

Single-Use customised products

Scalable platforms for:

1. Batch/fed-batch mammalian cell cultivation
2. Continuous cell cultivation at very high cell density
3. Microbial fermentation



CellVessel



Customer designed CellVessel 3 litre, MST drive, dual impeller, extra In&Out, extra hoses, head space gas exchange.



Option examples - Aeration devices, Micro – PP body with 15 µm pore, Macro – multiple 500 µm holes in tube, L-sparger with 10 x 0.3 mm holes in OD8 mm tube.

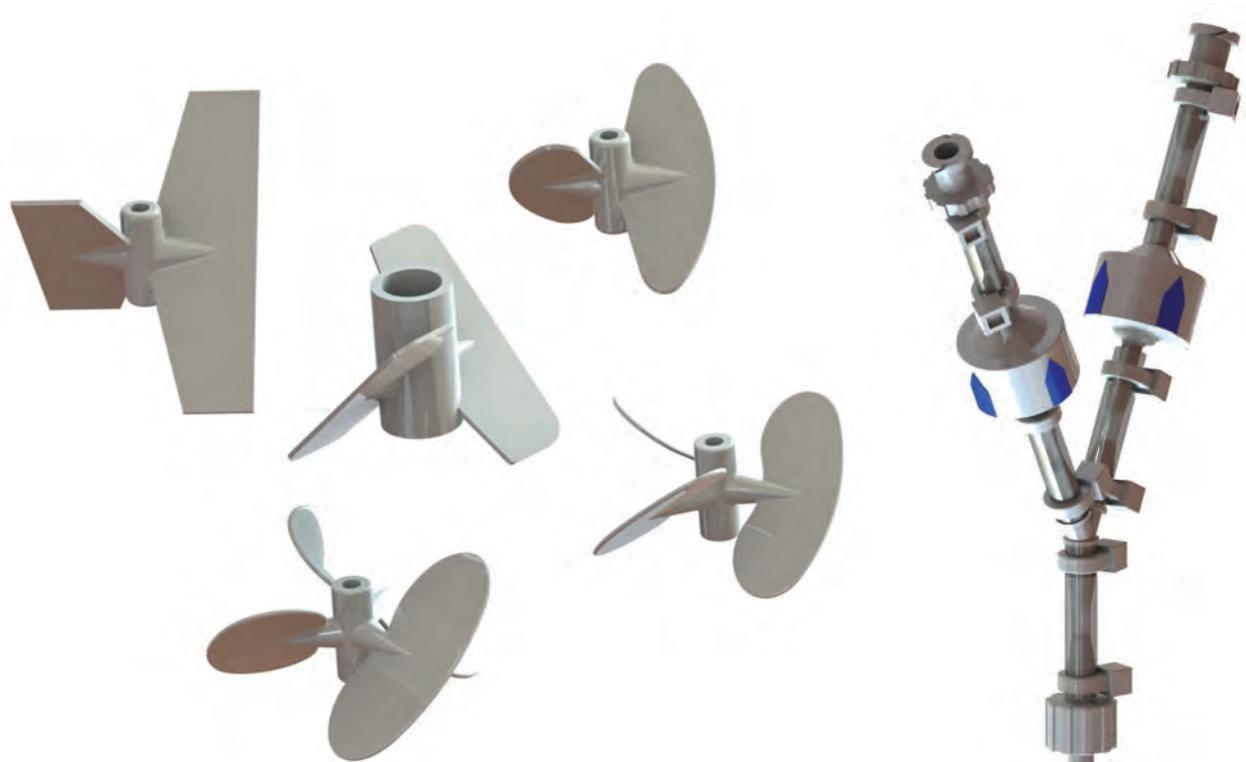


Option example - VisiFerm DO sensor well incl cap



Option example - Gas inlet or outlet

Worlds first configurable Single-Use-Bioreactor from bottom up



One of many option examples - Impellers for various diameter, design, applications.

Option example - Inlet / outlet device with twin one-way valves.

CellVessel™ Single-Use-Bioreactors (SUB) for batch and fed-batch cultivation of various cell lines in suspension are unique as they are fully configurable and meet any design request in a scalable platform ranging 1-25 litre Working-Volume (WV).

