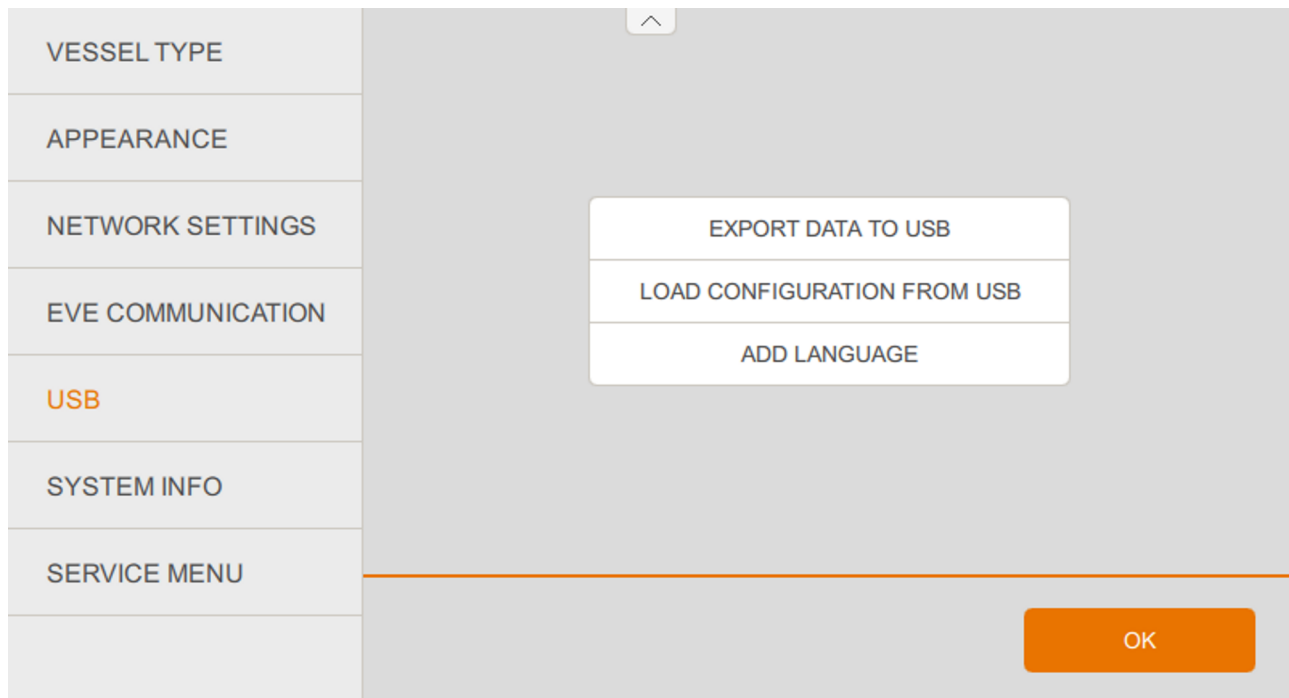
SERVER ACCESS

Determine whether the bioreactor is invisible (**Hidden**), only available for read access (**Read-Only**) or available for read and write access (**Read/Write**) in the OPC UA.

Operation

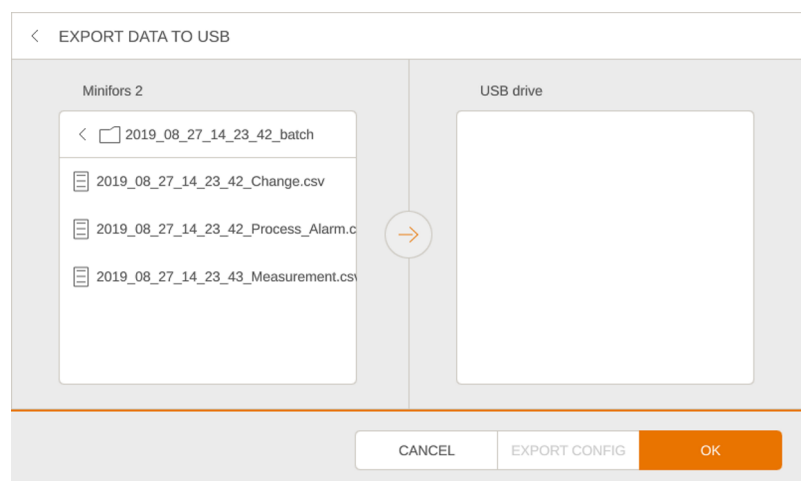
9.2.6 USB Data Export and Import from a USB Stick

In the *USB* menu, a USB stick connected with the device's USB port can be used to import or export data.



EXPORT DATA TO USB

Opens the menu for data export.



The selection menu in the left-hand screen section contains the files that can be moved across to the USB stick using the arrow button in the middle.

- **EXPORT CONFIG:** to export a backup of the current device configuration as zip file to the USB stick, which can be imported again by *LOAD CONFIGURATION FROM USB*.
- **CANCEL:** to cancel and leave the menu without changes.
- **OK:** to confirm data export and leave the menu.

Three files are created per batch and are ready for export. Each file name contains the start date and start time of the batch:

Time specification in file name

yyyy	=	Year
mm	=	Month
dd	=	Day
hh	=	Hours
ii	=	Minutes
ss	=	Seconds

The three files contain the following:

yyyy_mm_dd_hh_ii_ss_Change.csv

Log of the changes during the batch, e.g. manual input of setpoints, in CSV format. In combination with the initial state at batch start (**EXPORT CONFIG**) the current configuration can be determined at any time.

The columns of the CSV file are:

- DateTime: absolute date and time
- Parameter: parameter that was changed
- Property: property of the parameter that was changed
- NewValue: property of the newly allocated value
- OldValue: the old value of the property

Operation

yyyy_mm_dd_hh_ii_ss_Measurement.csv

Log of the actual values of all parameters during the batch in CSV format. The recording interval is 1 min. If higher precision is required, SCADA software, e.g. the bioprocess platform software eve®, can be connected via OPC UA and used for recording.

The columns of the CSV file are:

- DateTime: absolute date and time
- ProcessTime: relative time to batch start (batch time)
- <ParameterName>: actual value of the corresponding parameter

yyyy_mm_dd_hh_ii_ss_Process_Alarm.csv

Log of all alarms that occurred during the batch (e.g. deviations from the setpoints and actual values) and events (e.g. sampling) in CSV format.

The columns of the CSV file are:

- DateTime: absolute date and time
- AlarmType: type of alarm or event
- ProcessTime: relative time to batch start (batch time)
- EndAlarmTime: time at which the alarm state was resolved
- ConfirmedTime: time at which the alarm was confirmed on the operating panel

LOAD CONFIGURATION FROM USB

Opens the menu for importing a device configuration from the USB stick (see also **EXPORT CONFIG** in **EXPORT DATA**) including set-points, cascades and PID settings.

ADD LANGUAGE

A selection menu for data import appears. A language can be added or updated.

9.2.7 SYSTEM INFO – System Information

The *SYSTEM INFO* menu displays some important system information.

VESSEL TYPE	^ HMI SERIAL NUMBER GFMM01746640 VERSION 3.2.3.21 Cell Culture CONTROLLER VERSION iMC-Board Controller Version 2.04 MIF2 Jul 2 2019 OS VERSION Linux 4.1.15-rocko-2.0-6-g3f4f318644fe OPERATING HOURS 0d 21h 21min 38s MAC ADDRESS eth0: 00:07:8E:1A:A6:D0	
APPEARANCE		
NETWORK SETTINGS		
EVE COMMUNICATION		
USB		
SYSTEM INFO		
SERVICE MENU		
	LICENSE INFO	OK

- *HMI SERIAL NUMBER*: serial number of the operating panel
- *VERSION*: current firmware version & version of the device (for microorganisms or cell cultures)
- *CONTROLLER VERSION*: controller version
- *OS VERSION*: version of the operating system
- *OPERATING HOURS*: operating hours of the device since startup
- *MAC ADDRESS*: hardware address

LICENSE INFO

Pressing **LICENSE INFO** opens a menu with the licenses of all software libraries used.

Operation

9.3 Parameter – Parameter Groups

9.3.1 Overview

On the main screen, up to eight parameters can be simultaneously monitored and controlled. The parameters are divided into five parameter groups:

MINIFORS 2		14:06:45			
FAVORITES MAIN EXTENDED EXIT GAS PUMPS	PARAMETER	VALUE	SETPOINT		
	Temperature	10.0 °C	37.0 °C	☐	
	Stirrer	0 min ⁻¹	55 min ⁻¹	☐	
	pH	2.00	7.00	☐	
	pO ₂	0.0 %	21.0 %	☐	
Batch Time (since inoc.) 00:12:30 EDIT VIEW SAMPLE NOW STOP BATCH					

- **FAVORITES:** allows you to compile up to eight parameters from the other four parameter groups. This can be done using the **EDIT VIEW** button (→ Chapter 9.13 'EDIT VIEW' on page 130).
- **MAIN:** contains the *Temperature*, *Stirrer*, *pH*, *pO₂*, *Total Flow*, *GasMix* and *Foam* parameters.
- **EXTENDED:** contains the *Air Flow*, *Gas2Flow*¹⁾, *N₂ Flow*²⁾, *O₂ Flow*²⁾, *CO₂ Flow*²⁾, *Air Headspace*²⁾, *Analog IO1* and *Analog IO2* parameters as well as the optional parameters *Balance*, *Turbidity* and *Redox*, if available.
- **EXIT GAS:** contains the *Exit Gas O₂* and *Exit Gas CO₂* parameters, provided the exit gas analysis option is available.
- **PUMPS:** contains the *Pump1* to *Pump4* parameters and also offers the *FILL* and *EMPTY* functions.

¹⁾ Version for microorganisms only

²⁾ Version for cell cultures only

9.3.2 Parameters – Displays and Functions

Columns

Irrespective of the selected parameter group, every parameter menu has the same three columns.

FAVORITES	PARAMETER	VALUE	SETPOINT	
MAIN	Temperature	10.0 °C	37.0 °C	☐  
	Stirrer	0 min ⁻¹	55 min ⁻¹	☐ 
EXTENDED	pH	2.00	7.00	☐   
EXIT GAS	pO ₂	0.0 %	21.0 %	☐   
PUMPS	TotalFlow	0.000 L min ⁻¹	0.000 L min ⁻¹	☐ 
	GasMix	NaN %O ₂	21 %O ₂	☐  
	Foam	0		☐  

- *PARAMETER*: display of the parameter
- *VALUE*: display of the actual value of the parameter
- *SETPOINT*: entry of the max. setpoint of the parameter

If the right-hand display is shown, further functions are available depending on the selected parameter group and parameter.

ON/OFF



Switches control of the selected parameter on or off.



ON/OFF is only available when a batch is running. First start the batch with **START BATCH** and, if necessary **INOCULATE**.

Calibrating



Opens the calibration menu of the selected parameter.



The "calibration" function is only available for the parameters *pH*, *pO₂* and *Turbidity* (variant ASD12-N).

Operation

Editing



Opens the editor menu with the various settings for the selected parameter. Not all parameters have an editor menu.

E.g. cascades can be set here, PID settings can be adjusted, parameter alarms can be switched on or off or the pump functions can be selected.

The settings are described along with the corresponding parameter in the later parameter chapters.

Information



Opens a dialogue box containing basic information on the selected parameter.



Display of the info button is switched on or off in the *APPEARANCE* menu for system settings.

9.3.3 SETPOINT – Setting the Setpoint

Setting the Setpoint

The setpoints can be entered in any operating state of the device for parameters that are not controlled via cascade and have a controller output. Parameter control is however only active when a batch has been started using **START BATCH** and the corresponding parameter has been activated using **ON/OFF**.

PARAMETER	VALUE	SETPOINT
Temperature	10.0 °C	37.0 °C
Stirrer	0 min ⁻¹	55 min ⁻¹
pH	2.00	7.00
pO ₂	0.0 %	21.0 %
TotalFlow	0.000 L min ⁻¹	0.000 L min ⁻¹
GasMix	NaN %O ₂	21 %O ₂
Foam	0	

SETPOINT STIRRER

50 min⁻¹ ☐

DELETE

1	2	3
4	5	6
7	8	9
ABC	0	.

CANCEL

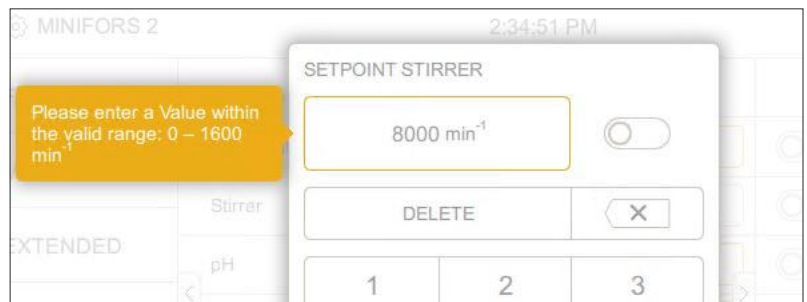
After pressing the input field in the *SETPOINT* column of the desired parameter, the key pad appears for typing in the setpoint and, if necessary, for activating the parameter (using **ON/OFF**).

- **OK** confirms the input, the key pad disappears.
- **CANCEL** makes the key pad disappear without making any changes.

Inadmissible Setpoints

If an inadmissible setpoint is entered, an error message is generated that prompts a correct entry within the permissible parameter setpoints.

Example (version for microorganisms): The *Stirrer* setpoint entry is too high. Make a new entry within the permissible values of 0 to 1600 min⁻¹.



9.3.4 Parameter Alarms

Alarm Displays

If a parameter is activated and the batch inoculated, parameter alarms are generated after a predefined waiting time if there are unexpected deviations from the actual values and setpoints. Parameter alarms are additionally signalled by the green blinking light of the LED status indicator on the basic unit.

Parameter alarms are displayed as follows:

FAVORITES 1		PARAMETER	VALUE	SETPOINT
MAIN 1		Temperature	32.2 °C	37.0 °C
		Stirrer	24 min ⁻¹	24 min ⁻¹
EXTENDED		pH	7.00	7.00
EXIT GAS		pO ₂	100.0 %	100.0 %
PUMPS		TotalFlow ← pO ₂	8.00 L min ⁻¹	8.00 L min ⁻¹
		GasMix	NaN %O ₂	21 %O ₂
		Foam	0	

Batch Time (since inoc.)

00:03:18

EDIT VIEW

SAMPLE NOW

Operation

- In the parameter group that contains the parameters in question, a number on a red background appears. This indicates the number of existing parameter alarms.
- The parameter in question is displayed with a red bar and an actual value in red.
- A red exclamation mark highlighted in white on a red background appears in the footer.

Pressing the symbol or swiping upwards opens the *Equipment Alarm* menu (➔ Chapter 9.10 'Alarms – Equipment Alarm Menu' on page 184).

Parameter alarms are also logged in the batch log file (➔ Chapter 9.2.6 'USB Data Export and Import from a USB Stick' on page 140).

Parameter Alarm pH and pO₂

If necessary, the triggering of parameter alarms can be suppressed for the two parameters *pH* and *pO₂*. This means that the function can be switched on and off in the editor menu of the corresponding parameter. For all other parameters, this function is always activated ex-factory and is neither visible for nor editable by the operator.

EDIT pH

ALARM OFF ☒ ON

Example to the left: Editor menu of parameter *pH* with function switched on.

Parameter Alarm Limit Factory Settings

Parameter	Alarm limit	
	Value	Unit
Temperature	2	°C
Stirrer ¹⁾	50	min ⁻¹
Stirrer ²⁾	15	min ⁻¹
pH	0,5	pH
pO ₂	10	%
Total Flow ¹⁾	0,3	L min ⁻¹
Total Flow ²⁾	10	mL min ⁻¹
GasMix	10	%
Air Flow	0,3	L min ⁻¹
Gas2 Flow ¹⁾	0,3	L min ⁻¹

Parameter	Alarm limit	
	Value	Unit
N ₂ Flow ²⁾	10	mL min ⁻¹
O ₂ Flow ²⁾	10	mL min ⁻¹
CO ₂ Flow ²⁾	10	mL min ⁻¹
Air Headspace ²⁾	10	mL min ⁻¹

¹⁾ Version for microorganisms

²⁾ Version for cell cultures

9.3.5 Cascades

Cascades can be configured for some parameters. A cascade can be used to assign a parameter to another parameter as an actuator.

