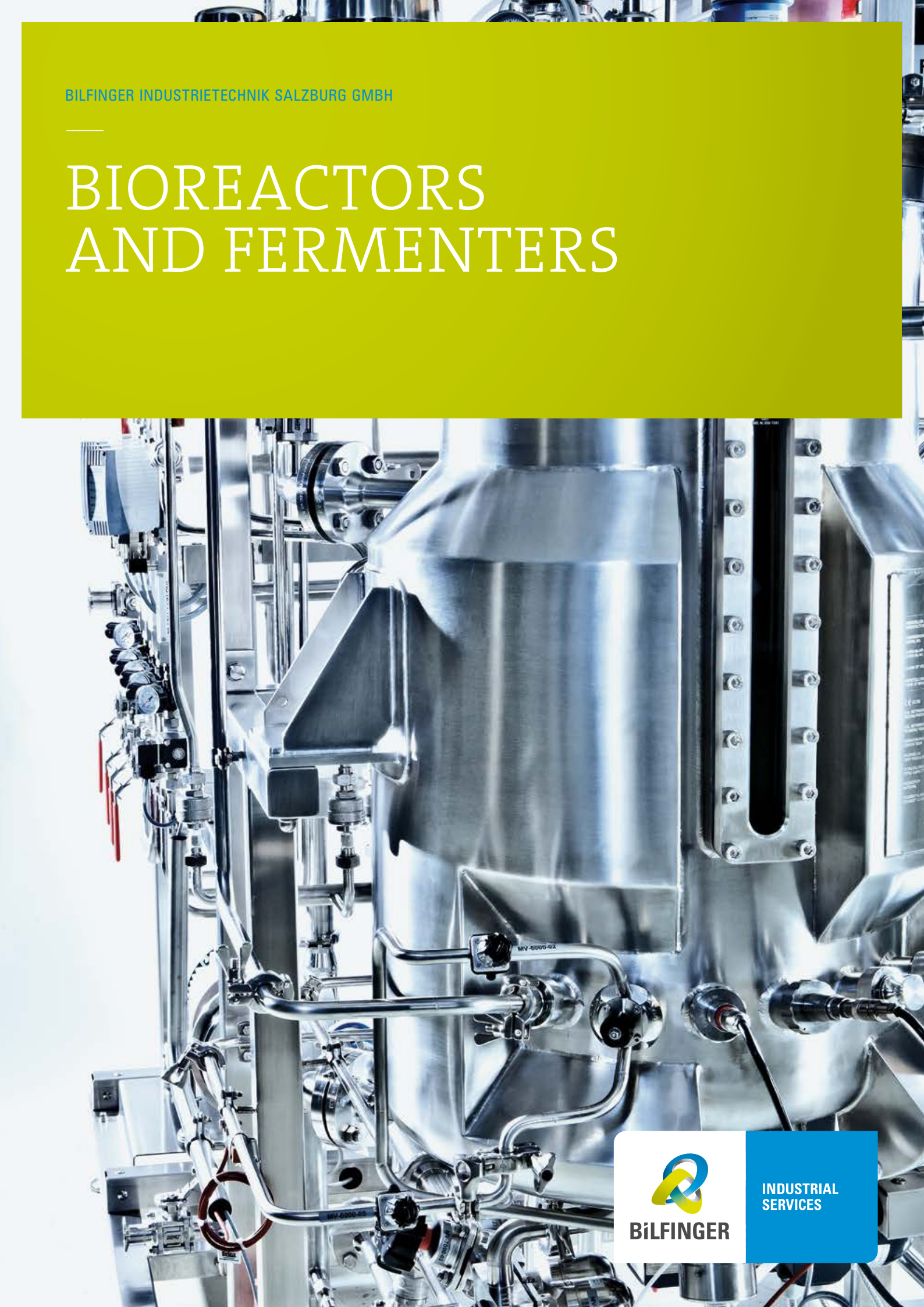
BILFINGER INDUSTRIETECHNIK SALZBURG GMBH

BIOREACTORS AND FERMENTERS



BILFINGER INDUSTRIAL SERVICES

BILFINGER INDUSTRIETECHNIK SALZBURG

At Bilfinger Industrietechnik Salzburg, we have decades of experience which we have gained from completing many successful projects. Our company was incorporated in 1955. We completed our first pharmaceuticals plant in 1964 and our first biotech plant in 1986. Our core skills cover the engineering, fabrication and construction of piping, systems and plants for the biotechnology, pharmaceuticals and fine chemicals industries.

