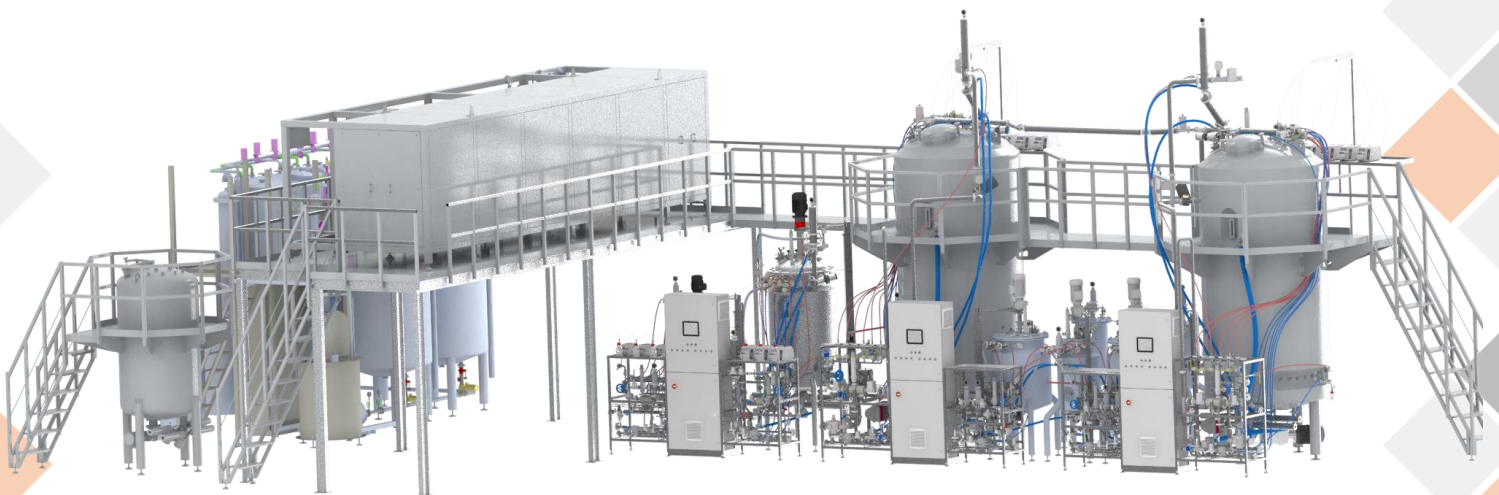




# PILOT & INDUSTRIAL BIOREACTORS


## PRODUCT BROCHURE



**Bioreactors.net AS**

 Dzerbenesstr. 27, Riga, Latvia, LV1006

 +(371) 6755 35 18

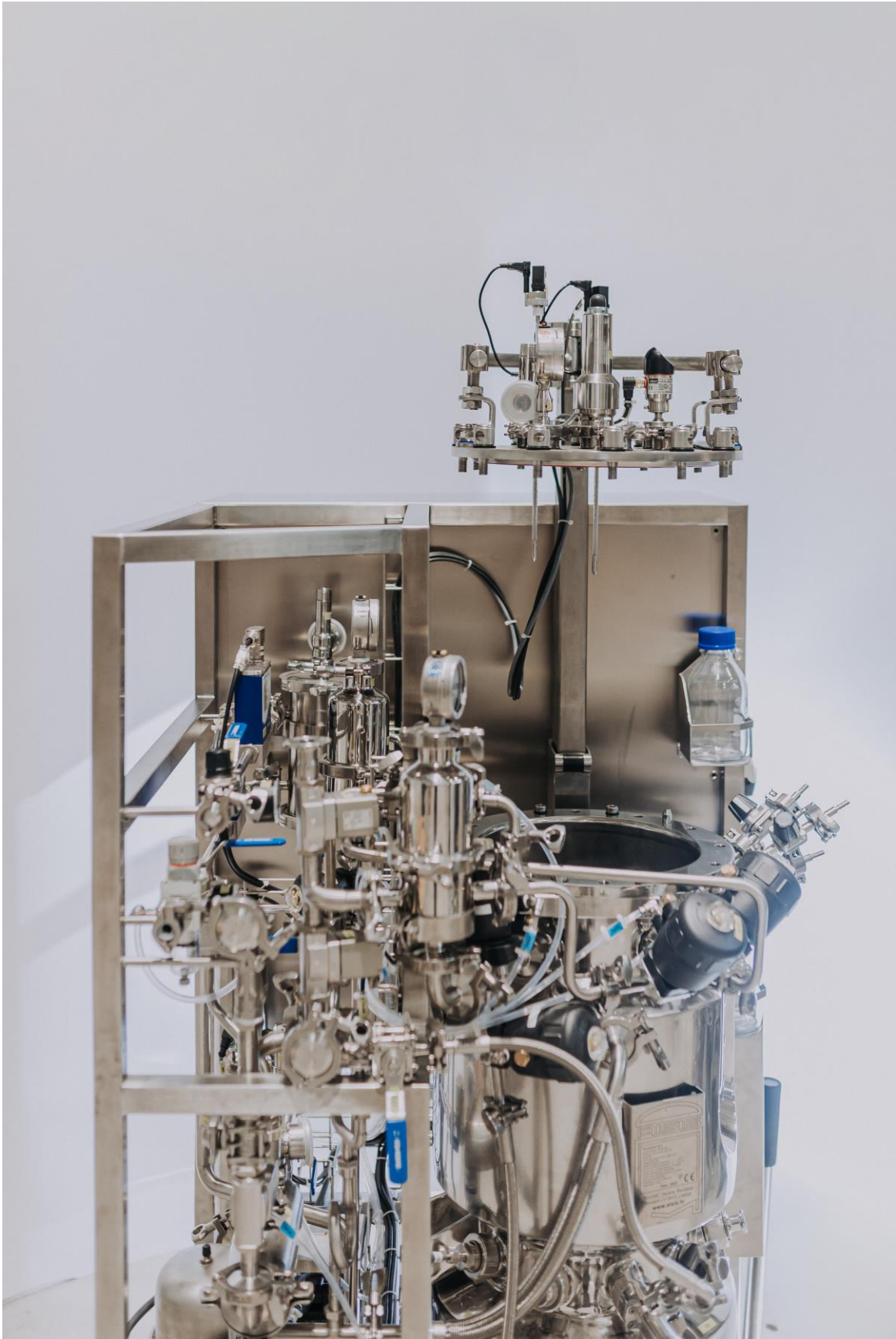
 [info@bioreactors.net](mailto:info@bioreactors.net)