CellVessel SUB is designed for connection to any Process-Control-System (PCS) and replaces all traditional glass/metal STR. CellVessel comes for bottom drive (Magnetic-Stirrer-Table - MST) or top drive (Head-Plate-Drive - HPD) accepting any PCS servo motor.

Basic specifications for CellVessel are:

- PC (polycarbonate) vessel in 5 different diameters and 5 different heights
- PC cover with 7 - 12 PG13.5 ports according to the vessel diameter
- Rigid design for stable servo motor connection

Fully configurable CellVessel may be created by selecting components from:

- A range of impeller(s), any rotation for up-flow / down-flow / axial / radial fluid circulation for any application
- MST drive or HPD for connection to any servo motor (a servo motor specific adapter is required)
- SUB temperature controlled with electrical heating blankets and/or with water borne Flexible-Heating-Cooling blanket
- Various aeration methods; micro pore spargers, hole spargers, L-sparger, head space gas exchange
- Baffled stator for axial vortex mixing, donut shape flow pattern for improved mass transfer for increased productivity
- Several height liquid level / foam sensors
- Many different exhaust methods
- Several different liquid In&Out methods
- May be pre-installed with a range of Single-Use-Sensor (SUS)

Worlds first Single Use-Fermenter for microbial applications



OD80 mm turbine integrating porous PP sparger bodies in the core, 4 magnets for MST drive at 1500 rpm



Option example - 4 ports with female Luer-Lok = one sample line with swabable valves 40 mm above bottom, one harvest line to vessel bottom, two headspace lines, ground SS probe integrated

Option example - Gas-cooler - one OD 50 mm sterile filter on 80 mm long 8 x 12 mm hose – Luer-Lok/barb water connection



BactoVessel™ Single-Use-Fermenter (SUF) for batch and fed-batch microbial applications are unique as they are fully configurable in a scalable platform ranging 1-25 litre WV.

BactoVessel SUF is designed for connection to any Process-Control-Systems (PCS) and replaces traditional glass/metal fermenters. BactoVessel are for bottom drive on Magnetic-Stirrer-Table (MST) accepting most PCS servo motors.

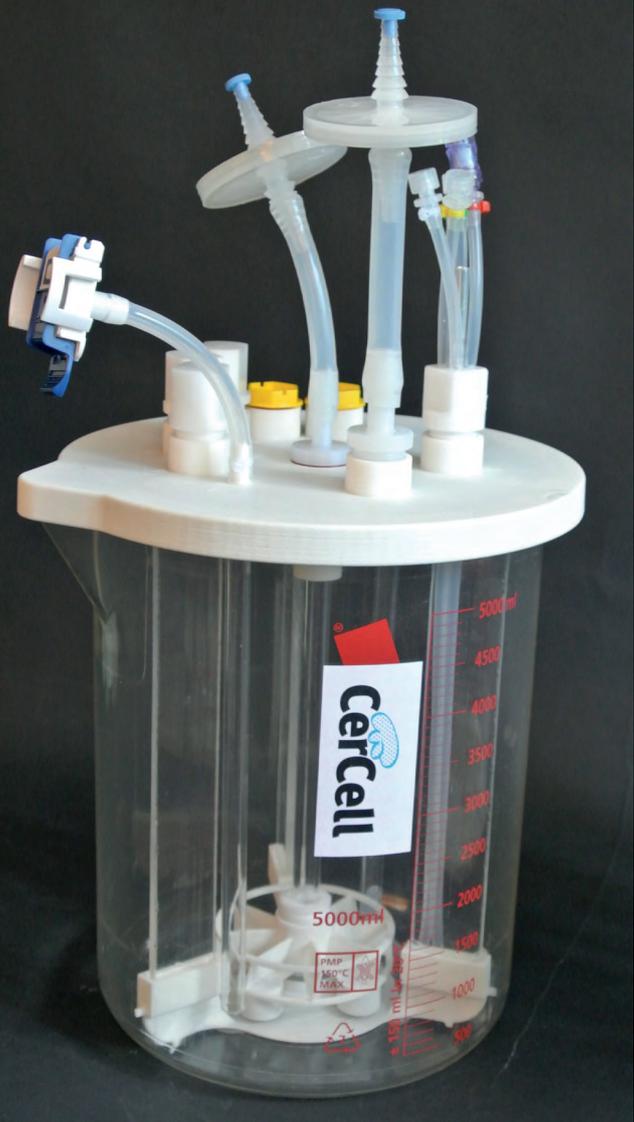
Basic specifications for BactoVessel are:

- PC (PolyCarbonate) vessel in 5 different diameters and 5 different height covering 1-25 litre WV
- PC cover with a number of PG13.5 ports according to the vessel diameter
- Rigid design for stable servo motor connection

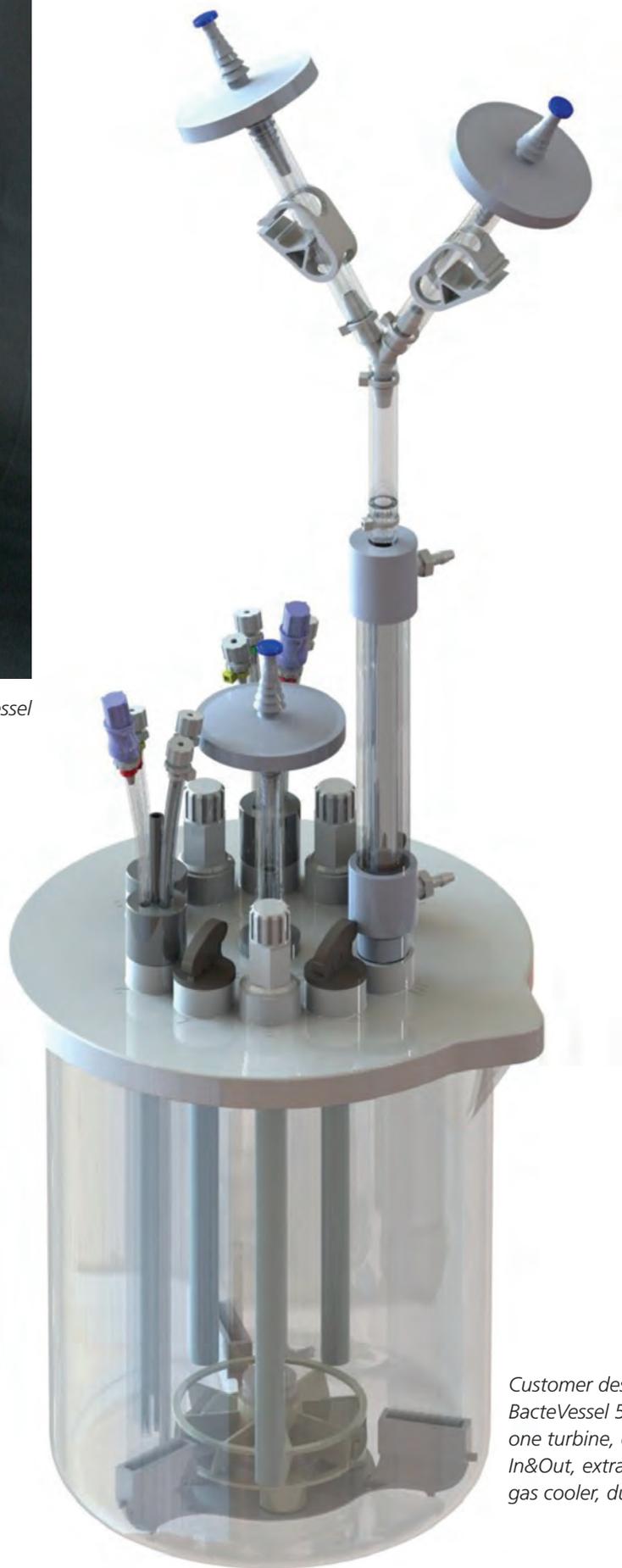
Fully configurable BactoVessel may be created by selecting components from:

- A range of turbines for clockwise rotation / up-flow combined axial / radial fluid circulation
- MST drive for connection to powerfull servo motor (a servo motor to MST specific adapter is required)
- SUF temperature controlled with water borne Flexible-Heating-Cooling blankets
- Aeration through turbine core integrated micro pore spargers
- Baffled stator for axial vortex mixing, donut shape flow pattern
- Several height liquid level / foam sensors
- Many different exhaust methods
- Several different liquid In&Out methods
- May be pre-installed with a range of Single-Use-Sensor (SUS)

BactoVessel



Customer designed 5 litre BactoVessel



Customer designed BactoVessel 5 litre, one turbine, extra In&Out, extra hoses, gas cooler, dual filter



Option example - 500 ml foam collection bottle with two OD 50 mm sterile filter on Y-connector, 2 hose clamps

CellCore for continuous operation

Mammalian cells lines are harboured inside a 3D matrix / scaffolding and a steady flow of nutrients are constant fed to the cells, giving a continues harvest for an extended period.

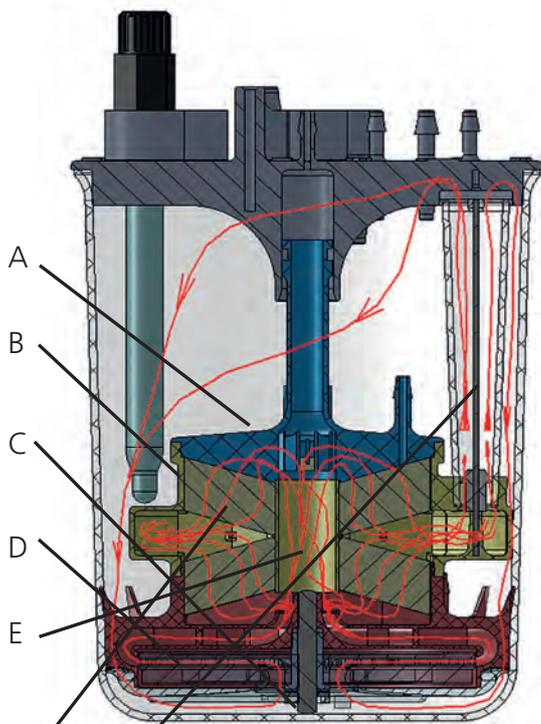


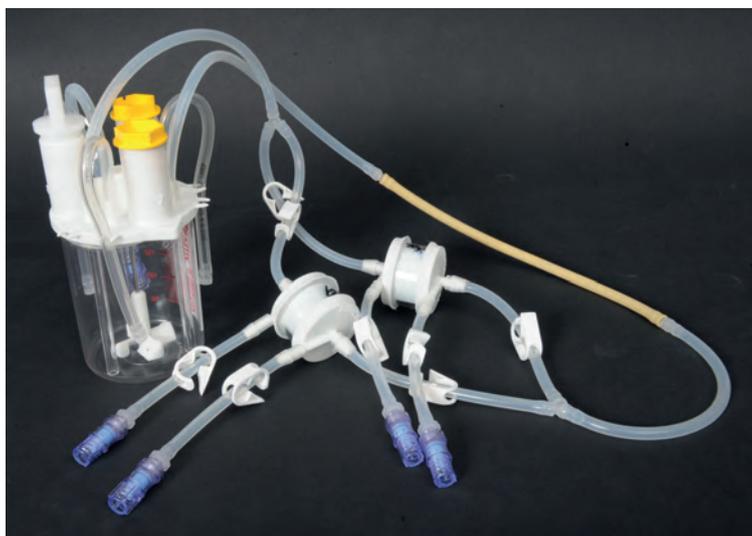
Illustration of constant media re-circulation and flow pattern in CellTank insuring cells obtain gradient free access to nutrient

The platform is engineered to:

- Cultivate 100-150 mio adherent or suspension cells per ml
- Immobilized suspension cells in the cell retention scaffolding
- Allow continues cultivation for months with constant harvest
- Steady state feeding of nutrient and removal of disposed media
- Accept a variety of scaffoldings / matrix materials inside each envelope harbouring a variety of adherent as well as suspension mammalian cell lines for expression of a product
- Eliminate gradients where cells are harboured
- Retain cells in the matrix and hereby avoid external arranged cell retention membrane devices
- Hook up with conventional Process-Control-Systems (PCS)
- Integrate classical signal Single-Use-Sensor (SUS) pH sensors, DO non-invasive well and bio mass sensors
- Precision E-beam sterilized and ready to use
- Operate on MST coupled to a variety of servo motors
- Avoid contact between aeration bubbles and cells
- 0.05 nano liter per cell per day media perfusion rate



Light weight rigid plastics CellTank compared with 5 litre jacketed glass/steel STR. Equal total cell density and daily product expression though CellTank offer 4-8 times the cultivation time.