INNOVATIVE BIOREACTOR LINE MADE BY AN **EXPERIENCED PARTNER**

Our new bioreactor line represents the essence of our expert knowledge and has been designed with utmost care taking into account the state-of-the-art sterile design. The bioreactors are equipped with modern, user-friendly E/I&C and automation. Whether for bacterial or cell culture cultivation, it offers the right solution.

Bilfinger's bioreactors incorporate the results of systematic and quality-oriented engineering. Yet, they are more than just products as we offer comprehensive services throughout their entire life cycle. This makes them an end-to-end solution.

We at Bilfinger Industrietechnik Salzburg have many years of experience in engineering, fabricating and commissioning of customer-specific and tailor-made bioprocess equipment.

Our process-oriented project management and coherent quality assurance system enables us to realize your project fully matching your specifications and to meet even challenging milestones and timelines.

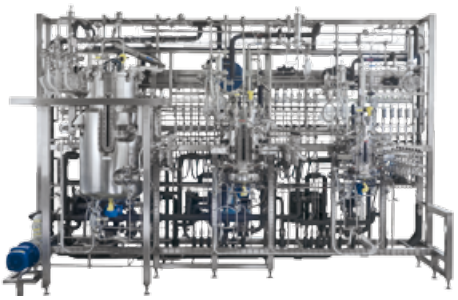
Skids and superskids are prefabricated in our factory, designed specifically for cGMP-compliant construction and applying state-of-the-art machinery and technology.

BILFINGER'S NEW BIOREACTOR LINE

DESIGN PRINCIPLE	YOUR BENEFIT
STRICTLY ACCORDING TO GMP GUIDELINES	
– Design and fabrication of piping and sterile valve arrangement in line with the 2D rule and thus avoiding dead-ends – Fully self drainable pipes – Temperature monitoring in relevant condensate pipes – Separate automatic sterilisation and CIP of the supply air and exhaust air groups	– Guaranteed sterility – also for long processes – Recording of sterilisation processes – Increased process safety: filters can be changed during operation
SKID DESIGN	
The bioreactors are manufactured in Salzburg, tested comprehensively and shipped to clients around the world as a unit.	– Short and unproblematic start-up and site acceptance test (SAT)
MODULAR SYSTEM	
The modular system provides the basis for configuring the bioreactor. This involves combining basic functions in assembly groups for which preconfigured engineering modules are available.	– The customer adapts the bioreactor to his/her specific needs – Optional or alternative configurations or individual configurations can be easily implemented – Short delivery periods
STATE-OF-THE-ART COMPONENTS	
We use commercial-grade, high-quality, industrial-standard components.	– State-of-the-art technology – Reliable during operation
USER-FRIENDLY DESIGN	
The bioreactor has been developed from the user's perspective in every respect.	– Optimum ergonomics and serviceability