 [www.bioreactors.net](http://www.bioreactors.net)



# TABLE OF CONTENTS

1. INTRODUCTION .....	5
2. PILOT SCALE BIOREACTORS.....	6
2.1 TECHNICAL SPECIFICATION .....	7
3. INDUSTRIAL BIOREACTOR LINES.....	10
3.1 Applications of stainless-steel vessels.....	12
4. AUTOMATED CIP EQUIPMENT.....	13
4.1 MOBILE CIP EQUIPMENT.....	14
4.2 STATIONARY CIP EQUIPMENT.....	15
5. APPLICATIONS AND PAST EXPERIENCES .....	16



# 1. INTRODUCTION

---

Welcome to our innovative company, where we specialize in the design and manufacture of laboratory and pilot scale bioreactors. **Our state-of-the-art bioreactors are equipped with the latest technologies, including model-based control of fed-batch fermentation and a novel magnetic drive,** resulting in innovative solutions that meet up-to-date requirements.

At our laboratory, **we test our new bioreactor solutions through real fermentation processes to ensure their reliability and performance.** Our bioreactors have been designed to be easily adapted to a wide range of applications, and we manufacture laboratory bioreactors for the cultivation of bacteria, mammalian cells, and micro-algae, using a common basic solution.

We also manufacture pilot scale bioreactors made of components such as vessels, technological stands, and control cabinets, and each of these can be supplied as a separate product. **With extensive experience in implementing our pilot scale bioreactors in fully automated production lines** for various applications, such as vaccines, enzymes, bio-fertilizers, and bioremediation, we have installed production facilities with up to 15 bioreactors, using volumes up to 20 m<sup>3</sup>.

**Our bioreactors are equipped with novel magnetic coupling mixers and ensure compliance with GMP rules by using SCADA software according to the requirements of CFR Title 21 Part 11** from the US Food and Drug Administration. We also provide our equipment with IQ (Installation Qualification) and PQ (Performance Qualification) to ensure top-quality performance.

Join us and discover the innovation behind our bioreactors, where quality and performance meet the highest standards.

## 2. PILOT SCALE BIOREACTORS

We provide a wide range of stainless-steel bioreactors, starting from 10 liters going up to 50,000 liters. Additionally, we offer bioreactor lines that include other technological vessels.



An autonomous bioreactor is comprised of three essential components:

- The bioreactor vessel equipped with an agitator
- The technological skid
- The control cabinet, which includes a Process Logic Controller (PLC).