CellCompact 33-0015 for testing of scaffolding parameters to cell line adaption or small scale continues expression of a product

Platform scalable >1:1000

- CellCompact 5 ml (33 series - 1 discs)
- CellTank 150 ml (34 series - 2 discs)
- CellReactor 1,500 ml (36 series - 4 discs)
- CellDream 15,000 ml (38 series - 8 discs)

How does CellTank work?

1. The CellCore platform is a reactor core A designed as a cylinder with stacked two slightly angled and circular envelopes B. The envelopes are arranged parallel with radial / axial inlet / outlet. As the envelope diameter and pair number are variable the scalability is created.
2. The matrix in the CellTank are polyester fiber non-woven scaffolding F which create the millions of sites to harbour both suspension and / or adherent cells.
3. Internal re-circulation of media inside the SUB insures constant, gradient free access to nutrient and gasses for constant expression of product.
4. Media pump on CellTank inlet C is at the very bottom. The media passes the impeller D driven by external magnetic forces (not shown) and exits the pump into the reactor core centre E into the triangular volumes and flows further perpendicularly through each of the envelopes / matrix discs F. Having passed the matrix, media is collected in the hollow circumference collection volume in direct correspondence with the built-in media mass flow instrument G capable of 0.4 - 2.4 liter/ min.
5. The centrifugal pump D capacity is 0-3 liter/min at 250-600 rpm depending on cell density ranging up to max practical 1.5×10^8 ml matrix. 25 Watt of power is required to overcome the 0-50 mBar pressure difference accros the cell packed matrix/scaffolding.
6. Each of the two envelopes B has 50 cm² inlet surface area and close to 80 ml volume. This is also how CerCore creates the 4 - 24 cm/min flux / media velocity accros the 18 mm thick envelopes B in order to avoid gradients.

Sensors in CellTank

Sensor package

3D cut through the CellTank illustrates a 120 mm pH SUS on the left and the re-usable Visiform™ DO sensor on the right fitted to the non-invasive well with the SUS optical membrane in the front.

The 120 mm SUS bio mass sensor is seen behind the pH sensor.