LABQUBE

PILOTQUBE



PROQUBE

MODULAR SYSTEM FOR BIOREACTORS AND FERMENTERS

SUPPLY AIR GROUP

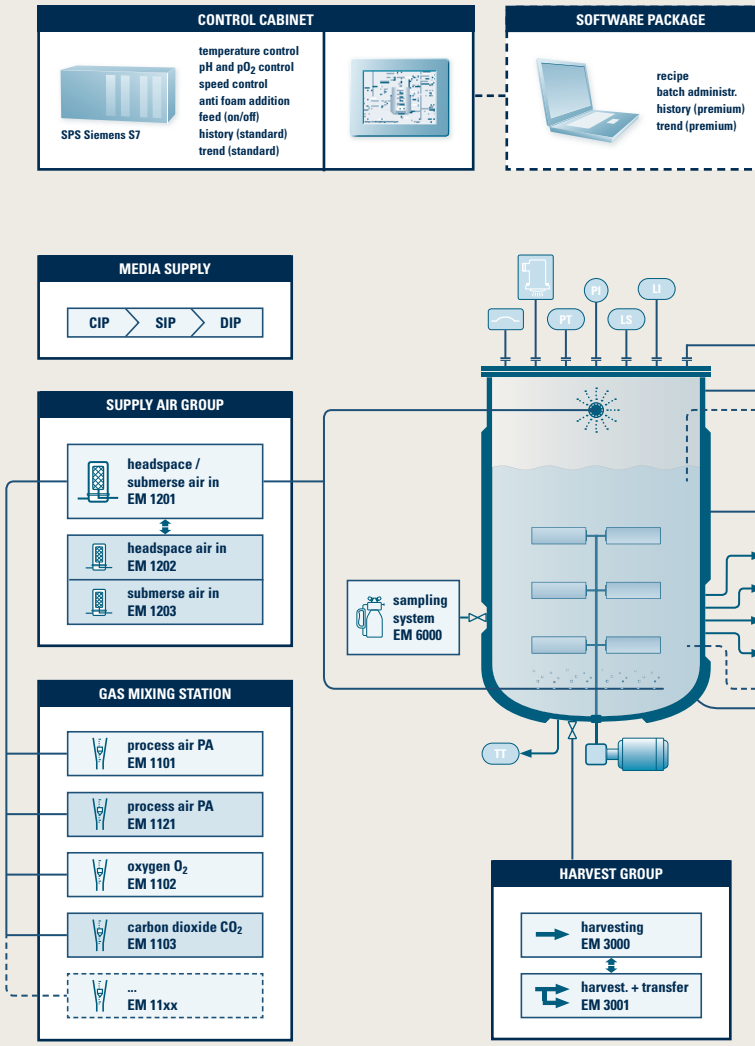
The gases can be introduced via the headspace and/or as submerse aeration via a ringsparger or frit into the bio-reactor. The submerse and headspace aeration systems are both equipped with individual sterile filters and corresponding piping and can be sterilised and cleaned as separate units.

GAS MIXING STATION

The gas mixing station permits the introduction of specific gas flows, such as CO_2, O_2, N_2 and air. The required volume of gas can be set by means of massflow controllers.
The adjustment of pO_2 and pH levels is possible via the corresponding gas flows.

SAMPLING SYSTEM

Sampling and the sterilisation of the valve is done manually. Various options are possible, such as CIP function, automatic operation or a closed sampling system in glass bottles.

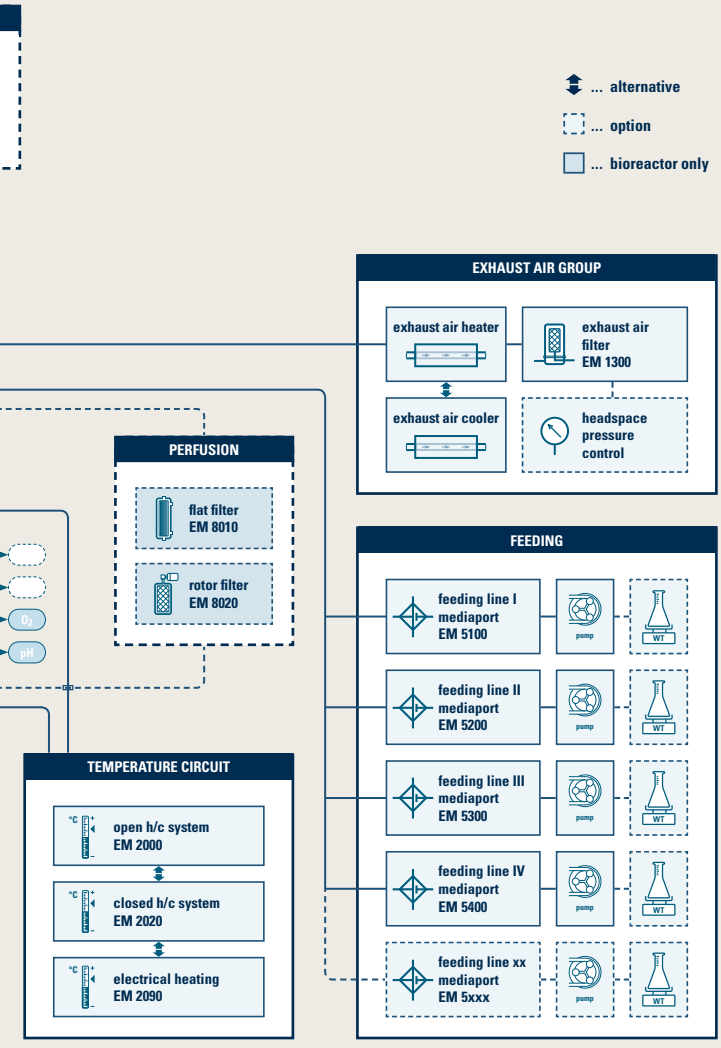


HARVEST GROUP

The bottom drain valve is SIP-ready. Optionally, the harvest group can be fitted with a valve configuration for sterile transfer. A CIP function of the valve and the transfer pipe is also optional.