## STAINLESS STEEL BIOREACTORS FOR MICROBIOLOGY AND CELL CULTURES

Vessel design	<p><b>Jacketed with heat insulation.</b> Removable lid (up to 800 liters). The hydraulic lifting device of the lid.</p> <p><b>Vessels over 800 liters have manhole of corresponding size.</b> Side glass on the lid and in the upper cylindrical part of the vessel.</p>
Total volume (L)	15 – 50 000 (customized)
Working volume (L)	10 – 35 000 (customized)
H/D range	1,1 – 3,2 (customized)
Surface quality	<p><b>Inner vessel wall:</b> surface roughness lower than 0.63 µm.</p> <p><b>Outer vessel wall:</b> surface roughness lower than 0.8 µm (passivated).</p>
Materials	<ul style="list-style-type: none"> <li>• The material of the parts, in contact with the product is <b>stainless steel 316L</b>;</li> <li>• For parts, not in contact with the product (e.g., the jacket) – stainless steel 304;</li> <li>• O-ring gaskets and membranes in contact with the product – <b>EPDM, Silicone, Viton, PTFE</b></li> <li>• <b>Insulation</b> – chlorine free mineral wool;</li> <li>• <b>Sight glass</b> – borosilicate glass;</li> <li>• <b>Peristaltic pump tubing</b> - platinum cured silicone</li> </ul> <p>All bioreactors have insulation over the jacket. The outside surface of insulation is covered by stainless steel 304</p>
Pressure and temperature	<p>For all vessels the <b>maximal design pressure inside the vessels – 3.5 bar</b>, in jacket –4.0 bar (can be customized).</p> <p><b>Maximal temperature - 135 °C.</b></p>

### AGITATION, AERATION

Mixing	<p><b>Novel magnetic coupling mixing</b> with top- or bottom placed motor with reduction gear.</p> <p><b>For microbial cultures</b> 2 – 4 standard Rushton turbine type agitators are used for mixing media. To improve oxygen transfer rate an extra agitator can be added.</p> <p><b>Optionally pitched blade or marine impellers</b> for shear sensitive conditions, and special agitators for viscous media.</p> <p>Mixer rotation speed maximal range (for standard Rushton turbine mixing system, can be customized):</p> <p><b>Mixing speed depends on the design and size of the mixer</b></p>
--------	--

Aeration	<p>The aeration system may be configured for both microbial and cell culture, and includes:</p> <ul style="list-style-type: none"> <li>• Filter-Reducer with pressure gauge to set up supplied air pressure;</li> <li>• <b>Flow switch or MFC</b> for measuring supplied air flow in the range of 0 - 2 vvm (volume of air per volume of fluid per minute);</li> </ul> <ul style="list-style-type: none"> <li>• <b>Chemically inert PTFE membrane filter cartridges</b> which are inherently hydrophobic used as air and gas-sterilizing filters for incoming and outgoing air. Filters are installed in the steam sterilizable stainless-steel housings;</li> <li>• <b>Automatic gas flow control system</b> (e.g., O<sub>2</sub>, N<sub>2</sub>, CO<sub>2</sub>, NH<sub>3</sub>) using a mass flow controller (the MFC) (optional);</li> <li>• <b>The measurement of the O<sub>2</sub> / CO<sub>2</sub> concentration ratio</b> in the exhaust air (optional);</li> <li>• <b>Automatic pressure control system</b> in the fermenter vessel, mounted on the exhaust gas line (optional)</li> </ul>
<b>CONTROL</b>	
Automation	Siemens Simatic S7 - 1500 series PLC. Touch panel 15" TFT, 1024 x 768mm, 262k colours
Frame	Stainless steel power cabinet
Communication	Profinet connection to LAN or WAN
Sensors (basic)	Temperature, pH, pO <sub>2</sub> , foam, alarm level, pressure
Sensors (optional)	Optical density, pCO <sub>2</sub> , O <sub>2</sub> / CO <sub>2</sub> gas analyser, redox potential, methanol, integrated weighing system.
Control of fermentation and sterilization processes	<p>The following processes and parameters are controlled:</p> <ul style="list-style-type: none"> <li>• Temperature, pH, pO<sub>2</sub> (according cascade control), foaming, high level, inlet air or gas flow, overpressure (optional), methanol (optional) and ethanol (optional) concentrations;</li> <li>• Substrate feeding according to adjusted profiles (optional)</li> <li>• Fully automated sterilization in place of empty and filled (with substrate) vessel, including the sterilization of inlet and outlet filters, and cooling of vessel after sterilization.</li> </ul>





### 3. INDUSTRIAL BIOREACTOR LINES

Bioreactors.net has an extensive experience in developing complex bioreactor systems for biotechnological production.