Example: For control of the pO_2 by changing the *Gasmix* parameter, a cascade to the *Gasmix* parameter is configured for the pO_2 . If the pO_2 actual value is below the prescribed setpoint, the *Gasmix* is increased by the controller until the desired setpoint is reached for the pO_2 .

Display

Parameters that are used in a cascade are identified in the main menu with an arrow and the name of the controlling parameter, and manual setpoint entry is deactivated.

FAVORITES	PARAMETER	VALUE	SETPOINT
MAIN	Temperature	11.9 °C	37 °C
	Stirrer ← pO ₂	3 min ⁻¹	60 min ⁻¹
EXTENDED	pH	6.99	7
EXIT GAS	pO ₂	19.1 %	21 %
PUMPS	TotalFlow	0.000 L min ⁻¹	0.000 L min ⁻¹
	GasMix	NaN %O ₂	21 %O ₂
	Foam	0	

Example: *Stirrer* is used in a cascade for pO_2 control. It is not possible to enter a setpoint for *Stirrer*.

Operation

Configuration

The cascades can be configured using the editor menu of the parameter. The procedure is described in the parameter description for the parameters for which this is possible.

9.4 MAIN Parameter Group

The *MAIN* parameter group contains all parameters that are available by default, as well as the two parameters *GasMix* and *TotalFlow* for flow control of the individual gasses.

9.4.1 Temperature

Measures and controls the temperature in the culture vessel. The temperature controller is optimised by default for a minimum overshoot during adjustment (setting *Default*).

Settings (only Version for Microorganisms)

Alternatively to the default setting *Default*, the controller can be set *Aggressive* so that temperature changes occur more quickly, but the setpoint can be exceeded for a short time during adjustment. The controller can be switched in the editor menu of the parameter.

EDIT Temperature

CONTROL

Default Aggressive

CANCEL OK

The only menu item *CONTROL* contains the two options mentioned above.

9.4.2 Stirrer

Measures and controls the speed of the stirrer. Rotation speed depends on factors such as the size of the motor, vessel volume, culture viscosity, number and kind of impellers etc.

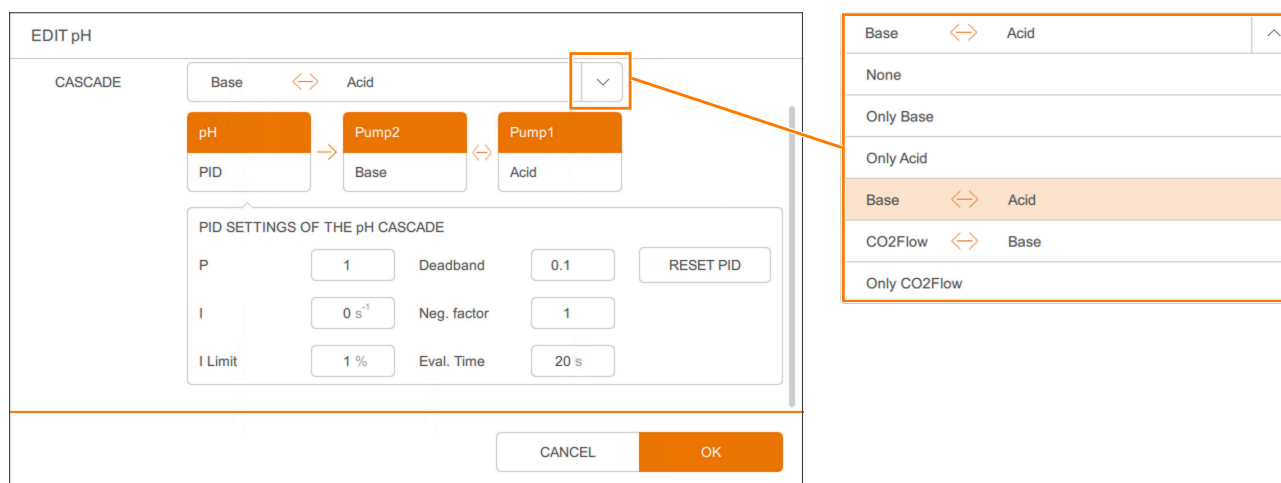
Stirring speed is often used in a cascade for pO_2 control. Cascades for pO_2 control can be configured in the editor menu of the pO_2 parameter.

9.4.3 pH

Measures and controls the pH in the culture vessel. The pH control can be configured using a cascade and takes place by default by adding acid and base via the two peristaltic pumps *Pump1/Acid* and *Pump2/Base*. For details on the pumps, see Chapter 9.7.1 'PUMPS Parameter Group' on page 164.

Settings

The settings for the cascade are made in the editor menu of the parameter.



At the *CASCADE* menu item, the drop-down list is used to call up the pre-defined cascades for pH control. The figure above shows the drop-down list of the version for cell cultures.

The following settings are available for selection:

- *None*: no control, pH is only measured
- *Only Base*: pH control takes place by adding base from *Pump2*.
- *Only Acid*: pH control takes place by adding acid from *Pump1*.
- *Base – Acid*: default setting, pH control takes place by adding base and acid.

Operation

Additional choice for version for cell cultures:

- *CO₂ Flow – Base*: pH control takes place by adding base and CO₂ (instead of liquid acid).
- *Only CO₂ Flow*: pH control only takes place by adding CO₂ (instead of liquid acid).

The selected setting is represented visually. In the following example, the standard setting with control via the acid and base pumps is shown.

The PID menu is activated.

The screenshot shows the 'EDIT pH' menu. At the top, there is a 'CASCADE' section with a dropdown menu set to 'Base' and 'Acid'. Below this, a diagram shows 'pH' connected to 'Pump2' (Base) and 'Pump1' (Acid). The 'PID SETTINGS OF THE pH CASCADE' section is highlighted with an orange box. It contains the following settings:

Parameter	Value	Parameter	Value
P	1	Deadband	0.1
I	0 s ⁻¹	Neg. factor	1
I Limit	1 %	Eval. Time	20 s

There is a 'RESET PID' button next to the 'Deadband' field. At the bottom of the menu are 'CANCEL' and 'OK' buttons.

The PID settings can be adjusted here as required or, if necessary, can be reset to factory settings using **RESET PID** (→ Chapter 9.9 'PID Controller – Basic Principle' on page 182).

After setting the desired cascade, entries are confirmed using **OK**.

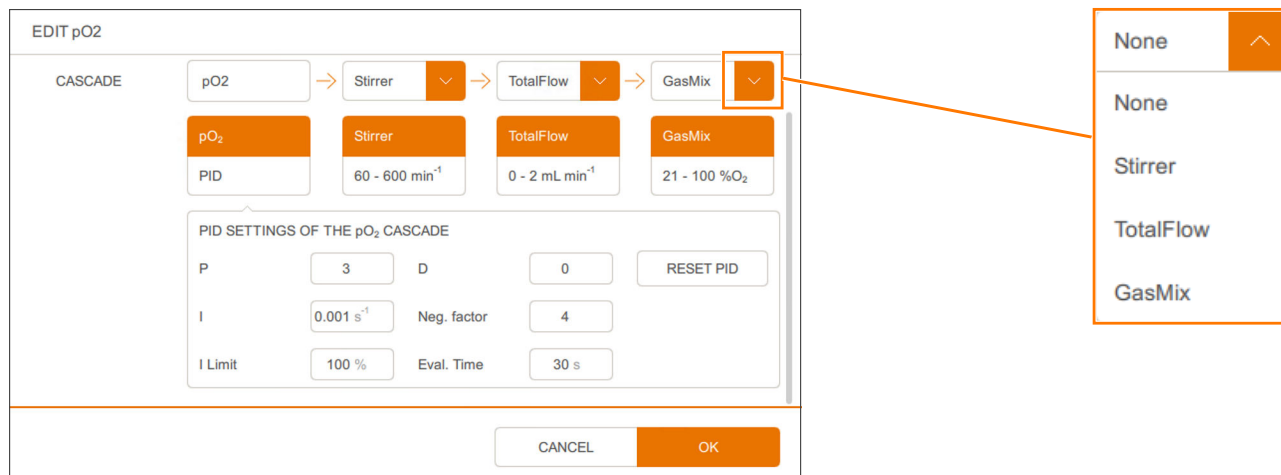
9.4.4 pO₂

Measures the dissolved oxygen in the culture. Unlike measurements such as pH, which are calibrated to absolute measurement values, the oxygen measurement is always calibrated to a relative reference point. For this purpose, the calibration is set to 100 % relative oxygen saturation, usually with air at max. stirring speed and maximum gas flow rate. The absolute concentration of dissolved oxygen in mmol L⁻¹ may therefore vary at 100 % saturation, depending on the process.

Since the pO₂ value cannot be directly influenced by the bioreactor, actuators must be assigned to the PID controller of the pO₂ parameter. This takes place using cascades with other parameters, such as *Stirrer* (stirrer speed), *Total Flow* (gas flow) or *GasMix* (gas mixture).

Settings

The settings for the cascade are made in the editor menu of the parameter.



EDIT pO2

CASCADE

pO2 → Stirrer → TotalFlow → GasMix

pO2 Stirrer TotalFlow GasMix

PID PID PID PID

60 - 600 min⁻¹ 0 - 2 mL min⁻¹ 21 - 100 %O₂

PID SETTINGS OF THE pO₂ CASCADE

P 3 D 0 RESET PID

I 0.001 s⁻¹ Neg. factor 4

I Limit 100 % Eval. Time 30 s

CANCEL OK

None

None

Stirrer

TotalFlow

GasMix

At the *CASCADE* menu item three drop-down lists are available. They contain all the parameters available for configuring a serial cascade of up to 3 stages for pO₂ control.

The following settings are available for selection:

- *None*: no control, pO₂ is only measured
- *Stirrer*: pO₂ is controlled using *Stirrer*
- *Total Flow*: pO₂ is controlled using *Total Flow*
- *GasMix*: pO₂ is controlled using *GasMix*



GasMix is only available if more than one gas is used and this is set accordingly in the editor menu of the *GasMix* parameter.

Serial cascades:

- *Stirrer – Total Flow*: pO₂ is first controlled by *Stirrer* and, after reaching its maximum, it is controlled by *Total Flow*.
- *Stirrer – GasMix*: pO₂ is first controlled by *Stirrer* and, after reaching its maximum, it is controlled by *GasMix*.
- *Stirrer – Total Flow – GasMix*: pO₂ is first controlled by *Stirrer* and, after reaching its maximum, it is controlled by *Total Flow* and, after reaching its maximum, it is controlled by *GasMix*.



Changing the cascade(s) and restricting/expanding the ranges requires setting/checking the PID values.

Operation

The selected setting is represented visually. The following example shows the setting with control using *Stirrer* (stirrer speed).

The screenshot shows the 'EDIT pO2' window. Under the 'CASCADE' section, a sequence of controls is shown: pO2 → Stirrer → TotalFlow → GasMix. Below this, a table lists the parameters for each control:

Control	Parameter	Value
pO ₂	PID	
Stirrer	PID	60 - 600 min ⁻¹
TotalFlow	PID	0 - 2 mL min ⁻¹
GasMix	PID	21 - 100 %O ₂

Below the table, the 'PID SETTINGS OF THE pO₂ CASCADE' are displayed:

P	3	D	0	RESET PID
I	0.001 s ⁻¹	Neg. factor	4	
I Limit	100 %	Eval. Time	30 s	

At the bottom, there are 'CANCEL' and 'OK' buttons.

The PID settings can be adjusted here as required or, if necessary, can be reset to factory settings using **RESET PID** (→ Chapter 9.9 'PID Controller – Basic Principle' on page 182).

If necessary, the value ranges used for the cascaded parameter(s) can be adjusted here. In the following example the cascaded parameter *Stirrer* is selected for this purpose in the visual representation, and the input fields for *Minimum* and *Maximum* become visible.

The screenshot shows the 'EDIT pO2' window with the cascade control setup. The 'Stirrer' parameter is selected, and its range is being adjusted. The 'Range Stirrer' section is expanded, showing the following fields:

Minimum	60 min ⁻¹
Maximum	600 min ⁻¹

At the bottom, there are 'CANCEL' and 'OK' buttons.

After pressing an input field, the key pad appears for typing in the value.

After setting the desired cascade, entries are confirmed using **OK**.

9.4.5 Total Flow

Measures and controls the sum of the volume flows of air (*Air Flow*) and one or two connected gas(es):

- Version for microorganisms: gassing with a second gas (oxygen OR nitrogen) possible, parameter *Gas2 Flow*.
- Version for cell cultures: gassing with two gases (oxygen AND nitrogen) possible, parameters *O₂ Flow* and *N₂ Flow*.

The mixing ratio of air with one or two connected gas(es) is controlled by the *GasMix* parameter. The controller calculates the setpoints for *Air Flow* and the additional flow parameter(s) on the basis of the setpoints for *Total Flow* and *Gasmix*. This allows, for example, the volume flows to be kept constant in the event of a changed gas composition, or the gas composition to be kept constant in the event of a changing volume flow. The measurement value is displayed in L min⁻¹ (version for microorganisms) or in mL min⁻¹ (version for cell cultures).

The sum of the volume flows, *Total Flow*, is often used in a cascade for pO₂ control. Cascades for pO₂ control can be configured in the editor menu of the *pO₂* parameter.

9.4.6 GasMix

Controls the oxygen concentration in the inlet air. This is done by mixing air and oxygen (O₂) or air and nitrogen (N₂). For the version for cell cultures, the 3-gas mixing system of air, nitrogen and oxygen is also available

Settings

The configuration is made in the editor menu of the parameter, see next figure, example of version for cell cultures.

EDIT GasMix

FEATURE

Only Air Air/O₂ Air/N₂ Air/N₂/O₂

CANCEL OK

Operation

The only menu item available here, *FEATURE*, has the following options:

- *Only Air*: air is exclusively used, with no addition of a second gas. The gas mixture always contains 21 % oxygen. The *Total Flow* corresponds to *Air Flow*. Parameter *GasMix* is not available for use in the pO₂ cascade.
- *Air/O₂*: the setpoint can be varied between 21 % (only air) and 100 % (only O₂). *Total Flow* therefore remains constant, the ratio of *Air Flow* and *Gas2 Flow*¹⁾ or *O₂ Flow*²⁾ is adjusted automatically on the basis of the setpoint of *GasMix*.
- *Air/N₂*: the setpoint can be varied between 0 % (only N₂) and 21 % (only air). *Total Flow* therefore remains constant, the ratio of *Air Flow* and *Gas2 Flow*¹⁾ or *N₂ Flow*²⁾ is adjusted automatically on the basis of the setpoint of *GasMix*.
- **Version for cell cultures only:** *Air/N₂/O₂*: the setpoint can be varied between 0 % (only N₂), 21 % (only air) and 100 % (only O₂). *Total Flow* therefore remains constant, the ratio of *Air Flow* and *O₂ Flow* and *N₂ Flow* is adjusted automatically on the basis of the setpoint of *GasMix*.

¹⁾ *Version for microorganisms*

²⁾ *Version for cell cultures*



The oxygen content of air is 20.95 %. The device works with the rounded value 21 % for easier display.



The 3-gas mixing system always requires air and cannot be used to mix nitrogen and oxygen. Set *GasMix* to *Only Air* and control *N₂ Flow* and *O₂ Flow* individually in the parameter group *EXTENDED*.

After selecting the desired option, entry is confirmed using **OK**.

The gas composition *GasMix* is often used in a cascade for pO₂ control. Cascades for pO₂ control can be configured in the editor menu of the pO₂ parameter.

9.4.7 Foam

In the standard setting, measures foam formation (*Antifoam* feature) and controls the addition of antifoam agent from *Pump3*. The antifoam pump is activated as soon as the antifoam sensor comes into contact with foam.