TEMPERATURE CIRCUIT

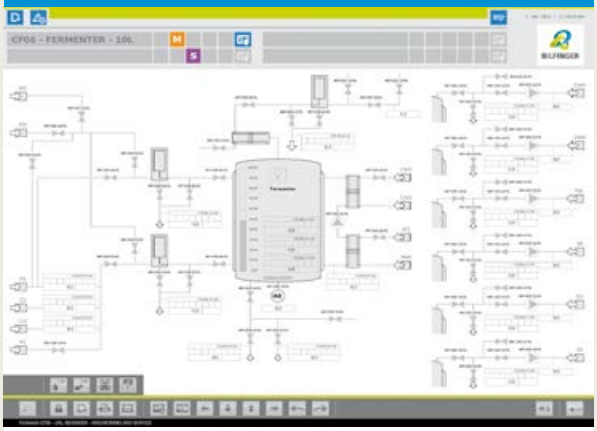
Depending on the size of the vessel, either an open or closed system with a separate expansion vat is used. The temperature of the content of the vessel is subject to follow-up control. For this purpose, the sensor inside the vessel is the main regulator for the temperature sensor in the temperature circuit.



FEEDING

Three feeding lines permit the precise addition of media or corrective reagents such as alkali or antifoam agents. A further feeding line allows the inoculum to be added to the vessel. All feeding lines are SIP-ready together with the system as a whole and also individually without any interruption to the ongoing fermentation process. Sterilisation is monitored via the temperature sensors. All feeding lines are CIP-ready and are each equipped with a peristaltic pump.

CONTROL SOFTWARE



The bioreactors are equipped with an automation solution based on Siemens process control products. HMI software PCS 7 flexible and automation software Step7 are used.

- Configuration of time-dependent set-point profiles
- Real-time trend visualization
- Alarm handling based on PCS 7 flexible messaging module
- Management, visualization and historical process data
- Fully automatic sequences for SIP, CIP, pressure test and operation sequences such as submerse aeration, headspace/submerse aeration, etc.

EXHAUST AIR GROUP

The exhaust air group permits the heated and/or cooled removal and filtering of exhaust gases. In addition, there is a connection for exhaust air analysis. An optional module also allows the headspace pressure to be regulated. The exhaust air group can be sterilised and cleaned separately from the bioreactor vessel.

AUTOMATION

Process	■ batch ■ continuous	■ fed-batch
SIP	■ automatic	▫ manual
Control system	■ temperature control ■ pH control ■ foam detection ■ stirring speed control ■ history (standard) ▫ software package: recipes, batch administration, history (premium), trend (premium), laptop optional	■ pO_2 control ■ level control ■ feed (on/off) ■ visualisation ■ trend (standard)
Hardware	■ 15“ Touch Multipanel ■ with Profinet and Profibus interface	■ Simatic S7
Programming	■ ANSI / ISA-88	▫ GAMP5

VESSEL

	LABQUBE	PILOTQUBE	PROQUBE
Working volume	15 - 100 l	100 - 1000 l	≥ 1000 l
H:D ratio	■ 2:1	■ 3:1	
Guidelines	■ PED (AD-2000)	▫ ASME	
Material requirements	■ AISI 316L	▫ 1.4435	
Surf. spec. (interior)	■ Ra < 0,6 µm, electropolished	■ Ra < 0,8 µm, electropolished	
Operating values	■ pressure min/max: -1 / 3 barg	■ temperature min/max: 5 / 150 °C	
Double jacket	■ -1 / 6 barg		
Insulation	■ insulation jacket		
Accessories	■ sparger ■ vortex breaker ■ dip tube ■ manometer	■ ring sparger ■ longitudinal inspection glass ■ bursting disk ▫ lid opening device, automatic	

E/I&C

Pressure	■ PT: pressure transmitter	▫ headspace pressure control
Level	■ LT: level by guided radar ▫ LT: ball float type	▫ LT: differential pressure
Safety	▫ bursting disk monitoring	
Detection	■ AF: foam detection	▫ LS: high level detection
Analysis	■ pH measurement ■ pO_2 measurement	▫ pH measurement II ▫ pO_2 measurement II ▫ biomass
Others	■ stirrer speed detection ▫ vessel weight ▫ exhaust gas analyzer ▫ conductivity measurement CIP final rinse	■ temperature transmitter ▫ platform balance for feedings ▫ flow meter

GAS MIXING STATION

Gases	■ process air ■ oxygen	■ N_2 ■ CO_2
Accessories	■ mass flow controller (4 pcs.)	■ mass flow controller (2 pcs.)