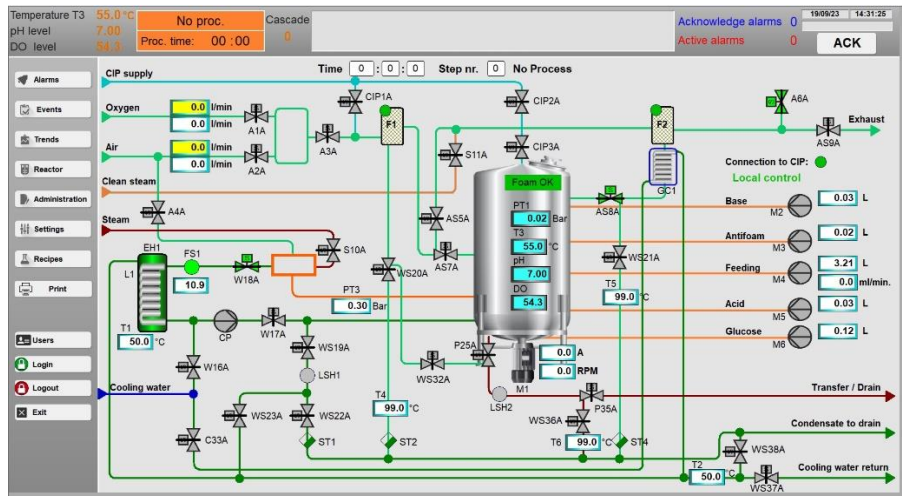
#### Wide range of fully automated bioreactors

#### From 10L to 50 000L reactors

Fully automated systems:

PLC Siemens Simatic ET200SP series (S7-1500) Based automation provides full automation of :

- Pressure hold test
- Vessel sterilization and filter sterilization
- Fermentation and temperature maintenance
- Temperature, pH, Dissolve Oxygen, Foam control, Pressure control
- Stirrer rotation speed
- Level and volume measurements with a help of hydrostatic pressure sensors
- Feeding rate according to feeding profile

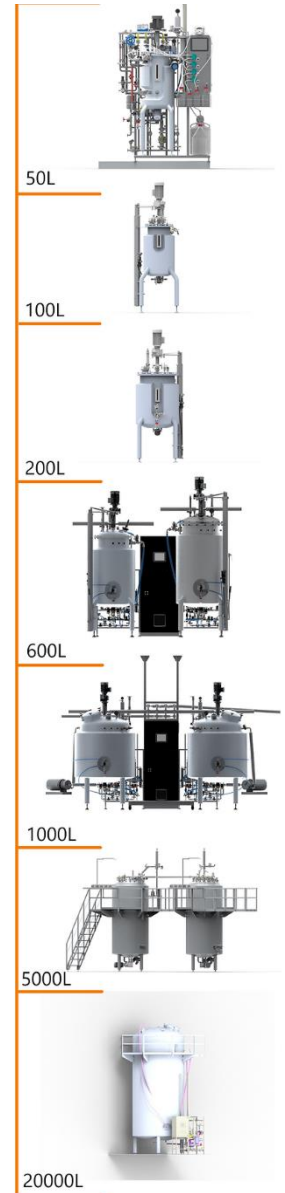


With integrate CIP (Clean-in-Place) module it is possible to automate

- Vessel rinsing with water
- Acid treatment of vessel
- Base treatment of vessel and rinsing

Full cycle service:

- Development of vessels engineering (modelling, Layouts, circuit wiring etc.)
- Programming controllers (PLC) and visualisation systems (SCADA);
- FAT (Factory acceptance test) DQ (Design Qualification), IQ/OQ (Installation/Operational Qualification);
- Installation and cabling of reactors and electrical equipment at site;
- SAT (Site acceptance test), PQ (Performance qualification);
- Staff training



# Industrial Bioreactor Order Process

## Timeline

### Start



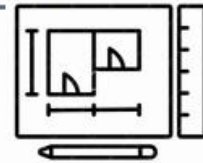
#### Offering & Contracting Order

We produce a custom offer, agree on the specifications and requirements from the client. Revise and agree upon deliverables, agree upon contract which is signed by both parties

### Layouts & Process Description

Physical bioreactor and supplementary equipment location in your facility, process nuances and other details are exchanged between your engineers and the ones on our side

### 1.Phase



### 2.Phase



#### Engineering, Design & Revision

We produce a 3D representation of your devices and layouts. Together we communicate and revise all the critical details of the bioreactors

### Manufacturing & Programming

The manufacturing takes place and the reactors are manufactured, control programs are developed, documentation prepared & certification process initiated

### 3.Phase



### 4.Phase



#### Factory Acceptance Test (FAT, DQ, IQ/OQ)\* & Delivery

We thoroughly test the produced equipment in our facility to make sure that everything works as expected. After the test is passed, we carefully pack the equipment and deliver it to end-user.