Alternatively, the antifoam sensor can be configured as a level sensor so that *Pump3* pumps medium/liquid into the culture vessel until the desired fill level has been reached, respectively the sensor detects liquid.



The direction of rotation of the pump cannot be changed. If, however, culture medium is to be pumped out of the culture vessel as soon as the sensor detects liquid, this can be done by selecting the feature *Antifoam* and reverse connection of the pump hoses. This allows, for example, the filling level in the culture vessel to be kept constant.

Note that when switching to "normal" function mode of the feature *Antifoam*, the pump hoses must be connected to *Pump3* as usual again!

Settings

Selection of the foam sensor functions, as well as other possible settings, takes place in the editor menu of the parameter.

EDIT Foam	
FEATURE	None Level Antifoam

The *FEATURE* item has the following three options:

- *None*: no control, foam/liquid is only detected
- *Level*: addition of culture medium (filling of the culture vessel) until sensor detects liquid
- *Antifoam*: addition of antifoam agent as soon as sensor detects foam

If the *Level* or *Antifoam* feature is selected, additional parameter settings are possible:

Operation

- *DOSE TIME*: duration (in seconds) of the addition of antifoam agent, respectively culture medium by *Pump3*
- *WAIT TIME*
 - Feature *Antifoam*: duration (in seconds) after the addition of antifoam agent to reduce foam before more antifoam agent is added.
 - Funktion *Level*: no waiting time is needed here, duration can be set to 0 (zero).
- *ALARM TIME*
 - Feature *Antifoam*: time (in seconds) after which a parameter alarm is triggered if foam is still detected despite the addition of antifoam agent.
 - Feature *Level*: time must be set to 0 (zero).

After pressing an input field, the key pad appears for typing in the value. All entries are confirmed with **OK**.

9.5 EXTENDED Parameter Group

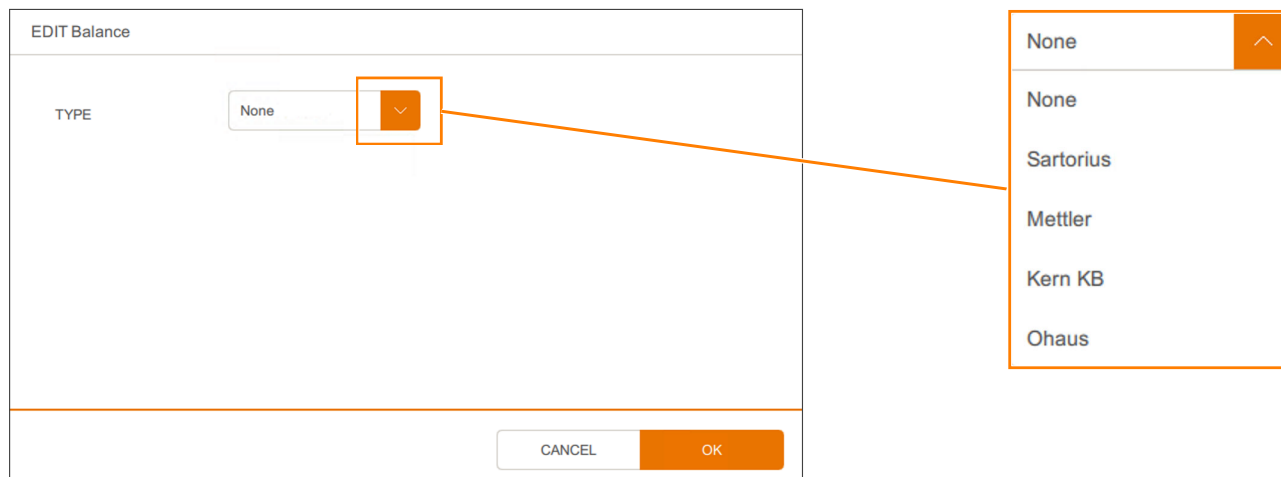
The *EXTENDED* parameter group contains all existing (Gas) *Flow* parameters, two parameters for analogue inputs/outputs and the optional parameters for weight measurement (*Balance*), turbidity (*Turbidity*) and the reduction/oxidation potential (*Redox*), if the respective option is connected.

9.5.1 Balance (Optional)

Measures a weight, e.g. a bottle with nutrient solution. Can be coupled with *Pump4* (feed) to carry out gravimetric feeding (➔ Chapter 9.7.6 'Pump4' on page 168).

Settings

The balance type can be configured in the editor menu of the parameter.



The *TYPE* menu item contains the drop-down list for selection of the balance manufacturers.



Balances must be configured with the following values: Baudrate 9600, 8 bits, no parity, 2 stop bits.

For a list of compatible balances or help with the connection, please contact your local INFORS HT service partner.

9.5.2 Flow Parameters

All *Flow* parameters measure and control the volume flow of the corresponding gas into the culture vessel via a mass flow controller (thermal mass meter with control valve). The measurement system is completely electronic and the measured value is displayed in L min⁻¹ (version for microorganisms) or mL min⁻¹ (version for cell cultures).

Depending on the device version, the following flow parameters are present by default:

- Version for microorganisms: *Air Flow* (air) und *Gas2 Flow* (for oxygen OR nitrogen).
- Version for cell cultures: *Air Flow* (air), *O₂ Flow* (oxygen), *N₂ Flow* (nitrogen), *Air Headspace* (air headspace) and *CO₂ Flow* (carbon dioxide).

The maximum gassing rate is determined by the vessel size used in the *VESSEL TYPE* menu. For values see ➔ Chapter 13.4.5 'Gassing System' on page 223.

Operation

Air Flow

Regardless of the existing device version and configuration of the gassing system, the setpoint for the air volume flow is ALWAYS set in the *TotalFlow* parameter. A setpoint can NEVER be set in the *Air Flow* parameter, as the oxygen concentration is ALWAYS controlled by the *GasMix* parameter, even if only air is used. For details about *TotalFlow* and *GasMix*, see the corresponding chapters in ➔ Chapter 9.4 'MAIN Parameter Group' on page 150.

O₂ Flow / N₂ Flow

Depending on which configuration is selected in the *GasMix* parameter, setpoints for the volume flow of oxygen and/or nitrogen can be set individually.

Air Headspace

The setpoint settings of the air volume flow for headspace gassing with air is independent of the parameters *GasMix* and *TotalFlow*.

CO₂ Flow

CO₂ can be used via parameter *CO₂ Flow* instead of liquid acid via the acid pump for pH control. Addition of CO₂ is either possible via sparger or headspace. The *CO₂ Flow* parameter can also be used separately from the pH control. In both cases, however, it is independent of the *GasMix* and *TotalFlow* parameters.

The settings are made in the editor menu of the parameter.

EDIT CO ₂ Flow	
OUTLET	Sparger Headspace
FEATURE	pH Manual
CANCEL OK	

The two menu items *OUTLET* and *FEATURE* have the following options:

- *Sparger / Headspace*: to select gas entry via sparger or headspace. Sparger gassing is set ex-factory.
- *pH / Manual*: to use CO₂ either for pH control (*pH*) or as individual gas flow parameter (*Manual*).

If the parameter is configured for pH control, it is automatically accepted in the pH parameter as an actuator in a cascade. In this case, the setpoint value can no longer be edited in the parameter. If it is used as a normal gassing parameter, the setpoint can be set as usual.

9.5.3 Turbidity (Optional)

This is used to determine the turbidity of the culture. The turbidity can be used to draw conclusions regarding the biomass concentration in the culture. The measurement range and the measurand of the parameter differ depending on the installed measurement system (→ Chapter 13.5.1 'Turbidity Measurement' on page 227).

9.5.4 Redox (Optional)

Measures the reduction/oxidation potential in the medium in mV (→ Chapter 13.5.3 'Redox Measurement' on page 228).

9.5.5 Analog IO1 & Analog IO2

These two parameters represent two analogue 4 – 20 mA inputs/outputs and are available for the connection of two external devices. Both parameters are calibrated and scaled to a range of 0 to 100 %



If external values are to be converted, this must be done via eve®, the platform software for bioprocesses.

Settings

In the editor menu can be set, whether the external device displays measured values only, e.g. a sensor, or whether setpoints can also be entered, e.g. for a pump.

Operation

EDIT Analog IO1

DEVICE

NONEPUMPCUSTOM

MODE

IN/OUTIN ONLY

CANCEL

OK

The two menu items *DEVICE* and *MODE* offer the following options:

- *DEVICE*: Setting the type of parameter, choice between *NONE*, *PUMP* or *CUSTOM* (customized)



Settings here are only relevant, if working with eve®, the platform software for bioprocesses.

- *MODE*: mode selection, choice between *IN/OUT* (with setpoint entry and display of actual value, e.g. pump) or *IN ONLY* (measured only, display of actual value, e.g. sensor)

9.6 EXIT GAS Parameter Group

The *EXIT GAS* parameter group contains the parameters for the optional exit gas analysis (➔ Chapter 13.5.2 'Exit Gas Analysis' on page 228).

Details on technical data, usage and maintenance requirements for the gas sensors can be found in separate documentation provided by the manufacturer.

9.6.1 Exit Gas O₂

Measures the oxygen concentration in Vol.% O₂ in the exit gas of the bioreactor using a combined gas sensor from the manufacturer BlueSens. The measurement range can vary depending on the installed measurement system and sensor type (➔ Chapter 13.5.2 'Exit Gas Analysis' on page 228).

9.6.2 Exit Gas CO₂

Measures the carbon dioxide concentration in Vol.% CO₂ in the exit gas of the bioreactor using a combined gas sensor from the manufacturer BlueSens. The measurement range can vary depending on the installed measurement system and sensor type (➔ Chapter 13.5.2 'Exit Gas Analysis' on page 228).

Operation

9.7 PUMPS Parameter Group

9.7.1 Overview

FAVORITES	PARAMETER	VALUE	SETPOINT	FILL	EMPTY
MAIN	Pump1	0 ~ml	0 %	FILL	EMPTY
EXTENDED	Pump2 ← pH	0.0 ~ml	0.0 %	FILL	EMPTY
EXIT GAS	Pump3	0.0 ~ml	0.0 %	FILL	EMPTY
	Pump4	0.0 ~ml	0.0 %	FILL	EMPTY
PUMPS	OPEN AUTO FILL/EMPTY				

In the *PUMPS* parameter group, the delivery rate of the pumps can be set or monitored and the function mode of the pumps can be configured.

In addition, the pump hoses can be manually filled or emptied by pressing and holding **FILL** or **EMPTY**. By pressing **AUTO FILL/EMPTY**, the submenu opens with the option to set a time control for the filling and emptying of every pump.

For details on automatic filling/emptying, see ➔ Chapter 9.7.7 'AUTO FILL/EMPTY – Automatically Filling/Emptying Pump Hoses' on page 169.

Function Modes

Depending on the function mode, the pumps run in analogue (continuous) operation with variable speed, or digital operation with fixed speed.

Example:

- Analogue: 50 % = half speed = half delivery capacity
- Digital: 50 % = 100 % speed, but only active 50 % of the time = half delivery rate

In digital operation, pumping is used as an actuator for other parameters such as pH or Foam and receive their setpoint from the corresponding controller. This means that it is not possible to enter a setpoint. When pumping in analogue operation, setpoints can be specified in % of pump capacity.

The totalled actual value of a pump is displayed, depending on the configuration, in the number of rotations or as an estimated volume in mL or for *Pump4* as a weight in grams in the *VALUE* column on the main screen.

Default Settings

The pumps are configured as follows ex-factory:

Pump	Version for microorganisms	Version for cell cultures
<i>Pump1</i>	<i>Acid</i> ■ addition of acid, digital ■ controlled by the <i>pH</i> parameter	<i>Feed</i> ■ addition of nutrient solution, analogue ■ controlled by the user
<i>Pump2</i>	<i>Base</i> ■ addition of base, digital ■ controlled by the <i>pH</i> parameter	<i>Base</i> ■ addition of base, digital ■ controlled by the <i>pH</i> parameter
<i>Pump3</i>	<i>Antifoam</i> ■ addition of antifoaming agent, digital ■ controlled by the <i>Foam</i> parameter	<i>Feed</i> ■ addition of nutrient solution, analogue ■ controlled by the user
<i>Pump4</i>	<i>Feed</i> ■ addition of feed solution, analogue ■ controlled by the user	<i>Feed</i> ■ addition of nutrient solution, analogue ■ controlled by the user

9.7.2 Configuring the Pumps

The editor menu of every pump has four menu items for configuration. The figure below shows the editor menu of *Pump 1* as an example.

EDIT Pump1

TUBE TYPE

Ø 0.5 mm

Ø 1.0 mm

Ø 2.5 mm

FEATURE

Acid

Feed

DISPLAY COUNT UNIT

Count

~ml

VALUE

0 ~ml

RESET COUNT

CANCEL

OK

Operation

TUBE TYPE

Ø 0.5 mm	Ø 1.0 mm	Ø 2.5 mm
----------	----------	----------

To select the pump hose used.

The following pump hoses are available: 0.5 mm, 1.0 mm (standard) or 2.5 mm. On the basis of the selected hose diameter, the pumped volume can be estimated and used for the display of the totalled actual value (selection under *DISPLAY COUNT UNIT*).



An incorrectly set hose diameter results in an incorrectly totalled actual value.

FEATURE

Acid	Feed
------	------

To configure the pump function operating mode.

Since the four pumps have different functions, they are described in the following chapters.

DISPLAY COUNT UNIT

Count	~mL
-------	-----

To configure the display of the totalled actual value.

Either *Count* (number of rotations of the pump head) or *~mL* (the pumped volume estimated on the basis of the hose diameter selected under *TUBE TYPE*) can be selected.



If a balance (*Balance*) is connected and linked with *Pump4, g* (measured pumped weight) is also available at *Pump4*.

VALUE

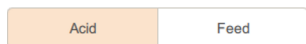
0.0

RESET COUNT

Displays the totalled actual value and to reset the counter.

The totalled actual value of the pump is displayed here and can be reset to 0 by pressing *RESET COUNT*.

9.7.3 Pump1



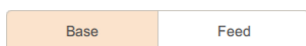
Pump1 can be configured for the *Acid* function or *Feed*.

- *Acid*: digital operating mode, is used in pH control to add acid.
- *Feed*: analogue (continuous) operating mode, can be used for addition of another nutrient solution, for example.



The function of *Pump1* can also be changed by making corresponding entries in the editor menu of the *pH* parameter.

9.7.4 Pump2



Pump2 can be configured for the *Base* function or *Feed*.

- *Base*: digital operation mode, is used in pH control to add base.
- *Feed*: analogue (continuous) operation mode, can be used for addition of another nutrient solution, for example.



The function of *Pump2* can also be changed by making corresponding entries in the editor menu of the *pH* parameter.

9.7.5 Pump3



Pump3 can be configured for the *AntiFoam* function, *Level* or *Feed*.

- *Antifoam*: digital operating mode, is controlled by the foam sensor (*Foam*) and used to add antifoaming agent.
- *Level*: digital operating mode, is controlled by the foam sensor (*Foam*), which is used as a level sensor, and is used to fill culture medium into the vessel.
- *Feed*: analogue (continuous) operating mode, can be used for addition of another nutrient solution, for example.

Operation



The direction of rotation of the pump cannot be changed. If, however, culture medium is to be pumped out of the culture vessel as soon as the sensor detects liquid, this can be done by selecting the feature *Antifoam* and reverse connection of the pump hoses. This allows, for example, the filling level in the culture vessel to be kept constant.

Note that when switching to "normal" function mode of the feature *Antifoam*, the pump hoses must be connected to *Pump3* as usual again!



The function of *Pump3* can also be changed by making corresponding entries in the editor menu of the *Foam* parameter.

9.7.6 Pump4

Pump4 can be configured for the *Feed* function or, provided an optional balance is connected and the *Balance* parameter is available, it can be configured for *Balance Feed* or *Dose*.