■ standard specification ▫ optional / alternative ■ standard specification - bioreactor only ■ standard specification - fermenter only

SUPPLY AIR GROUP

Filter	■ sterile filter 0,2 µm (2 pcs.) ■ connections for filter integrity test	■ sterile filter 0,2 µm (1 pc.)
Cleaning / Sterilisation	■ CIP ■ temperature transmitter	■ SIP

EXHAUST AIR GROUP

Heat exchanger	■ exhaust air heater	▫ exhaust air cooler
Filter	■ sterile filter 0,2 µm	■ connections for filter integrity test
Cleaning / Sterilisation	■ CIP ■ temperature transmitter	■ SIP
	■ connection for exhaust gas analysis	▫ additional parallel filter

SAMPLING SYSTEM

Valve	■ manually operated	▫ automatic
Cleaning / Sterilisation	▫ CIP	■ SIP
Type	■ open sampling system	▫ closed sampling system

HARVEST GROUP

Configuration	▫ transfer line	
Cleaning / Sterilisation	▫ CIP ▫ temperature transmitter	■ SIP

TEMPERATURE CIRCUIT

Configuration	■ closed circuit ▫ electrical heater	▫ open type with direct cooling

FEEDING

Feeding line 1	■ peristaltic pump (pulsation mode) ▫ glass bottle with disk filter ■ CIP	▫ analog version ■ SIP
Feeding line 2	■ peristaltic pump ▫ glass bottle with disk filter ■ CIP	▫ analog version ■ SIP
Feeding line 3	■ peristaltic pump ▫ glass bottle with disk filter ■ CIP	▫ analog version ■ SIP
Feeding line 4	■ peristaltic pump ▫ glass bottle with disk filter ■ CIP	▫ analog version ■ SIP
	▫ needle connection	

PERFUSION (OPTIONAL FOR BIOREACTOR)

■ flat filter ▫ rotor filter ■ connectable over sampling and feeding ports ▫ separate port for perfusion	

CONTACT US FOR YOUR OWN INDIVIDUAL OFFER!

The Bilfinger modular system is structured in such a way that individual specifications can be implemented swiftly and simply. We will be pleased to provide you with a quote for the bioreactor tailored to your specific requirements.

ASSISTANCE THROUGHOUT THE ENTIRE LIFE CYCLE

Assured quality from the outset

Systematic quality assurance is guaranteed in accordance with our HSEQ (health-safety-environment-quality) system throughout all stages of the process. Bilfinger Industrietechnik Salzburg is a company certified in accordance with ISO 9001 and SCC** (Safety Certificate for Contractors).

Factory acceptance test (FAT)

In addition to quality assurance during the production process, we perform systematic and comprehensive factory acceptance testing prior to delivery of the system to ensure compliance with all requirements specified and issue the corresponding qualification documentation. After the FAT has been successfully completed, the system is prepared for shipment, packed carefully and transported to the customer by selected logistics partners.

Insertion and installation

On request, the system will be inserted and installed under the supervision of Bilfinger Industrietechnik Salzburg. If necessary, we can handle all of the on-site activities and ensure that the bioreactor is fully integrated in the entire production environment.

Start-up and site acceptance test (SAT)

After the system has been successfully reassembled and installed, we start up the process and ensure that the individual sub-systems are integrated correctly. The SAT confirms that the system has been started up correctly.

Qualification

On request, we perform DQ, IQ and OQ and issue full documentation in accordance with cGMP requirements. Qualification is closely linked with project management in the interests of achieving balance between time/cost minimisation and the design requirements stipulated by cGMP.

Services

With our comprehensive range of services, we ensure that the system operates perfectly. Customer proximity and uncomplicated support are very important to us in this regard – and are made possible by having company-owned subsidiaries in Austria, Germany and Switzerland as well as numerous locations of the Bilfinger Group and agencies in many countries. Our service contracts cover servicing, inspection and maintenance, delivery of spare parts and consumables, calibration, passivisation and de-rouging.

Engineering &
Technologies

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