- DQ (Design Qualification), IQ/OQ (Installation/Operational Qualification)

### Assembly & Site Acceptance Test (SAT & PQ)

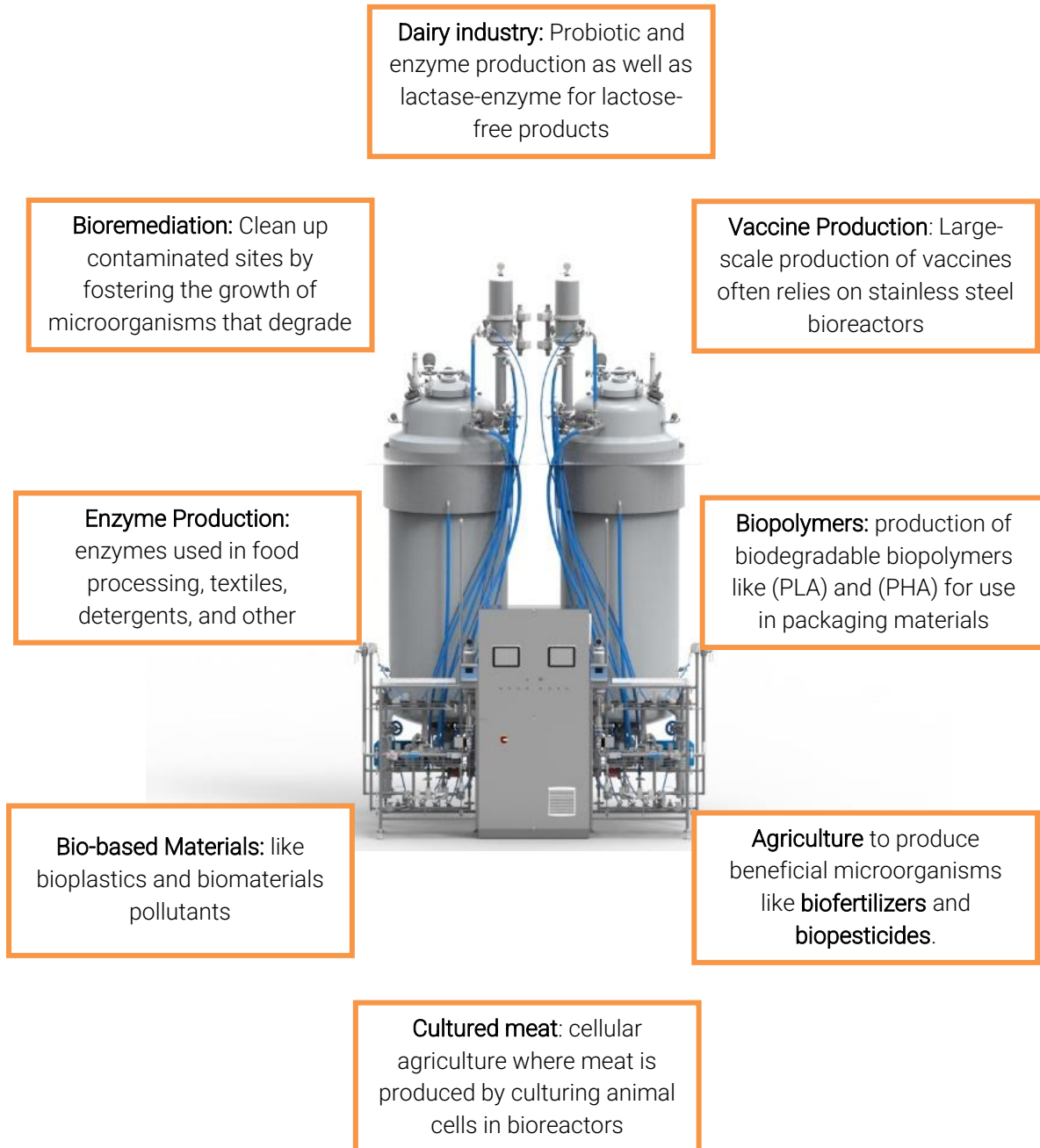
When the bioreactors have arrived on site then the devices are assembled and site acceptance test (SAT) is performed with process of choice to ensure that the equipment is fully operational. PQ (Performance Qualification) is optional

### Finish



Each order is individual and we accommodate our process and timeline accordingly to each order.