Feed Balance Feed Dose		
PARAMETER	VALUE	SETPOINT
Pump1 ← pH	0.0	0.0 %
Pump2 ← pH	0.0	0.0 %
Pump3 ← Foam	0.0	11.1 %
Pump4	0.0 g	100.0 %

- *Feed*: analogue (continuous) operating mode, is used for the addition of nutrient solution.

The setpoint value is entered in % of pump capacity.

Feed Balance Feed Dose		
PARAMETER	VALUE	SETPOINT
Pump1 ← pH	0.0	0.0 %
Pump2 ← pH	0.0	0.0 %
Pump3 ← Foam	0.0	11.1 %
Pump4	0.0 g	100.0 g h ⁻¹

- *Balance Feed*: analogue (continuous) operating mode, is used for the addition of nutrient solution. The delivery rate is controlled on the basis of the signal of the balance on which the bottle with nutrient solution is positioned (*Balance* parameter) to guarantee precise dosing.

The setpoint value is entered in g/h.

Feed	Balance Feed	Dose
------	--------------	------

PARAMETER	VALUE	SETPOINT
Pump1 ← pH	0.0	0.0 %
Pump2 ← pH	0.0	0.0 %
Pump3 ← Foam	0.0	11.1 %
Pump4	0.0 g	START DOSE

- *Dose*: analogue (continuous) operating mode, is used for the addition of a defined weight of nutrient solution.

The desired feed rate in grams is entered by pressing **START DOSE**.

The key pad appears for typing in the desired dosing weight.

PARAMETER	VALUE	SETPOINT
Pump1 ← pH	0.0	0.0 %
Pump2 ← pH	0.0	0.0 %
Pump3 ← Foam	0.0	11.1 %
Pump4	0.0 g	STOP DOSE

As soon as the dosing process starts, **STOP DOSE** is available. By pressing **STOP DOSE**, the dosing process can be stopped at any time, and by pressing **START DOSE** again, the dosing process can be resumed in the same way.

After the defined amount of nutrient solution has been added, a new dosing process can be started with a new setpoint value.



For the *Balance Feed* and *Dose* functions, the additional input fields for adjusting the parameters of the PID controller are available in the editor menu of *Pump4* (→ Chapter 9.9 'PID Controller – Basic Principle' on page 182).

9.7.7 AUTO FILL/EMPTY – Automatically Filling/Emptying Pump Hoses

Pressing **OPEN AUTO FILL/EMPTY** in the pump menu, opens the submenu for automatic filling and emptying of the pump hoses.

Operation

^

PARAMETER	VALUE	SETPOINT	FILL	EMPTY
Pump1	0 ~ml	0 %	FILL	EMPTY
Pump2 ← pH	0.0 ~ml	0.0 %	FILL	EMPTY
Pump3	0.0 ~ml	0.0 %	FILL	EMPTY
Pump4	0.0 ~ml	0.0 %	FILL	EMPTY

OPEN AUTO FILL/EMPTY

Auto fill/empty

Parameter	Filling duration		Emptying duration	
Pump1	20 s	FILL	20 s	EMPTY
Pump2	20 s	FILL	20 s	EMPTY
Pump3	20 s	FILL	20 s	EMPTY
Pump4	20 s	FILL	20 s	EMPTY

CANCEL

OK

For each pump, an individual filling duration as well as an individual emptying duration can be defined. Pressing **FILL** or **EMPTY** starts the filling or emptying procedure for the corresponding pump and the pump hose is filled or emptied for the set filling or emptying duration.

Filling duration	
16 s	STOP
16 s	STOP
20 s	FILL
17 s	STOP

If a filling or emptying procedure is active, the remaining filling or emptying time is displayed. The filling or emptying process can be stopped at any time by pressing **STOP**. Pressing **FILL** or **EMPTY** again will restart the process.

The menu cannot be closed while at least one filling or emptying procedure is active. The menu can be closed using **OK** as soon as all filling or emptying procedures are completed.

9.8 Calibrating the Sensors

Sensors for measuring the pH, pO₂ and turbidity (ASD12-N) are usually calibrated before each cultivation.

Depending on the sensor and measurement system, either a 2-point calibration should be used, or a 1-point calibration and a zero point adjustment is sufficient.



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

9.8.1 Calibrating the pH Sensor

General Information

pH sensors must be calibrated before autoclaving, i.e. before installing in the culture vessel.



If the pH sensor has already been calibrated externally, the bioreactor will use this data and the calibration procedure on the operating panel is not necessary.

Depending on the variant selected, the device is configured for pH measurement with the digital pH sensors of the type InPro 3253i ISM from the manufacturer METTLER or the type Easyferm Plus ARC from the manufacturer HAMILTON. The pH buffers and their temperature dependencies are stored in these pH sensors and are automatically detected during calibration. It is therefore not necessary to carry out a separate temperature measurement of the buffer solution.

Calibrating

To calibrate a pH sensor at the operating panel, proceed as follows:

1. ➔ Connect the sensor cable (➔ Chapter 7.3.10 'Connecting the pH Sensor' on page 116).

Operation

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

! NOTICE

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



Only sensor type Easyferm Plus ARC: an *ERROR Glass resistance too high* that might appear after initialization can be ignored. This can occur if the sensor is in contact with air or non-conductive liquid such as distilled water.

3. ➔ Call up the calibration menu of the *pH* parameter.
➔ The menu display changes after a short initialization phase:

- Header: date and time of the last calibration
- **1-POINT CALIBRATION:** to select 1-point calibration
- **2-POINT CALIBRATION:** to select 2-point calibration
- **PRODUCT CALIBRATION:** to select product calibration (➔ Chapter 9.8.2 'pH Sensor Product Calibration' on page 175).
- **SHOW SENSOR STATUS:** shows data and values produced by the firmware of the sensor manufacturer that is integrated in the sensor (➔ 'Sensor Status' on page 174).
- HAMILTON sensors only: shows sensor quality within a range of 0 to 100 % in the footer.

4. Select 2-point calibration.

➡ The menu display changes to the first calibration point and shows the following:

- Left-hand side: guides step-by-step (1 – 5) through the calibration of the first reference value.
- Right-hand side:
 - Drop-down list for selection of the reference value. If the connected sensor allows the use of different calibration buffers or an automatic detection of the calibration buffer (*AUTO*), it can be selected. Otherwise, the calibration buffer to be used is displayed.
 - Measured value display
 - **CALIBRATE POINT**: to start calibration for 1st reference.
 - **CONFIRM NOW**: to confirm calibration and continue with 2nd reference.

5. ➡ Hold the pH sensor into the appropriate buffer solution of the first calibration point (step 1).

6. ➡ If possible, select the reference value or automatic buffer recognition (step 2).

➡ The current pH measured value appears, **CALIBRATE POINT 1** is activated, i.e. the button turns orange.

7. ➡ Wait until the measured value is stable (step 3).

Operation

CALIBRATE POINT 1

CONFIRM NOW

8. ➞ Press **CALIBRATE POINT 1** to start calibration (step 4).

➞ **CONFIRM NOW** slowly turns orange and indicates the ideal waiting time until a stable measured value is reached.



If the measured value is assumed to be already stable, the waiting time can be skipped by pressing **CONFIRM NOW** to continue with the second calibration point.

9. ➞ Press **CONFIRM NOW** (step 5).

➞ The calibration point is stored.



If the calibration process fails, an error message is displayed with a corresponding notice. In this case, restart the calibration.

If the calibration is successful, the menu display changes automatically to calibrate the second calibration point. The step-by-step guide (steps 6 - 10) through the calibration remains the same as for the first point (steps 1 - 5). After rinsing the pH sensor with distilled water, the same ERROR may occur. This can also be ignored here.

After successfully storing the 2nd calibration point via **CONFIRM NOW**, the calibration is completed and the menu can be exited via **OK**.

Sensor Status

SHOW SENSOR STATUS is used to show data and values produced by the firmware of the sensor manufacturer integrated in the sensor. In addition to information on the sensor type and information on calibration, the following two values are displayed for METTLER ISM sensors:

- *ACT* (Adaptive Calibration Timer): adaptive calibration timer in days, determines the time of the next calibration to ensure that optimal measurement performance is guaranteed. After successful calibration, it is reset to its start value.
- *DLI* (Dynamic Lifetime Indicator): dynamic display of the lifetime. Shows the number of days remaining and is pre-set by the sensor manufacturer.

9.8.2 pH Sensor Product Calibration

General Information

It is possible to adjust the calibration curve to the current process conditions using product calibration. This could be necessary if there is a possibility of drift of the displayed pH during a long-term cultivation, for example.



Product calibration can only be carried out and is only effective if the externally measured and entered pH value does not deviate from the original pH value by more than 2 pH units.

Calibrating

PRODUCT CALIBRATION

Proceed as follows for a product calibration:

1. ➔ Call up the calibration menu of the *pH* parameter.
2. ➔ In the menu display that follows the initialisation phase, press **PRODUCT CALIBRATION**.
 - ➔ The menu display changes and now displays the following:

< PRODUCT CALIBRATION PH !

1 Take a sample for offline measurement and confirm **CONFIRM**

Sample was taken at

2 Measure the pH of the sample and enter the value

3 Start the calibration **CALIBRATE**

SENSOR QUALITY 94.0 % **CANCEL** **OK**

- Left-hand side: guides step-by-step (1 – 3) through the product calibration.
- Right-hand side:
 - **CONFIRM**: to confirm sampling and generate a time stamp.
 - Display of the generated time stamp.
 - Input field: to enter the externally measured pH value of the sample.
 - **CALIBRATE**: to start product calibration.

Operation

3. ➤ Take a sample from the process (in the culture vessel). There are two possible approaches:

- Variant A: confirm the sampling (generate a time stamp), carry out a laboratory measurement of the pH value for the sample, enter the measured value and carry out product calibration.
- Variant B: confirm the sampling (generate a time stamp), leave the calibration menu and carry out the product calibration with an external measured value at a later time.

Variant A

The sequence of screens for Variant A calibration is as follows:

- A screen with an orange button labeled **CONFIRM**.
- A screen displaying the pH value **6.9**.
- A screen with an orange button labeled **CALIBRATE**.
- A screen displaying **PRODUCT CALIBRATION** and **ACTIVE**.

Proceed as follows:

1. ➤ Press **CONFIRM**.

➡ The date and time of the sampling are now displayed.

2. ➤ Carry out a laboratory measurement of the pH value for the sample.

3. ➤ Enter the measured pH value of the sample, in the example to the left, pH 6.9.

4. ➤ Press **CALIBRATE** to start calibration.

5. ➤ Wait until the calibration is complete.

6. ➤ Confirm the calibration with **OK** and leave the menu.

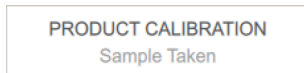
➡ In the calibration menu, *ACTIVE* is displayed under *PRODUCT CALIBRATION* to show that a product calibration was carried out and is active.

➡ Date and time are displayed in the header of the menu.



A new 2-point or 1-point calibration cancels the product calibration.

Variant B



Proceed as follows:

1. ➔ Press **CONFIRM**.
 - ➔ The date and time of the sampling are now displayed.
2. ➔ Leave the calibration menu using **OK** and carry out a laboratory measurement of the pH value for the sample at a later time of your choosing.
 - ➔ In the calibration menu, *Sample Taken* is displayed under *PRODUCT CALIBRATION* to show that sampling was carried out but product calibration is not yet active.

If a sample is lost, step 1 can be repeated.
3. ➔ To carry out product calibration, proceed as in Variant A) from step 3.

9.8.3 Calibrating the pO₂ Sensor

General Information

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

Depending on the variant selected, the device is configured for pO₂ measurement with the digital pO₂ sensors of the type InPro 6860i ISM from the manufacturer METTLER or the type Visiferm DO ARC from the manufacturer HAMILTON.



pO₂ sensors are preconfigured by the device manufacturer to the measured value %-sat. Replacement sensors must also be configured by the device manufacturer.

Calibrating

The following example describes a 2-point calibration of a pO₂ sensor in the medium after autoclaving. For the 100 % calibration, gassing with air is used, for the 0 % calibration, nitrogen is used.

For this, both gases must be connected and ready for operation, unused gases must be switched off.



If necessary, enter setpoints for temperature and pH, activate parameters and press **START BATCH** and wait until the desired operating temperature and the expected pH have been reached.

Proceed as follows:

Operation

1. ➤ Call up the calibration menu of the pO_2 parameter.

➡ The menu display changes after a short initialization phase:

CALIBRATE PO2 (LAST CALIBRATION: 7/24/19 10:23 AM) ⓘ

1-POINT CALIBRATION

2-POINT CALIBRATION

SHOW SENSOR STATUS

SENSOR QUALITY 37.0 %

CANCEL OK

- Header: date and time of the last calibration
- **1 POINT CALIBRATION**: to select 1-point calibration
- **2 POINT CALIBRATION**: to select 2-point calibration
- **SHOW SENSOR STATUS**: shows data and values produced by the firmware of the sensor manufacturer that is integrated in the sensor (➡ Chapter 9.8.1 'Calibrating the pH Sensor' on page 171).
- HAMILTON sensors only: shows sensor quality within a range of 0 to 100 % in the footer.

2. ➤ Select 2-point calibration.

➡ The menu display changes to the first calibration point and shows the following:

< 2-POINT CALIBRATION PO2 ⓘ

First Calibration Point

1 Select the value of the first calibration point 100 ▾

2 Optionally set setpoints for 100% pO_2 SET TO 100%

3 Evaluate the sensor data 104.5

4 Perform the calibration at the first point CALIBRATE POINT 1

5 Confirm measure or restart first calibration CONFIRM NOW

SENSOR QUALITY 37.0 %

CANCEL OK

- Left-hand side: guides step-by-step (1 – 5) through the calibration of the first reference value.
- Right-hand side:
 - Drop-down list for selection of the reference value. If the connected sensor allows the use of different reference values or an automatic detection of the reference value ("AUTO"), it can be selected. Otherwise, the calibration buffer to be used is displayed.
 - **SET TO xx%**: setpoint setting to activate gassing and the stirrer for calibration in the medium.
 - Measured value display
 - **CALIBRATE POINT**: to start calibration for 1st reference.
 - **CONFIRM NOW**: to confirm calibration and continue with 2nd reference.

3. ➤ If possible, select the reference value 100 % (step 1).

➔ **CALIBRATE POINT 1** is activated, i.e. the button turns orange.



This enables a calibration of the sensor outside the medium, i.e. without active gassing for a standard calibration outside the medium, which is not described here.

SET TO 100%

4. ➤ Press **SET TO 100%** (step 2).

➔ The gassing with air is activated, the stirrer is switched on at the same time.

5. ➤ Wait until the medium is saturated with oxygen, i.e. wait until the measured value is stable (step 3).

6. ➤ Press **CALIBRATE POINT 1** to start calibration (step 4).

➔ Gassing and stirrer are stopped.

➔ **CONFIRM NOW** slowly turns orange and indicates the ideal waiting time until a stable measured value is reached.



If the measured value is assumed to be already stable, the waiting time can be skipped by pressing **CONFIRM NOW** to continue with the second calibration point.

7. ➤ Press **CONFIRM NOW** (step 5).

➔ The calibration point is stored.

CALIBRATE POINT 1

CONFIRM NOW

Operation



If the calibration process fails, an error message is displayed with a corresponding message. Restart the calibration in this case.

If the calibration is successful, the menu display changes automatically to calibrate the second calibration point. The step-by-step guide (steps 6 - 10) through the calibration remains the same as for the first point (steps 1 - 5).

Proceed with the second point (0 % calibration) in the same way as for 100 %. After pressing **SET TO 0 %**, a dialogue will appear asking to check whether nitrogen is connected (version for microorganisms) or whether the nitrogen supply is turned on (version for cell cultures). If necessary, perform the corresponding step and confirm with **OK**. Then the gassing with nitrogen is activated, and the stirrer is switched on at the same time.

After successfully storing the 2nd calibration point via **CONFIRM NOW**, the calibration is completed, and the menu can be exited via **OK**.

9.8.4 Calibrating the Turbidity Sensor

General Information

Turbidity sensors ASD12-N are pre-calibrated ex-factory. Inserts are available for reference measurement. Due to the different light absorption of different media, zero point calibration of the turbidity sensor should be performed before each cultivation process. This can be done either before or after autoclaving, depending on the application in question.

Conditions for zero point calibration of the sensor: the sapphire windows of the turbidity sensor must be clean and free of air or gas bubbles. The light absorption of the medium before activation of the gassing and before inoculation can be used as a reference value for the zero point.

Calibrating

To calibrate the zero point of the turbidity sensor (option, ASD12-N only), proceed as follows:

1. ➤ Connect the sensor cable.
2. ➤ Call up the calibration menu of the *Turbidity* parameter.
 - ➡ The menu shows:

The screenshot shows a screen titled "CALIBRATE Turbidity (LAST CALIBRATION: 19.08.19)". The screen is divided into two main sections. The top section contains a list of two steps: "1 Wait until measurement is stable" and "2 Perform zero point calibration". To the right of these steps, the value "00" is displayed. Below the steps, there is an orange button labeled "CALIBRATE". At the bottom of the screen, there are two buttons: "CANCEL" and "OK".

- Header: date of the last calibration
- Left-hand side: calibration sequence (2 steps)
- Right-hand side: measured value and **CALIBRATE**: to calibrate the zero point.

3. ➤ Wait until the measured value is stable.

4. ➤ Press **CALIBRATE**.

- ➡ If the calibration was successful, **OK** is activated and can be pressed to confirm the calibration and leave the menu.

Operation

9.9 PID Controller – Basic Principle

For some parameters, PID controllers (Proportional Integral Derivative controller) are used.

9.9.1 Table with Settings for the PID Controller

Setting	Description
P (Prop. Term)	Proportional term: the greater the difference between setpoint and actual value, the greater the controller output.
I (Integ. Term [1/s])	The integral factor sums up all errors over the term. If the setpoint is not reached with the proportional factor, the integral factor successively adjusts the output until the setpoint is reached. If the integral factor is set too high, this leads to fluctuations of the control loop.
D (Diff Term [s])	The differential quotient calculates the change in the actual value over time and counteracts this change.
Neg. Factor	The negative factor can be used to weight a two-sided control (+100 to -100 percent) (e.g. strong acid, weak base). Here, 1 is the balance and 0.5 or 2 the corresponding halving or doubling of the controller output. Example: nitrogen affects the pO ₂ value less than oxygen, so a negative factor of 2 can rebalance the regulator's response.
Deadband	If a deadband value is entered, no control takes place within this value around the setpoint (symmetrical, +/-). That is, the controller output is = 0. The deadband is used for pH control.
I Limit (Integ. Limit [%])	To ensure that the integral factor cannot increase indefinitely, the integral influence is used. This limits the error summation. The integral influence is set between 0 % and 100 % of the controller output.
Eval Time [s]	The eval. time shows the intervals in seconds of the new calculation of the PID value. The controller speed is defined by this. 10 seconds is a good average value for the eval. time.

9.9.2 Tips for Readjusting a PID Controller

To readjust the PID controller, proceed as follows:

1. ➤ Start by setting the proportional factor when readjusting a PID controller. Choose the proportional bandwidth as large as possible.
2. ➤ Set the integral factor and differential quotient to zero.
3. ➤ Increase the proportional factor until the controller causes oscillations of the actual value.
4. ➤ Measure the period of oscillation, e.g. with the bioprocess platform software eve® of the device manufacturer.
5. ➤ Halve the proportional factor and vary the integral factor between the reciprocal of twice and four times the period of oscillation.

9.9.3 Adjusting PID Settings

! NOTICE

Inappropriate changes to the PID controller settings may have a negative effect on the bioprocess and cause loss of property.

Therefore, only change factory settings of the PID controller(s), if you are fully aware of the consequences! If necessary, the factory settings can be restored via **Reset PID**.

PID control may be configured for parameters *pH*, *pO₂* and *Pump4* (function *Balanced Feed*). This is done in the editor menu of the corresponding parameter and therefore described there.

Operation

9.10 Alarms – Equipment Alarm Menu

There are two types of alarm that appear in the *Equipment Alarm* menu:

- Parameter alarms: display of deviations from actual values and set-points for parameters after a predefined waiting time (➔ Chapter 9.3.4 'Parameter Alarms' on page 147).
- Equipment errors: if equipment errors occur repeatedly or cannot be resolved, inform an authorised INFORS HT service partner.

The *Equipment Alarms* only available when there are open or unconfirmed alarms. Otherwise the alarm symbol (a red exclamation mark highlighted in white on a red background) is hidden in the lower screen edge.

FAVORITES	1	PARAMETER	VALUE	SETPOINT
MAIN	1	Temperature	32.2 °C	37.0 °C
		Stirrer	24 min ⁻¹	24 min ⁻¹
EXTENDED		pH	7.00	7.00
EXIT GAS		pO ₂	100.0 %	100.0 %
PUMPS		TotalFlow ← pO ₂	8.00 L min ⁻¹	8.00 L min ⁻¹
		GasMix	NaN %O ₂	21 %O ₂
		Foam	0	

Batch Time (since inoc.)
00:03:18

EDIT VIEW

SAMPLE NOW

Pressing the alarm symbol or swiping upwards opens the *Equipment Alarm* menu.

MAIN	1	temperature	37.4 °C	37 °C	
		Stirrer ← pO ₂	20 min ⁻¹	20 min ⁻¹	
EXTENDED		pH	7.00	7	
EQUIPMENT ALARM (4)					
DESCRIPTION		STATE		CONFIRMATION	
● Alarm_PowerFailDuringRunningBatch		Resolved		☐	
● Alarm_ControllerCommunicationFailure		Open			
● Temperature too high		Open			
● TotalFlow too high		Resolved		☐	

- *DESCRIPTION*: describes the type of alarm.
- *STATE*: status display of the alarm, open or resolved .
 - Open alarms are displayed in red and with the word *Open*.
 - Resolved alarms are displayed in green and with the word *Resolved*.
- *CONFIRMATION*: to confirm the alarm and delete it from the list. The entry in the batch log remains.

9.11 Switching off the Device

1. ➔ Ensure that the batch (bioprocess) has been stopped. If necessary, stop it via **Stop Batch**.



Always stop the running batch on the operating panel. If it is stopped by pressing the power switch, it is akin to a power interruption. This means that when it is switched on again, the previous settings are adopted and the batch continues running where it was interrupted. This also applies, if the batch is controlled via eve®, the platform software for bioprocesses.

2. ➔ Press the power switch to switch off the device.
3. ➔ Close the supply lines (water, gas).
4. ➔ Let the motor cool down (device version for microorganisms).



CAUTION

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

5. ➔ If necessary, autoclave the vessel, built-in-parts and accessories in accordance with the internal safety regulations before cleaning.

Cleaning and Maintenance

10 Cleaning and Maintenance

The following chapters contain general descriptions regarding the cleaning of the culture vessel and its accessories, and how these can be stored.

In addition, the chapter contains a maintenance plan and corresponding descriptions for the procedures to be performed by the operator.

10.1 Cleaning Agent and Disinfectant

Purpose of use	Allowed products/tools
Culture vessel	Water and a non-scratch, non-abrasive sponge or washing-up brush; lab washer with special washing agent (for industry and lab use)
Cleaning agent for denaturation of proteins	0.1 N NaOH
Cleaning agent for smaller parts	Ultrasonic bath
Cleaning agent for surfaces	Water
Disinfectant for surfaces	Ethanol, 70 %
Decalcifier for the device	Amidosulphonic acid (liquid form)

CAUTION

Using spray bottles with ethanol can result in explosive mists being created!

All cleaning operations with ethanol must be carried out in an environment that is separate from the device, well ventilated and meets internal safety regulations.

10.2 Cleaning the Culture Vessel - Routine Cleaning

! NOTICE

Household washing-up liquid and soap (in particular cream soaps) can collect in glass pores and impair later cultivations.

Never clean culture vessels and accessories with household soap and use special cleaning agent (for industrial and lab use) in the lab washer.

The following method describes a routine cleaning between two cultivations. It takes place with the culture vessel completely assembled and the accessories completely mounted.

This does not include the sensors, with the exception of antifoam or level sensors from the device manufacturer. To avoid damaging the other sensors during the routine cleaning, they are first removed and then cleaned separately according to the third-party manufacturer guidelines and then stored, if necessary (→ Chapter 10.5 'Cleaning the Sensors' on page 195).

Proceed as follows to carry out a routine cleaning of the culture vessel:

1. ➤ Except antifoam/level sensors, carefully unscrew all sensors by hand from the vessel top plate ports and place them to the side for separate cleaning according to the manufacturer guidelines.
2. ➤ Completely fill the culture vessel with 0.1 N NaOH.
3. ➤ Fit the top plate on the vessel and secure it.
4. ➤ Hang the culture vessel on the basic unit.
5. ➤ Couple the motor.
6. ➤ Switch on the device at the power switch.
7. ➤ At the operating panel, start the Batch using **START BATCH** and stir strongly for 2 hours with the stirrer function (parameter *Stirrer*).



It is recommended to warm the 0.1 N caustic soda to 60 °C and to prolong the duration of stirring for dealing with persistent residue of foam or protein.

8. ➤ At the operating panel, stop the Batch using **INOCULATE** and **STOP BATCH**.
9. ➤ Switch off the device at the power switch.

Cleaning and Maintenance

- 10.** ➤ Let the motor cool down.
- 11.** ➤ When the motor has cooled down: Uncouple the motor.
- 12.** ➤ Remove the top plate and carefully place it so that it does not lie on top of components.
- 13.** ➤ Empty the culture vessel.
- 14.** ➤ Thoroughly rinse the culture vessel with distilled water.

10.3 Removing the Vessel Top Plate and Accessories

All accessories must be removed for thorough cleaning of the individual parts of the culture vessel. This is described in the following sections.

The cleaning itself is described in ➔ Chapter 10.4 'Cleaning and Storing Individual Parts' on page 194. The cleaning of the hoses with pump heads, the basic unit and the operating panel are described in separate sections.

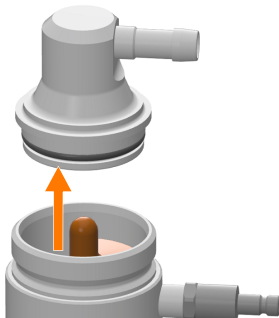
Sensors from third-party manufacturers are cleaned according to their manufacturer's specifications.

10.3.1 Removing the Exit Gas Cooler

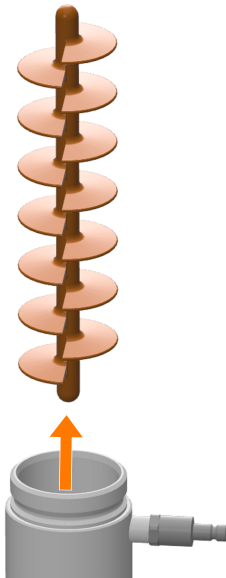
- 1.** ➤ Unscrew the exit gas cooler from the vessel top plate port by hand.
Ensure that the O-ring does not get lost.
- 2.** ➤ Remove the pressure hose with exit gas filter, dispose of the exit gas filter.
- 3.** ➤ Unscrew and remove the coupling nut on the lid by hand in counter-clockwise direction.



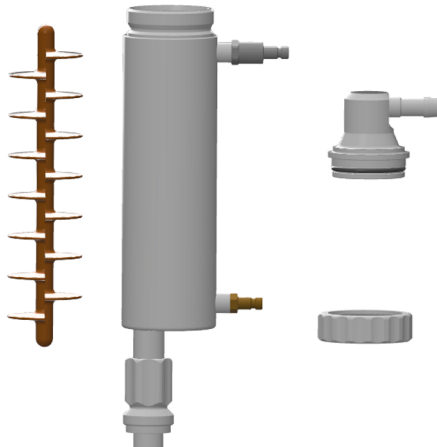
Cleaning and Maintenance



- 4.** → Remove the lid by hand. If necessary, wet the lid slightly with water to facilitate loosening of the lid.



- 5.** → Remove the silicone baffle from the exit gas cooler.



- 6.** → Clean the individual parts of the exit gas cooler (→ Chapter 10.4 'Cleaning and Storing Individual Parts' on page 194).

Cleaning and Maintenance

10.3.2 Removing the Sensors

10 mm ports (antifoam/level)

1. ➔ Loosen and remove the fastening screw beside the sensor by hand.
2. ➔ Loosen the slotted screw at the clamping adapter.
3. ➔ Carefully remove the sensor from the clamping adapter.
4. ➔ Pull the clamping adapter out of the vessel top plate port by hand.

Ensure that the outer O-ring at the clamping adapter does not get lost and that the insulation is not damaged.



The sensor can be pulled out of the vessel top plate port along with the clamping adapter. After subsequently unscrewing the slotted screw on the clamping adapter, the sensor can be pulled out of the clamping adapter.

12 mm / Pg13.5 ports (pH, pO₂, Redox, turbidity)

1. ➔ Carefully unscrew the sensors by hand from the vessel top plate ports.
2. ➔ Clean/service the sensors according to the sensor manufacturer guidelines.

Turbidity measurement, variant CGQ BioR: loosen the strap and remove along with sensor from the vessel.

10.3.3 Removing Hoses, Filters and Pump Heads

To later clean reagent hoses and pump heads, they must be removed from the reagent bottles and from components of the culture vessel.



To avoid damage, never dismantle the pump heads. Always replace a damaged pump head along with the pump hose, and vice versa.

Proceed as follows:

1. ➔ Remove cable ties (e.g. with a side cutter) so that the hoses are not damaged.
2. ➔ Pull hoses off the culture vessel and the reagent bottles.
3. ➔ Remove and dispose of filters for pressure equalisation and hoses from reagent bottles.

Cleaning and Maintenance

4. ➔ Ensure that the inlet air filter is clean, dry and not blocked. If this is not the case, dispose of it.



If the filter for pressure equalisation and the corresponding hoses have been used several times, ensure that the filters are always dry and clean.

5. ➔ Dispose of the exit gas filter (➔ Chapter 10.3.1 'Removing the Exit Gas Cooler' on page 188).

10.3.4 Removing Blanking Plugs

10 mm Ports

1. ➔ Loosen and remove the fastening screw beside the blanking plug by hand.
2. ➔ Pull the blanking plug out of the vessel top plate port by hand.
Ensure that the O-ring at the blanking plug does not get lost.

12 mm / Pg13.5 Ports

- ➔ Loosen the blanking plug with a hexagon socket spanner and remove it by hand.
Ensure that the O-ring does not get lost.

10.3.5 Removing the Septum Collar and Septum

1. ➔ Loosen the blanking plug with a hexagon socket spanner in the septum collar and remove it by hand.
Ensure that the O-ring does not get lost.
2. ➔ Unscrew the septum collar out of the port by hand.
3. ➔ Remove the septum from the port and dispose of it.

Cleaning and Maintenance

10.3.6 Removing Addition Port Adapters, Feed Needle and Temperature Sensor Immersion Pocket

1. ➤ Loosen and remove the fastening screw between the addition port adapters and/or feed needle(s) as well as beside the immersion pocket by hand.
2. ➤ Pull the addition port adapters and if necessary, the feed needle(s) from the vessel top plate ports by hand.
3. ➤ Pull the temperature sensor pocket out of the vessel top plate port.

Ensure that the O-rings on the addition port adapters and at the immersion pocket do not get lost.

10.3.7 Removing the Vessel Top Plate

! NOTICE

If the vessel top plate presses against long components they could bend because of the weight of the top plate.

Always position the vessel top plate so that it does not lie on top of components.

Proceed as follows to remove the vessel top plate:

1. ➤ As far as possible, remove mounted parts before lifting the top plate.
2. ➤ Remove the knurled nuts on the top plate by hand and place them to the side.
3. ➤ Hold the glass vessel with one hand and carefully lift the top plate vertically upwards from the vessel with the other until the stirrer shaft and other long components can no longer come into contact with the glass vessel.