**Stainless-steel bioreactors have a wide range of uses and are tailor-made for each specific process.**

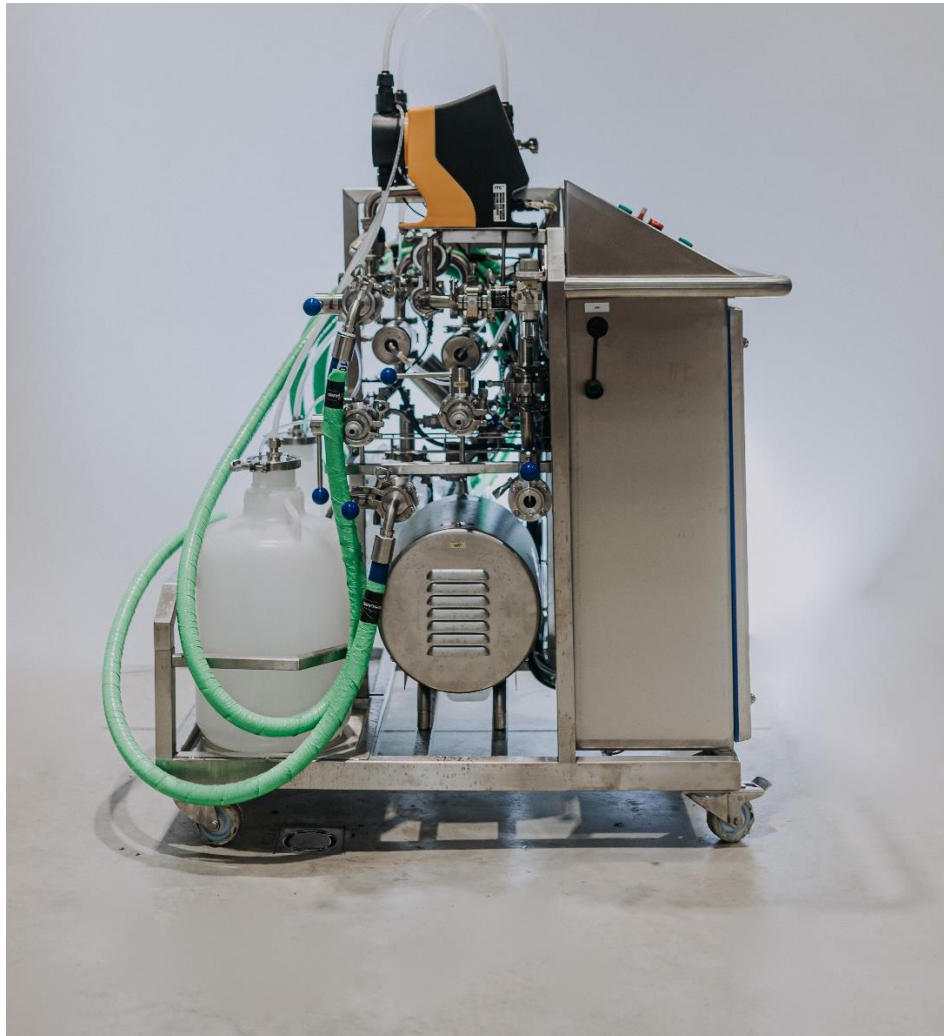


## 4. AUTOMATED CIP EQUIPMENT

We have a selection of CIP (Cleaning-in-Place) equipment available in two different types:

- Mobile CIP equipment
- Stationary CIP equipment

Our CIP equipment is designed to provide efficient and effective cleaning solutions for various industrial and commercial applications.



This CIP (Cleaning-in-Place) system is designed to be mobile and can be easily moved between production units. It can be connected to fermenters or other technological vessels and can achieve a maximum detergent circulation speed of 5000 L/h, ensuring fast and efficient cleaning.

The system includes:

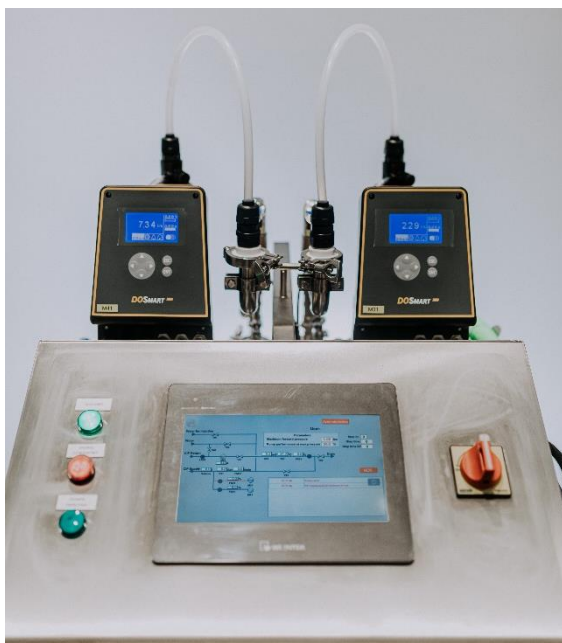
- self-priming pump for CIP circulation and discharge
- 2 dosing pumps
- A control cabinet
- Valves for manual and automatic control

This configuration allows for the effective cleaning of fermenters and other equipment with total volumes ranging from 20 up to 1000 litres.

## 4.1 MOBILE CIP EQUIPMENT

This CIP installation is capable of using both manual and fully automatic cleaning modes. For automatic control, the CIP cleaning mode must be adjusted or selected, which can be done through the control cabinet.

The CIP cleaning mode consists of multiple stages, with each stage divided into several steps that use selected parameters such as temperature, time for CIP cleaning and discharge output, detergent conductivity, speed of concentrate supply, mixer rotation speed, CIP cleaning pump productivity, and cleaning duration.



Automatic control is achieved by adjusting or selecting the CIP cleaning mode through the control board.

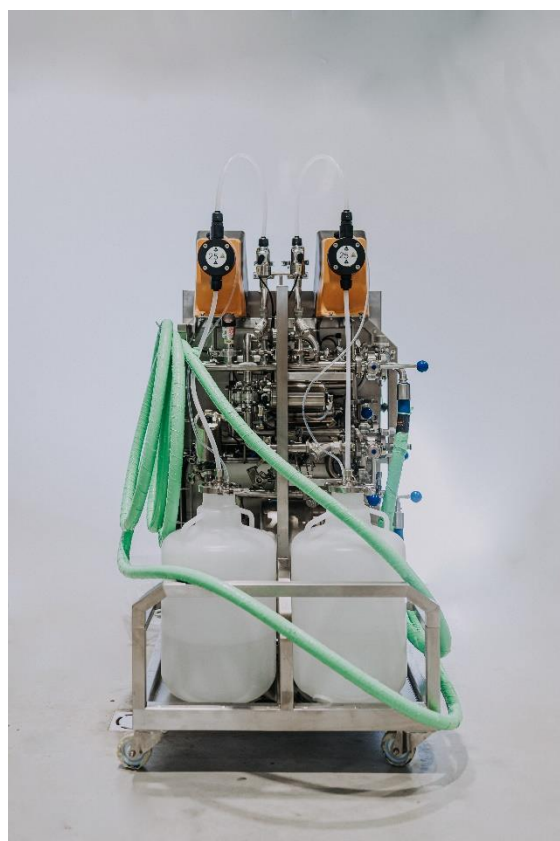
The CIP cleaning mode consists of multiple stages, with each stage divided into several steps that use selected parameters such as temperature, time for CIP cleaning and discharge output, detergent conductivity, speed of concentrate supply, mixer rotation speed, CIP cleaning pump productivity, and cleaning duration.

These parameters are carefully selected to ensure an effective and thorough cleaning process.

In automatic mode, the following CIP cleaning operations can be performed:

- Preliminary rinsing
- Cleaning with alkaline detergent
- Rinsing
- Cleaning with acidic detergent
- Final rinsing

Customized operations can also be implemented to suit specific cleaning requirements. This CIP installation can operate in both manual and fully automatic cleaning modes. Automatic control is achieved by adjusting or selecting the CIP cleaning mode through the control board.



## 4.2 STATIONARY CIP EQUIPMENT



operator panel or SCADA system.

The CIP/SIP processes are fully automated, but can also be controlled manually if required for any reason.

The automatic CIP/SIP process is carried out based on the selected recipe that includes stages and steps with corresponding parameters. Each cleaning phase consists of a specific sequence of steps, which may vary depending on the selected cleaning mode.

In automated mode, the following phases can be performed:

- Preliminary rinsing with cooled water;
- Preliminary rinsing with hot water;
- Cleaning with alkaline detergent;
- Rinsing with cooled water;
- Cleaning with acidic detergent;
- Final rinsing with cooled water;
- Final rinsing with injection solution;
- Cleaning and sterilization of pipelines.

It is possible to add a new phase as per specific production requirements. The parameters of each phase can be adjusted to ensure optimal working of CIP/SIP.

The stationary CIP equipment is customized according to the specific requirements of the production process. This equipment is designed for CIP/SIP cleaning of bioreactors, other technological vessels, and pipeline connections. Customized CIP/SIP systems can be installed with more than one vessel, providing versatility and flexibility in the cleaning process.

The stationary CIP/SIP equipment has two working modes: cleaning and sterilization. These regimes can be adjusted either from the operator panel or by using the SCADA system, providing an efficient and user-friendly interface for the operator.

There are two ways to carry out CIP/SIP processes:

- 1) Locally, through direct control from the operator panel of the CIP/SIP equipment;
- 2) Centrally, by remote control from an



## 5. APPLICATIONS AND PAST EXPERIENCES

### SUBSTANCES FOR BIOREMEDIATION OF SOIL FROM OIL POLLUTION

This fermentation system is designed for the bioremediation of soil that has been contaminated with oil over a long period. The system utilizes a bacterial consortium that has been cultivated from oil-contaminated soil.