If the top plate cannot be easily lifted from the glass vessel, respectively the O-ring (top plate seal), execute slight tilting movements in order to detach it from the O-ring.

4. ➤ If necessary, now remove components that have not yet been removed.

Never remove the stirrer shaft!

5. ➤ Check the glass vessel for damage (cracks, fissures, scratches) and replace if necessary.

10.3.8 Removing the Sparger and the Dip Tube(s)

Straight spargers and dip tubes can be removed from the outside of the vessel top plate. Curved spargers and dip tubes can only be removed from the inside of the vessel top plate.

Since this device uses ring spargers and straight dip tubes, removal from the inside of the vessel top plate is described here. This means that the vessel top plate is already removed.

Proceed as follows:

- 1.** ➔ Loosen and remove the fastening screw beside the sparger/dip tube by hand.
- 2.** ➔ Loosen the slotted-head screw at the clamping adapter.
- 3.** ➔ Carefully pull the sparger/dip tube from the bottom out of the clamping adapter.
- 4.** ➔ Pull the clamping adapter out of the vessel top plate port by hand.

Ensure that the outer O-ring at the clamping adapter does not get lost.

10.3.9 Removing the Impellers

Before removing the impellers, it is advisable to measure and note the position for later correct mounting.



The mounting heights defined ex-factory for both impeller types (Rushton and pitched bladed) in all vessel sizes can be found in the technical data (➔ Chapter 13.4.3 'Stirrer' on page 219).

For removal proceed as follows:

- 1.** ➔ Loosen – do not remove! – the grub screws on the impellers with the hex key.
- 2.** ➔ Carefully pull the impellers off the stirrer shaft.

Cleaning and Maintenance

10.4 Cleaning and Storing Individual Parts

The procedure described here applies to the following individual parts:

- Vessel
- Exit gas cooler
- Accessories such as blanking plugs, spargers, dip tubes, addition port adapters etc.
- Reagent bottles
- Vessel top plate, with regard to its particular characteristics
- Cold finger (optional, version for microorganisms)

Particulars when Cleaning the Top Plate

- Do not place the top plate on the stirrer shaft.
- Never removed the drive hub and stirrer shaft!



Cleaning of the sensors, hoses, pump heads and the basic unit are described in separate sections.

Procedure

Proceed as follows for cleaning:

- 1.** → Clean parts with distilled water and a soft sponge or in the dishwasher.

Ensure that the deposits in the dip tubes, feed needles and in the exit gas cooler are removed. Use 0.1 N caustic soda solution followed by distilled water as necessary (→ Chapter 10.2 'Cleaning the Culture Vessel - Routine Cleaning' on page 187).
- 2.** → Dry all parts, including the inner parts of the dip tubes, spargers, exit gas cooler and feed needles.
- 3.** → Check all O-rings for cracks or damage. Replace them if necessary.
- 4.** → Store the vessel, vessel top plate and accessories in a clean, dry state in a location where they cannot be physically damaged (e.g. by falling), or prepare them for the next cultivation.

Cleaning and Maintenance

10.5 Cleaning the Sensors

Apart from antifoam and level sensor, all sensors are cleaned and maintained according to the descriptions of the sensor manufacturer.

1. ➔ Clean the sensors according to the sensor manufacturer guidelines.
2. ➔ Prepare the sensors for the next cultivation or, if necessary, service and/or store them according to the sensor manufacturer guidelines.

10.6 Cleaning the Hoses and Pump Heads

Proceed as follows to clean the reagent hoses and pump heads:

1. ➔ Thoroughly rinse the hoses with the pump heads with water.
2. ➔ Carefully dry all hoses and, if necessary, blow out with clean compressed air.



To avoid damage, never dismantle the pump heads. Always replace a damaged pump head along with the pump hose, and vice versa.

10.7 Cleaning the Super Safe Sampler

! NOTICE

Risk of damage to the sampling system from unsuitable cleaning methods or cleaning agent (such as acids, bases or solvents, for example).

- Only use water or a mild soap solution for cleaning.
- The sterile filter must remain dry at all times.

Proceed as follows to clean the sampling system:

1. ➔ Fill the culture vessel with water or a mild soap solution.
Or: Remove the sampling hose from the dip tube and hold it in a vessel, e.g. a beaker, with water or a soap solution.
2. ➔ Place the syringe on the automatic valve and pull out the plunger to rinse the sampling system.
3. ➔ When using a soap solution: Rinse the sampling system thoroughly with water.

Cleaning and Maintenance



If the test record requires that the culture is killed off after cultivation by autoclaving the culture vessel, the valves of the sampling system may become stuck due to residue of the culture solution. In such a situation, it would be better to autoclave the sampling system separately in a beaker of water (hoses filled with water, filter removed).

10.8 Cleaning the Basic Unit and Operating Panel

Proceed as follows to clean the surface of the basic unit and the operating panel as required:

1. ➤ Switch off the device at the power switch.
2. ➤ Disconnect the device from the power supply.
3. ➤ Wipe all surfaces with a damp cloth.
Clean with an appropriate disinfectant as necessary.
4. ➤ Clean the screen with a wipe suitable for computer or laptop screens.

10.9 Maintenance Plan



WARNING

Failure to observe the maintenance plan bears a significant risk.

Users are responsible for compliance with the maintenance plan; failure to comply with it will result in exclusion of liability (see GTC).

The following sections describe the maintenance work that is required for optimal and fault-free operation.

If increased wear is detected during regular checks, the required maintenance intervals must be shortened in accordance with the actual signs of wear. Contact the manufacturer if you have questions about maintenance work and intervals.

Cleaning and Maintenance

Interval	Maintenance work	Personnel
Prior to each use	Check hose lines and connections.	Operator
	Check cables for damage and kinks.	Operator
	Check all O-rings and gaskets and replace if necessary.	Operator
	Check the integrity of all glass parts (vessel, reagent bottles) and replace if necessary.	Operator
	Check all filters and replace if necessary. Replace the exit gas filter.	Operator
	If necessary, calibrate the sensors.	Operator
After each use	Autoclave and clean the culture vessel and accessories.	Operator
Every 6 months	Check functionality of measurement sections (temperature, pH, etc.), use simulator, where possible.	Technician
Annually	Full maintenance of the device.	INFORS HT service technician or licensed dealer
As required	Clean the basic unit and operating panel.	Operator
	Decalcify the device.	Operator

10.10 Decalcifying the Device

Limescale could block installed parts, lines or valves in the basic unit. It may be necessary to decalcify the device if certain faults occur in the temperature control or gassing system.

Note the following points before beginning the procedure:

- Be sure to respect the in chapter “Technical Data” specified inlet pressure.
- To warm up the decalcifier and pump it into the basic unit, use a chiller or a water bath and an external pump.
- During decalcification, the decalcifier flows in a circuit between the basic unit and the chiller/water bath.
- Use amidosulfonic acid in liquid form as decalcifying agent.
- For the mixture, calculate 5 litres of water plus the capacity of the water bath/chiller including the hoses.

Cleaning and Maintenance

! NOTICE

Amidosulfonic acid can crystallise in case of overdosage and cause loss of property!

When preparing the decalcifying liquid, observe and follow the manufacturer's instructions for correct dosage and application!

Proceed as follows for decalcifying:

- 1.** ➤ Mount the exit gas cooler into the port of the vessel top plate and connect to the basic unit.

Ensure that the valve for the exit gas cooler water supply is open. Open it, if necessary.
- 2.** ➤ Hang the culture vessel on the basic unit (hang the vessel holder on hooks on the thermal block).
- 3.** ➤ Fill the chiller/water bath with the prepared decalcifying liquid.
- 4.** ➤ Connect the chiller or water bath to the water inlet and outlet on the basic unit using hoses.
- 5.** ➤ To open the corresponding valves in the basic unit, set the temperature on the operating panel to 4 °C (cool).
- 6.** ➤ Set the chiller/water bath to 20 °C to 40 °C.
- 7.** ➤ Switch on the pump at the chiller/water bath.
- 8.** ➤ Let the decalcifier flow through the device for an hour.
- 9.** ➤ Connect the water inlet hose on the device to tap water.
- 10.** ➤ Hang the water outlet hose of the device at the spout.
- 11.** ➤ Rinse the device for an hour.

11 Rectifying Faults

The following chapter describes possible reasons for faults and how to resolve them. Reduce the service intervals in correspondence with the actual loads if faults become increasingly common. Contact the manufacturer or licensed dealer in case of faults that cannot be resolved by following the notices below.

11.1 General Faults

Fault description	Cause	Remedy	Personnel
Device does not work.	Device is not switched on.	Switch on the device at the power switch.	Operator
	Power supply of the device is interrupted.	1. Check if the plugs are plugged in correctly. 2. Check the mains connection.	Operator
	Device fuse is blown.	1. Replace the fuse. 2. If the fault occurs more than once, contact the INFORS HT representative.	Operator
	LED flashes red, Equipment Alarm is shown on the display, power failure during a running batch.	→ Acknowledge the alarm message. ➡ The batch is automatically started again.	Operator
	LED flashes red, Equipment Alarm is shown on the display, control system communication is interrupted.	1. Acknowledge the alarm message. 2. If the alarm occurs more than once, contact the INFORS HT representative.	Operator
	LED flashes red, Equipment Alarm is shown on the display, pressure in the culture vessel is too high.	1. Acknowledge the alarm message. 2. If necessary replace the exit gas filter or reduce the gas flow rate.	Operator

Rectifying Faults

11.2 Faults Drive System

Fault description	Cause	Remedy	Personnel
Motor does not start.	Motor is not properly connected.	1. ➔ Switch off the device. 2. ➔ Check cable connections and connect correctly as necessary.	Operator
	The <i>Stirrer</i> parameter is not activated.	Activate the <i>Stirrer</i> parameter.	Operator
	<i>Stirrer</i> parameter setpoint = 0.	Set <i>Stirrer</i> parameter setpoint > 0.	Operator
	The pO_2 is activated and set to oxygen control via the stirrer (cascade).	Switch off the cascade and test operation via the <i>Stirrer</i> parameter.	Operator
Unusual sounds when the stirrer is switched on.	Impeller is in contact with other built-in-parts, e.g. sensors.	1. ➔ Stop the batch and switch off the device. 2. ➔ Correctly mount the built-in-parts in the culture vessel and test stirrer with water in the vessel. 3. ➔ If interference persists, contact INFORS HT representative.	Operator
Motor control is volatile, irregular or stops.	The motor cable was plugged out when the basic unit was switched on.	Replace the motor.	INFORS HT service technician or licensed dealer

Rectifying Faults
11.3 Faults Temperature Control System

Fault description	Cause	Remedy	Personnel
No temperature control.	Temperature control is not activated.	Activate the <i>Temperature</i> parameter.	Operator
	Stirrer is not activated and/or setpoint = 0.	Activate the <i>Stirrer</i> parameter; if necessary, set the setpoint to > 0.	Operator
No cooling or inadequate cooling.	No water supply or inadequate flow.	Check the water supply and turn on the supply tap if necessary.	Operator
	Temperature sensor is not inserted.	Insert the temperature sensor into the immersion pocket in the vessel top plate.	Operator
	Cooling lines are blocked due to lime-scale.	1. ➤ Decalcify the device. 2. ➤ If fault persists, contact INFORS HT representative.	Operator
	Ambient temperature in laboratory too high or/and device with high heat radiation in the immediate vicinity (➔ Chapter 13.6 'Operating Conditions' on page 229).	1. ➤ Reduce room temperature and/or increase air circulation. 2. ➤ If this is not possible, reposition the device.	Operator

Rectifying Faults

11.4 Faults Gassing System

Fault description	Cause	Remedy	Personnel
No gassing / air bubbles in the culture vessel.	The on-site gas supply has been interrupted.	1. Stop the batch. 2. Check the on-site gas supply and switch it on, if necessary.	Operator
	<i>Flow</i> parameter is/are not activated.	Activate <i>Flow</i> parameter(s).	Operator
	Setpoint in <i>Flow</i> parameter(s) = 0.	Set the setpoint in the <i>Flow</i> parameter(s) > 0.	Operator
	<i>TotalFlow</i> parameter = 0 and/or <i>GasMix</i> parameter is/are not activated.	Set the <i>TotalFlow</i> parameter > 0 and activate the <i>GasMix</i> parameter.	Operator
	Hose connection(s) between the basic unit and the culture vessel is/are kinked or clamped.	1. Check whether the hose connection(s) is/are clamped, if necessary open the clamp(s). 2. Check hose connection(s) for kinks, if necessary route them again or replace them under observation of the sterility requirements.	Operator
	Inlet air filter is blocked.	Replace the inlet air filter under sterile conditions.	Operator
	Exit gas filter is blocked, over-pressure sensor switches gassing off for 10 s.	Replace the exit gas filter under sterile conditions.	Operator
Overpressure alarm <i>Gas pressure high</i> is displayed, the desired gas flow rate is not reached.	Blocked holes on the sparger.	1. Stop the batch. 2. Clean the sparger.	Operator
	Inlet air filter is blocked.	Replace the inlet air filter under sterile conditions.	Operator
	Exit gas filter is blocked, over-pressure sensor switches gassing off for 10 s.	Replace the exit gas filter under sterile conditions.	Operator

Rectifying Faults

Fault description	Cause	Remedy	Personnel
Alarm <i>Gas pressure low</i> is displayed, the desired gas flow rate is not reached.	Connection pressure is too low ($< 2 \pm 0.5$ bar).	Check the connection pressure and adjust if necessary.	Operator
Sudden increase in evaporation losses in the culture vessel.	The exit gas cooler does not cool, the <i>Temperature</i> parameter is activated.	Check the water supply to the exit gas cooler, restore it if necessary.	Operator
	The exit gas cooler does not cool, the exit gas cooler or basic unit is calcified.	Decalcify the device.	Operator
	The exit gas cooler does not cool, the control valve for water flow is closed.	Open the control valve.	Operator

Rectifying Faults

11.5 Faults pH Control

Fault description	Cause	Remedy	Personnel
No display or incorrect display of pH. Digital measurement systems: error message <i>ERROR</i> instead of actual value.	Sensor cable is not connected or not properly connected.	Connect the sensor cable correctly.	Operator
	pH drift during long cultivation.	Recalibrate pH with offline values (→ Chapter 9.8.2 'pH Sensor Product Calibration' on page 175).	Operator
	Faulty pH sensor.	1. → Test calibration with pH 4 and pH 7 buffer. 2. → Digital measurement systems: observe the error message when calling up the calibration menu (<i>Show Sensor Status</i>). 3. → Regenerate or replace the sensor, if necessary. Consult the documentation of the sensor manufacturer!	Operator
No pH control.	The <i>pH</i> parameter is not activated.	Activate the <i>pH</i> parameter.	Operator
	The pumps are not switched on.	Switch on Pump 1 (<i>Acid</i>), Pump 2 (<i>Base</i>).	Operator
	Incorrect deadband setting in PID.	Check the deadband (<i>Dead Band</i> in the <i>PID</i> parameter option): switch off or enter a small value.	Operator
	No addition of reagents (acids and base).	1. → Check the reagent bottles: refill if necessary. 2. → Check the hose connections between the reagent bottle and the culture vessel: connect properly if necessary. 3. → Remove/open clamps if necessary.	Operator

Rectifying Faults

Fault description	Cause	Remedy	Personnel
No pH control.	The (base/acid) pump does not operate properly.	Check the pump (<i>Acid</i> , <i>Base</i>) functionality using the operating panel (switch on/switch off).	Operator
	Pump hose is damaged, pump does not rotate: defective pump head	Replace pump head.	Operator
The pH value drifts up and down over time or acid and base are added almost continuously in turn.	The PID settings in the <i>pH</i> parameter are incorrect.	Check the PID settings (<i>PID</i> parameter option) and correct if necessary. Specifically, change the proportional factor (<i>Prop. Term</i>) or the <i>Deadband</i> setting.	Operator
	Incorrect strength of reagents: concentration is too weak or too high.	Check the strength of the reagents. Adjust if necessary: 0.1 mol to 2.0 mol.	Operator