The fermentation system is composed of bioreactors with capacities of 30, 100, and 800 liters. An additional 800-liter reactor is used for storing substrate.



### ENZYMES FOR DAIRY INDUSTRY

The bioreactor system described below is specifically **designed to produce ferments used in the dairy industry**. The system utilizes microorganisms such as *Lactococcus lactis*, *Streptococcus thermophilus*, and *Candida* strains.

The **system includes seeding-fermenters** with working volumes of 10 and 100 liters, and **one production fermenter** with a working volume of 1000 liters.

Additionally, three vessels with volumes of 100, 150, and 1000 liters are utilized for medium preparation, aseptic technological solution, and product storage. All fermenters are connected via pipelines to create a technological line which can be cleaned and sterilized using CIP/SIP equipment



### VACCINES FOR ANIMALS

**Two state-of-the-art bioreactor lines designed specifically for the cultivation of mammalian cells** used in the production of vaccine preparations for farm animals. Our fully closed system is comprised of the following key elements:

Two identical manufacturing lines, each equipped with bioreactors of varying volumes: 20, 100, 500, and 3000 liters.





## PROBIOTICS FROM WHEY LACTOSE

Bioreactors that utilize whey lactose as a nutrient medium for producing probiotics.

**Main equipment configuration of the fully automated system:**

- Bioreactors with total volumes 35, 350, 4000 and 2 x 15000 litres;
- CIP / SIP with 4 x 4000 litre vessels;
- SCADA, including 2 PC.



## BIO-FERTILIZERS

Two bioreactor lines for manufacturing biological products that enhance soil fertility. The main products of these bioreactors consist of bacteria that can fix nitrogen, release phosphorus, enhance potassium absorption, and prevent plant diseases caused by fungi.

**Main equipment configuration of the fully automated system:**

- Two bioreactor lines:
  - First line – Bioreactors with total volumes of 50, 500, 5000 and 20000 litres;
  - Second line - Bioreactors with total volumes of 50, 500 and 5000 litres;
- 500 litres mixing reactor for preparation of substrate;
- CIP / SIP with 4 x 4000 litres vessels;
- Circulation sterilizer;
- SCADA, including 2 PC.



### ***P. PASTORIS* FERMENTATION LINE FOR ENZYME AND PROTEIN PRODUCTION**

This bioreactor line is for the cultivation of *Pichia pastoris* to manufacture enzymes and proteins.

The system is fully closed and automated, consisting of the following key elements:

- 1) 50, 500 and 2 x 5000 litre bioreactors (total volumes);
- 2) Stationary CIP / SIP for automated cleaning and sterilization of bioreactors, reactors and connecting pipelines;
- 3) Circulation sterilizer for sterilization of substrate;
- 4) Feeding reactors for glycerol and methanol;
- 5) Connecting heat - insulated pipelines and the group of pneumatically controlled membrane valves.



### ***E. COLI* FERMENTATION-BASED INSULIN MANUFACTURING**

Our state-of-the-art GMP manufacturing line is **designed to produce high-quality insulin with strict adherence to Good Manufacturing Practices (GMP) guidelines.**

**Line consists of four bioreactors, two of which are 100 liters each and the other two are 1000 liters each.** These bioreactors are used for the fermentation process in which *E.coli* bacteria is grown and then used to produce insulin. Our bioreactors are equipped with advanced technology that allows us to control and optimize the fermentation process for maximum yield and quality.



In addition to the bioreactors, **manufacturing line also includes a CIP/SIP system.**

## BIO-LEACHING

Bioleaching is the extraction of metals from their ores with a help of the living microorganisms. This method can be applied for example, to recover copper, zinc, lead, arsenic, antimony, nickel, molybdenum, gold, silver, cobalt.

- 1) Two 6 litre bioreactors for preparation of the inoculate and four 6 litre bioreactors with feeding reactor connected in sequence by peristaltic pumps. All inner parts of bioreactors are from glass, PTFE or covered with special chemical resistant coating.
- 2) Three 30 and 80 litre bioreactors with an 80 litre feed reactor connected in sequence according to two options: by peristaltic pumps or gravity. All inner surfaces are covered with special chemical resistant coating.



# Bi●reactors.net

Bioreactors.net AS

27 Dzerbenes street, Riga  
LV-1006, LATVIA  
Phone/ fax: +371 67553518  
e-mail: [info@bioreactors.net](mailto:info@bioreactors.net)



ISO 9001:2015