Rectifying Faults

11.6 Faults pO₂ Control

Fault description	Cause	Remedy	Personnel
No display or incorrect display of pO ₂ . Digital measurement systems: error message <i>ERROR</i> instead of actual value.	Sensor cable is not connected or not properly connected.	Connect the sensor cable correctly.	Operator
	Faulty pO ₂ sensor.	1. → Check calibration. 2. → Digital measurement systems: observe the error message(s) when calling up the calibration menu (<i>Show Sensor Status</i>). 3. → If necessary, replace the pO₂ sensor. Consult the documentation of the sensor manufacturer!	Operator
No pO ₂ control.	The pO ₂ parameter and/or cascaded parameter is/are not activated.	Activate the parameter.	Operator
	The cascade settings are incorrect.	Check the cascade settings and change as necessary.	Operator
	No gas flow into culture vessel.	→ Chapter 11.4 'Faults Gassing System' on page 202.	Operator
	Fault with control of gas mixing unit.	1. → Check connections. 2. → Check gas lines.	Operator
Unstable pO ₂ control	Incorrect PID settings in the pO ₂ parameter.	Check the PID settings (<i>PID</i> parameter option) and correct if necessary. Specifically, the proportional factor (<i>Prop. Term</i>) and the deadband (<i>Dead Band</i>). The value in the deadband must be 0 (zero).	Operator

Rectifying Faults

11.7 Faults Antifoam/Level and Pump

Fault description	Cause	Remedy	Personnel
Foam/medium is not detected.	Sensor is not properly connected.	Check connections and connect properly as necessary.	Operator
Foam/medium is always/frequently detected.	Sheathing of antifoam sensor is damaged.	Have sheathing of anti-foam sensor replaced	INFORS HT service technician or licensed dealer
Antifoam pump does not work.	The <i>Foam</i> parameter is not activated.	Activate the <i>Foam</i> parameter.	Operator
	Pump 3 (<i>Antifoam</i>) is not activated.	Activate pump 3 (<i>Antifoam</i>).	Operator
No antifoam agent or medium supply or inadequate flow.	Reagent bottle is empty.	Refill reagent bottle.	Operator
	Incorrect antifoam agent or incorrect concentration.	Replace antifoam agent.	Operator
	Hose line is blocked or clamped.	1. → Check hose connection between reagent bottle and culture vessel, if necessary, connect correctly. 2. → Open closed clamp.	Operator
	The corresponding pump is not functioning correctly.	Check function of pump on operating panel.	Operator
	The pump hose is damaged.	Replace pump head.	Operator
	The pump head does not rotate: defective pump head.	Replace pump head.	Operator
	Incorrect hose type connected.	Check hose type, replace as necessary.	Operator

Rectifying Faults

11.8 Faults Feed and Pump

Fault description	Cause	Remedy	Personnel
No addition or inadequate addition of nutrient solution.	The <i>Feed</i> parameter (pump) is not activated.	Activate the <i>Feed</i> parameter (pump).	Operator
	<i>Feed</i> parameter (pump) setpoint = 0.	Set <i>Feed</i> parameter (pump) setpoint > 0.	Operator
	Hose line is blocked or clamped.	1. → Check connection between reagent bottle and culture vessel, if necessary, connect correctly. 2. → Open closed clamp.	Operator
	Reagent bottle is empty.	Refill the reagent bottle.	Operator
	Feed pump is not functioning correctly.	Check function of Feed pump on operating panel.	Operator
	Pump hose is damaged.	Replace pump head.	Operator
	Pump head does not rotate: defective pump head.	Replace pump head.	Operator
	Incorrect hose type connected.	Check hose type, replace as necessary.	Operator

Rectifying Faults
11.9 Interferences Turbidity Measurement

Fault description	Cause	Remedy	Personnel
Displayed measured value is not plausible/unusual.	Sensor cable is twisted or kinked or not properly connected.	1. → Check the connection of the sensor cable, connect it properly, if necessary. 2. → Check and ensure that the cable is not kinked or twisted.	Operator
	ASD12-N: sensor is not calibrated.	Calibrate the zero point.	Operator
	ASD12-N: window fouling on the sapphire windows.	Carefully clean the sensor.	Operator
	CGQ BioR: sensor is mounted in the wrong place / measures foam.	1. → Place the sensor at the level of the liquid. 2. → Make sure that there are no obstacles in front of the measuring window.	Operator
	Faulty sensor cable.	Replace the sensor cable.	INFORS HT service technician or licensed dealer
	Faulty sensor.	Replace the sensor.	Operator



If the temperature of the sensor (ASD12-N) rises above 50 °C during operation in the medium, an automatic switch-off takes place.

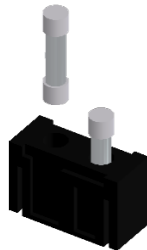
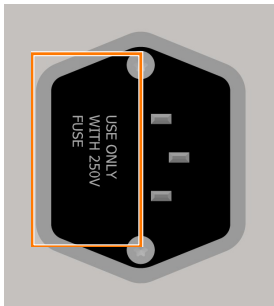
After the medium has cooled down, the measurement continues automatically.

Rectifying Faults

11.10 Replacing Device Fuses



The device fuses may only be replaced by fuses of the same rating. For information on the requirements regarding fuses, see ➔ Chapter 13.3.1 'Electrical Connection and Power Values' on page 215.



To replace a defective device fuse, proceed as follows:

1. ➔ Turn off the device and pull out the power plug.
2. ➔ Release the slot for the device fuses next to the mains connection by pressing together the two flaps and pulling out at the same time.
3. ➔ Remove the defective device fuse.
4. ➔ Insert a new device fuse with the correct number of Amperes.
5. ➔ Push the plug as far back in the opening as possible until it snaps in.
6. ➔ Restore the power supply to the device.

11.11 Behavior in Case of a Power Interruption

If the power supply to the device is interrupted during the running cultivation (e.g. by flicking the power switch or in case of a power failure), all parameter setpoints are stored. After restoring the power supply, the interrupted process is automatically continued with the last stored setpoints.

The system alarm *Restart after power failure* indicates that there has been a power interruption. However, the alarm provides no information on the duration of the event.

11.12 Returning for Repair

The provider must return the device or the faulty component part(s) to the manufacturer if, after consulting the service department of the local dealer or the manufacturer, on-site diagnosis and/or repair is not possible.



If the device, component or accessory has to be returned to the manufacturer for repair, a legally compliant declaration of decontamination is required for the safety of all parties involved and to comply with legal requirements (➔ Chapter 1.8 'Declaration of Decontamination' on page 19).

12 Disassembly and Disposal

The device must be disassembled and disposed of in an environmentally-friendly manner if it is not in use anymore.



If the device is to be returned to the manufacturer for disassembly and disposal, a legally compliant declaration of decontamination is required for the safety of all parties involved and to comply with legal requirements (→ Chapter 1.8 'Declaration of Decontamination' on page 19).

12.1 Disassembly

Prior to disassembly:

- Switch off the device and secure against reactivation.
- Physically disconnect the main energy supply from the device and wait for any components to fully discharge.
- Remove and dispose of all operating and auxiliary materials as well as remaining processing materials in an environmental acceptable manner.

Clean and disassemble component parts professionally with regard to any local regulations concerning employment and environmental protection. If possible, separate materials.

12.2 Disposal

Recycle disassembled components if no agreement is made concerning reclaim or disposal.

- Scrap metals.
- Recycle plastic components.
- Sort and dispose of the remaining components according their material composition.



WARNING

Electronic waste, electronic components, lubricants or other auxiliary materials/supplies are subject to hazardous waste regulations and may only be disposed of by registered specialist disposal firms.

Disassembly and Disposal

For disposal, the system units must be disassembled and dismantled into individual material groups. These materials must be disposed of according to the applicable national and local legislation. Local authorities or specialist disposal firms can provide information regarding environmentally acceptable disposal.

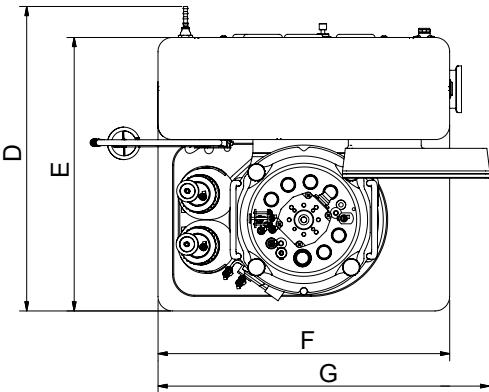
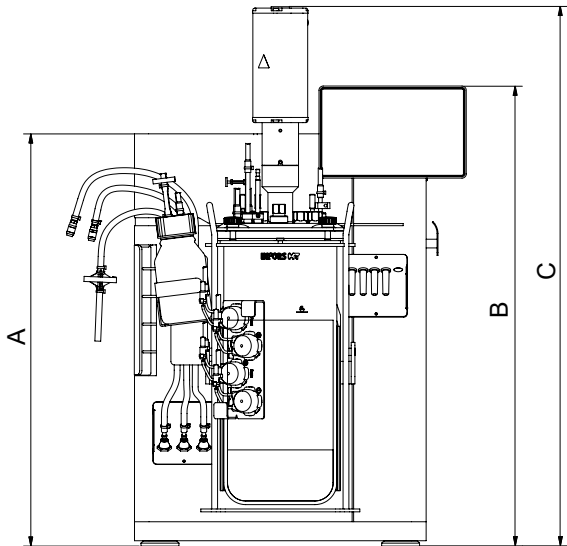
If no special arrangements have been made for return, Infors devices with the required declaration of decontamination can be sent back to the manufacturer for disposal.

Technical Data

13 Technical Data

13.1 Dimensions

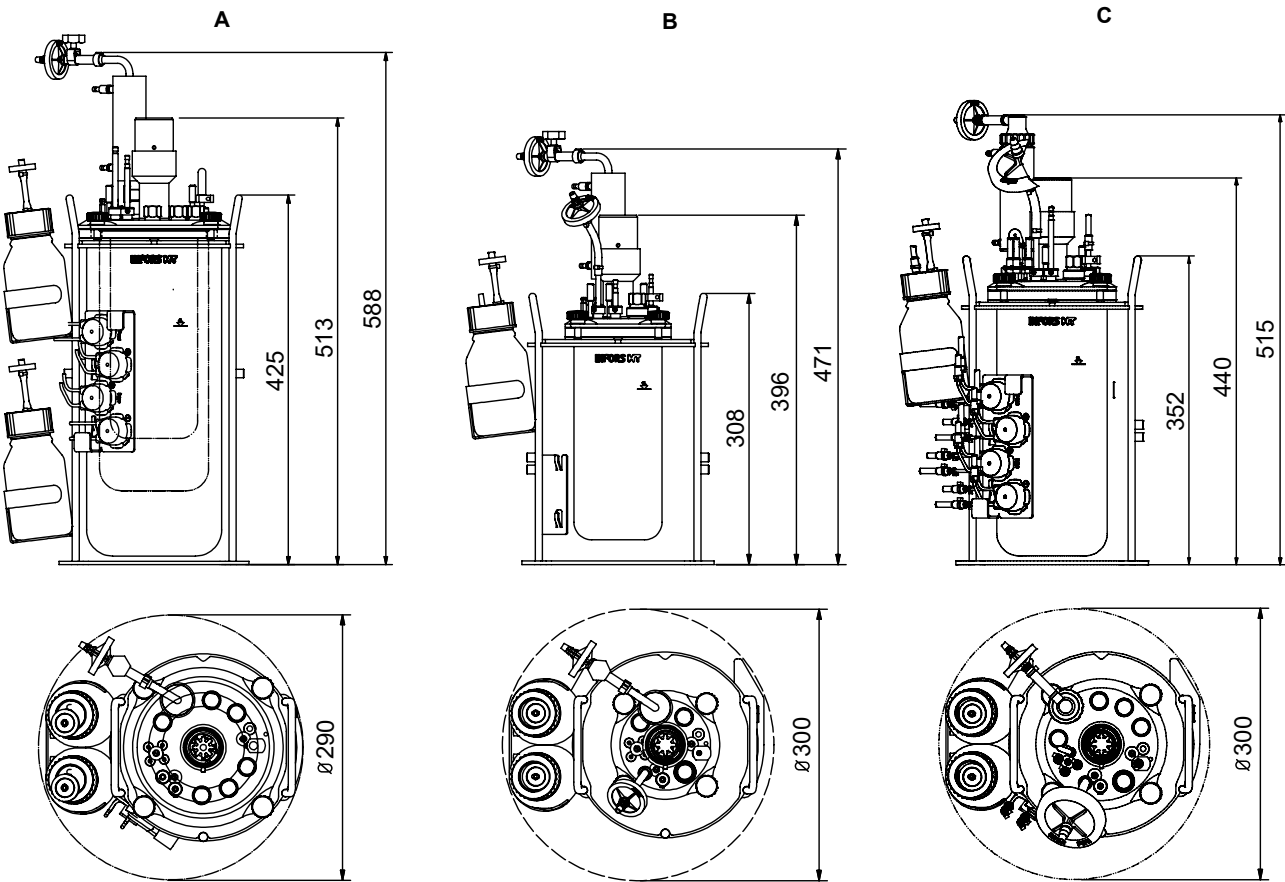
Front View and Top View Device



Pos.	Value	
A	565 mm	Both device versions
B	631 mm	
C	740 mm	Culture vessels DN 115 & DN 145 for microor- ganisms
	770 mm	Culture vessel DN 90 for microorganisms
	815 mm	Culture vessels, all sizes for cell cultures
D	415 mm	Both device versions
E	375 mm	
F	400 mm	
G	455 mm	

Technical Data

Culture Vessel



The dimension drawings (dimensions in mm) show a fully equipped culture vessel ready for autoclaving.

Pos.	Value	
A	Standard vessel holder	All culture vessels
B	Compact vessel holder	Culture vessels DN 90
C	Compact vessel holder	Culture vessels DN 115

13.2 Weight

Data	Value	Unit
Basic unit	23.5 ± 0.5	kg
Culture vessel DN 90	6.0 ± 0.5	kg
Culture vessel DN 115	7.0 ± 0.5	kg
Culture vessel DN 145	9.0 ± 0.5	kg



Equipped culture vessel, without medium, with vessel holder. The actual weight depends on design and allocation.

13.3 Connections and Connection Values

13.3.1 Electrical Connection and Power Values

Data	Value	Unit
Voltage	120/230	VAC
Frequency	50/60	Hz
Max. current	8	A
Max. power consumption ¹⁾	~ 800	W
Fuses (5 x 20 mm, slow-blown)	8	A

¹⁾ During heating phase, vessel with max. 4 L working volume, at max. rotation speed.

Technical Data

13.3.2 Water

Water Inlet Basic Unit

Data	Value	Unit
Connection pressure	2 ± 1	bar
Hose nozzle connection, nominal width	6	mm
Min. flow temperature	10	°C

Data	Value
Water quality	CaCO ₃ concentration 0 mmol L ⁻¹ to 1.5 mmol L ⁻¹

Water Outlet Basic Unit

Data	Value
Connection pressure	No backpressure

Data	Value	Unit
Hose nozzle connection, nominal width	6	mm

Technical Data

13.3.3 Process Gas

Data	Value	Unit
Constant connection pressure	2 ± 0,5	bar
Hose nozzle connection, nominal width	6	mm

Data	Value
General gas quality	Dry, clean and free of oil and dust
Recommended compressed air quality	Class 1,2,3,4 as per DIN ISO 8573-1



These specifications apply to all used gases except for the stated recommended quality of compressed air.

13.4 Specifications of the Basic Unit

13.4.1 Operating Panel

Data	Value
HMI	7" colour touch screen
Operating system	Embedded Linux
OPC server	OPC UA

13.4.2 Culture Vessel

Various

Data	Value
Operating pressure in culture vessel	Pressureless
Form	Cylindrical with flat bottom

Technical Data

Materials

Data	Value
Glass vessel	Borosilicate glass
Top plate and built-in parts	AISI 316L, electropolished ¹⁾
O-rings (in contact with product)	EPDM

¹⁾ Exception: impellers in culture vessel 1.5 L / DN 90 for microorganisms are made of PEEK.

Vessel Sizes

TV	Max. WV	Min. WV		DN	Height
		M	C		
1.5 L	1.0 L	0.3 L	0.3 L	90 mm	235 mm
3.0 L	2.0 L	0.6 L	0.7 L	115 mm	295 mm
6.0 L	4.0 L	1.1 L	1.5 L	145 mm	370 mm

Key:

- TV = Total volume
- WV = Working volume (maximum and minimum)
- DN = Nominal diameter (inner diameter vessel)
- M = Version for microorganisms
- C = Version for cell cultures



The volume markings on the glass vessels are only intended as visual aids. They do not represent precise measurements in litres.

Ports in Top Plate

Port		Quantity acc. to vessel DN		
Ø	Thread	DN 90	DN 115	DN 145
7.5 mm	None	4	4	4
10 mm	None	4	4	4
12 mm	Pg13.5	4	6	7

Technical Data
13.4.3 Stirrer
Drive General

Data	Value
Drive	Shaft with mechanical seal
Direction of rotation of drive shaft	Counter-clockwise = to left
Bearing	Outside vessel, in drive hub
Motor type	DC, brushless

Drive Version for Microorganisms

Data	Value	Unit
Nominal power of motor vessel DN 90	102	W
Nominal power of motor vessel DN 115 and DN 145	260	W
Range of rotation speed	150 to 1600	min ⁻¹
Accuracy measurement at 100 to 500 min ⁻¹	± 5	min ⁻¹
Accuracy measurement at > 500 min ⁻¹	1	% setpoint
Accuracy control	1	% Full Scale



Ranges of rotation speed are valid in liquid viscosity similar to water, without gassing, with 2 Rushton impellers.

Technical Data

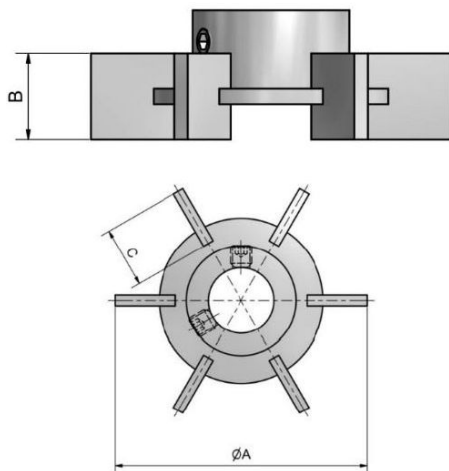
Drive Version for Cell Cultures

Data	Value	Unit
Nominal power of motor	74	W
Range of rotation speed	24 to 600	min ⁻¹
Accuracy measurement and control at 24 to 300 min ⁻¹	± 2	min ⁻¹
Accuracy measurement and control at > 300 to 600 min ⁻¹	± 4	min ⁻¹



Ranges of rotation speed are valid in liquid viscosity similar to water, without gassing, with 1 pitched blade impeller.

Impellers for Microorganisms



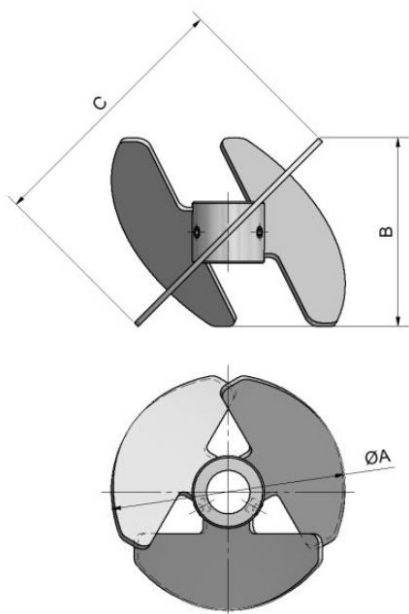
Data	Value
Type	Rushton impeller with 6 blades
Material impellers vessel DN 145 and DN 115	AISI 316L, electropolished
Material impellers vessel DN 90	PEEK

Dimensions and Quantity Impellers

Vessel	A	B	C	Quantity
6.0 L TV / DN 145	54 mm	11 mm	11 mm	2
3.0 L TV / DN 115	46 mm	11 mm	11 mm	2
1.5 L TV / DN 90	38 mm	9 mm	11 mm	2

Technical Data

Impellers for Cell Cultures



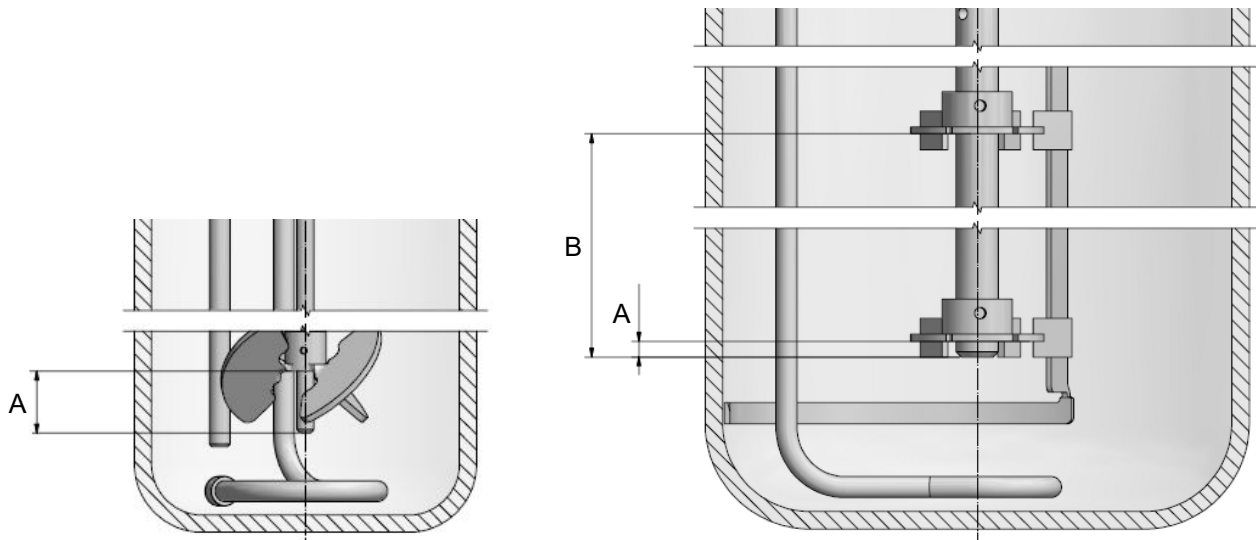
Data	Value
Type	Pitched blade impeller with 3 blades, angled 45°
Material	AISI 316L, electropolished
Flow direction blades	Standard: downwards, Option: upwards

Dimensions and Quantity Impellers

Vessel	A	B	C	Quantity
6.0 L TV / DN 145	85 mm	65 mm	90 mm	Standard: 1 Option: 2
3.0 L TV DN 115	65 mm	52 mm	72 mm	Standard: 1 Option: 2
1.5 L TV / DN 90	50 mm	30 mm	40 mm	Standard: 1 Option: 2

Technical Data

Impeller Mounting Heights ex-factory



Vessel	Pitched blade impeller	Rushton impellers	
	A	A	B
6.0 L TV / DN 145	16 mm	4.5 mm	137 mm
3.0 L TV DN 115	17 mm	6.0 mm	110 mm
1.5 L TV / DN 90	18 mm	3.0 mm	89 mm

13.4.4 Temperature Control System

Various

Data	Value
Heating	Electrical, thermal block 630 W
Cooling	Tap water ¹⁾ via thermal block and adapter
Sensor	Pt-100 class B, 1/3 DIN

¹⁾ A circulating cooler can be used instead of tap water for the cooling system.

Technical Data
Temperature Range and Accuracy

Data	Value	Unit
Measurement range	0 to 145	°C
Control range	Min. flow temperature + 5 to 60	°C
Accuracy measurement ²⁾	± 0.1	°C
Accuracy control ²⁾	± 0.2	°C

²⁾ at 20 °C to 60 °C

13.4.5 Gassing System
Version for Microorganisms

Data	Value	Unit
Gas entry	Sparger	
Specific gas flow rate, calculated for the max. working volume	8	L min ⁻¹

Gas(ses)	Flow control	Accuracy MFC
Air	2 Mass flow controllers (MFC)	± 0.05 L min ⁻¹
Air + O ₂		
Air + N ₂		

Technical Data

Version for Cell Cultures

Data	Value	Unit
Gas entry	Sparger, head space ¹⁾	
Specific gas flow rate, calculated for the max. working volume	2000	mL min ⁻¹

Gas(es)	Flow control	Accuracy MFC
Air	5 Mass flow control- lers (MFC)	± 4 mL min ⁻¹
O ₂		
N ₂		
CO ₂		

¹⁾ Air and/or CO₂ possible

Control Ranges of Gas Flow

Vessel sizes		Microorgan- isms	Cell cultures
Total volume	Max. working volume	L min ⁻¹	mL min ⁻¹
1.5 L	1.0 L	0.05 to 2.0	1.5 to 150
3.0 L	2.0 L	0.05 to 4.0	3.0 to 300
6.0 L	4.0 L	0.05 to 8.0	6.0 to 600



The mass flow controller is calibrated by the manufacturer ex-factory at standard conditions, i.e. at 1.013 bar and 20 °C. Therefore, for every gas flow rate the gas volume flow is given in L min⁻¹ and mL min⁻¹.

Technical Data

13.4.6 pH Control

Control

Data	Value
Control (via cascade)	Addition of acid and base via peristaltic pumps Acid and Base, Addition of CO ₂ ¹⁾ instead of acid possible
Control range	pH 2 to 12

¹⁾ Version for cell cultures only

Measurement System HAMILTON

Data	Value
Sensor type	Easyferm Plus ARC
Measurement principle sensor	Potential measurement against reference
Measurement range	pH 0 to 14



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

Measurement System METTLER

Data	Value
Sensor type	InPro 3253i, ISM with M100 transmitter
Measurement principle sensor	Potential measurement against reference
Measurement range	pH 0 to 12

Technical Data

13.4.7 pO₂ Control

Control

Data	Value
Control (via cascade)	Stirrer, gas flow, gas mixture (addition of O ₂ or N ₂)
Control range	0 % O ₂ -sat to 150 % O ₂ -sat

Measurement System HAMILTON

Data	Value
Sensor type	VisiPerm DO ARC / RS485-ECS
Measurement principle sensor	Optical
Measurement range	0.05 %-sat to 300 %-sat

Measurement System METTLER

Data	Value
Sensor type	InPro6860i, ISM
Measurement principle sensor	Optical
Allowed temperature range	0 °C to 60 °C
Measurement range	0 %-sat to 285 %-sat



The pO₂ sensors are preconfigured by the device manufacturer INFORS HT. Replacement sensors must be configured before use.

13.4.8 Antifoam Control

Data	Value
Sensor	Conductive with dosing needle
Control, digital	Pump 3: AF (antifoam)
Range	0 or 100 % (OFF or ON)

Technical Data

13.4.9 Pumps

Data	Value
Type	Peristaltic
Quantity	4
Control	Analogue or digital ¹⁾

¹⁾ Control (operating modes):

- Analogue = continuous operation with variable speed
- Digital = OFF/ON operation with fixed speed

Hoses

	Standard	Option 1	Option 2
Inside Ø	1.0 mm	0.5 mm	2.5 mm
Delivery rate ²⁾	3.5 mL min ⁻¹	1.1 mL min ⁻¹	16.1 mL min ⁻¹
Material	PharMed BPT		

²⁾ Typical figure with water measured at max. rotation speed

13.5 Specifications of the Options

13.5.1 Turbidity Measurement

Variant ASD12-N

Data	Value
Optical path length for higher cell densities ¹⁾	OPL05
Optical path length for lower cell densities ²⁾	OPL10

Data	Value	Unit
Measurement range absorption	0 to 4	CU

¹⁾ Version for microorganisms

²⁾ Version for cell cultures

Technical Data

Variant CGQ BioR

Data	Value
Measurement modes	Green (521 nm) or Infrared (940 nm)
Measurement range	0 to 1000

13.5.2 Exit Gas Analysis

For Aerobic Bioprocesses

Sensor type selection	Measurement range vol. % CO ₂	Measurement range vol. % O ₂
BlueInOne Ferm	0 to 10	1 to 50
BlueInOne Ferm	0 to 25	1 to 50
BlueVary with O ₂ cartridge ZrO ₂	0 to 25	0.1 to 50

For Aerobic and Anaerobic Bioprocesses

Sensor type selection	Measurement range vol. % CO ₂	Measurement range vol. % O ₂
BlueInOne Cell	0 to 10	0 to 100
BlueInOne Cell	0 to 25	0 to 100
BlueVary with O ₂ cartridge ec	0 to 25	0 to 100

13.5.3 Redox Measurement

Data	Value
Sensor type	Easyferm Plus ORP ARC
Measurement principle sensor	Oxidation reduction potential measurement against a reference

Data	Value	Unit
Measurement range	-1500 to +1500	mV

Technical Data

13.6 Operating Conditions

Data	Value	Unit
Ambient temperature	5 to 40	°C
Relative humidity, non-condensing	20 to 90	%
Altitude operating location	Max. 2000	m.a.s.l
Pollution degree as per EN 61010-1	2	
Min. distance from walls, ceilings and other equipment	150	mm

13.7 Emissions

Data	Value	Unit
Sound pressure level	< 70	dB(A)

EU Declaration of Conformity

14 EU Declaration of Conformity

EG-Konformitätserklärung

EC-Declaration of conformity

Déclaration CE de conformité

INFORS HT

Infors AG, Headoffice, Switzerland
Rittergasse 27, CH-4103 Bottmingen
T +41 (0)61 425 77 00
info@infors-ht.com, www.infors-ht.com

Gemäss der EG-Maschinen-Richtlinie 2006/42/EG, Anhang II 1 A

In accordance with directive on machinery 2006/42/EC, appendix II 1 A

D'après la directive relative aux machines 2006/42/CE 2006, annexe II 1 A

Hersteller

Manufacturer
Fabricant

Infors AG
Rittergasse 27
CH-4103 Bottmingen

Bezeichnung

Designation
Désignation

Tischbioreaktor
Bench-top bioreactor
Bioréacteur de paillasse

Typ

Type
Type

Minifors

Ab Release

From release
A partir du version

2.1

Ab Seriennummer

From serial number
A partir du numéro de série

S-000130198

Dieses Gerät entspricht den grundlegenden Anforderungen der Richtlinien

This device is in compliance with the essential requirements of directives

Cet appareil est conforme aux exigences essentielles des directives

Maschinenrichtlinie 2006/42/EG
EMV-Richtlinie 2014/30/EU

Directive on machinery 2006/42/EC
EMC directive 2014/30/EU

Directive relative aux machines 2006/42/CE
Directive CEM 2014/30/UE

Aussteller

Issuer
Editeur

Bevollmächtigter für die technische Dokumentation
Person authorised to compile the technical file
Person autorisée à constituer le dossier technique



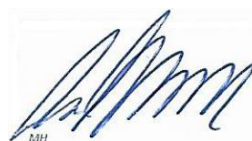
CR

C. Rutishauser

Infors AG
Rittergasse 27
CH-4103 Bottmingen

Anschrift
Address
Adresse

Konformitätsbeauftragter
Representative for conformity
Responsable de la conformité



M. Heuschkel
Chief Technology Officer

Bottmingen, 16. Nov. 2021

Ort, Datum
Place, date
Lieu, date

Digitize your bioprocesses

The platform software for your bioprocesses



eve® – the Bioprocess Platform Software

Able to do more than just plan, control and analyze your bioprocesses, eve® software integrates workflows, devices, bioprocess information and big data in a platform that lets you organize your projects in the cloud, no matter how complex they are.

Learn more at www.infors-ht.com/eve