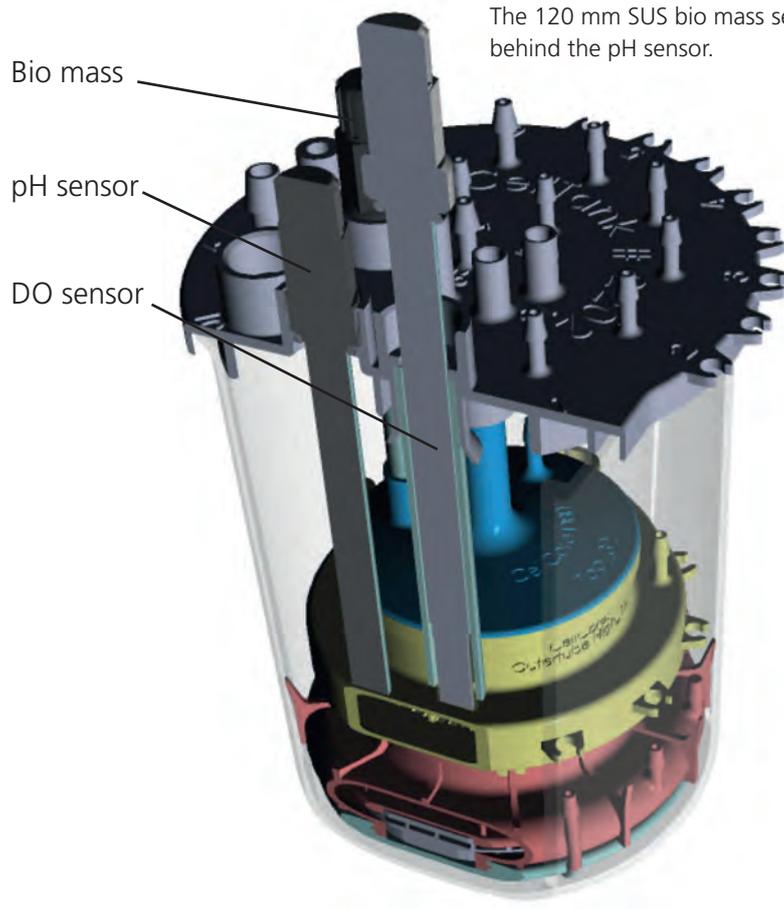


Photo of CellTank below shows

- Non-invasive well with inserted DO sensor
- Non-invasive well for temperature, (empty)
- Single-use pH sensor installed
- Single-use bio mass sensor installed
- Single-use mass flow rotameter installed



Bio mass sensor

CellTank's integration of re-usable or single-use capacitive sensing technology allows precise on-line monitoring of the cell mass, viable cell density as well as cell physiological state. Users can also track cell cycle changes, model apoptosis, and predict protein titer all in real time, and this from inside the scaffolding matrix harboring the cells.

Single-Use-Sensors (SUS) offer the following advantages

- Integrated SUS reduce contamination risk
- Saves hours of prep time and labor, as no autoclaving or cleaning is needed
- Enables SUS setup right on the bench – no biosafety cabinet / hood needed for operation



SUS in CellVessel and BactoVessel

Hamilton Single-Use-Sensors (SUS) for DO and pH

- Pre-installed single-use sensor cap on single-use well adapted for VisiFerm™ classical signal DO sensor
- Extends DO sensor life, as it is never autoclaved
- Classical dimension pH sensor for extended shelf lifetime offering months of operation
- Classical pH and DO sensor signal fits any PCS

C-CIT Single-Use-Sensors (SUS) for Glucose and Lactate

- CITSens Bio is a world-first system for online, in situ measurement of Glucose, Glutamate and Lactate. Real-time data capture of these process relevant parameters save costs for analysis and reduces the risk of contamination
- CITSens Bio sensors are based on screen printed electrodes, which are coated with an immobilized enzyme on a PG 13.5 type sensor body



Presens Single-Use-Sensors (SUS) for DO and pH

- Presens PG13.5 type sensor probes for oxygen, pH and carbon dioxide designed to measure in all CerCell SUBs and SUFs
- A variety of transmitters allows connection of SUS to any PCS as classical pH and DO sensors
- The Solaris PCS integrates Presens electro-optical modules for pre-installed DO and pH CerCell sensors



Io PCS

Io Process-Control-System (PCS)

for R&D bioreactor / fermenter

- Compact master control station, 100-240 VAC supply
- Gas mixing: up to 5 TMFC (Air, CO₂, N₂, O₂ and Overlay)
- Up to 2 vessels managed with one station
- Up to 8 software assignable peristaltic pumps, all speed controlled
- Accepts simultaneously classical Hamilton pH, DO and Presens pH, DO



BactoVessel on MST

Full package PCS + SUB or SUF

NEW



CellVessel with HPD

LEONARDO smart 18.5" touch screen controller for R&D bioreactors / fermenters

- Extended possibilities for software programming for continues operation
- Multi-level password protection
- Controller page to view set-points, process values and control mode, to set up customized PID (or use factory defaults) and alarm limits
- Continuous trends representation to track, print and export data
- Different dynamic zooms and configurations
- On-line parameters calibration of classical and Single-Use-Sensors
- Events log and alarm register
- Possibility of saving recipes for repeat usage
- Remote control, internet access for easy after-sales assistance



Heating / cooling method

- For water conveying Process-Control-System (PCS) the Flexible-Heating-Cooling (FHC) heat exchanger blanket is a simple hook-up to wrap around all CerCell SUB / SUF products.
- Connection of HFC to existing water heating / cooling system performed with standard couplings and hoses
- FHC simulates the traditional jacketed STR heating/cooling handling 10 - 60°C

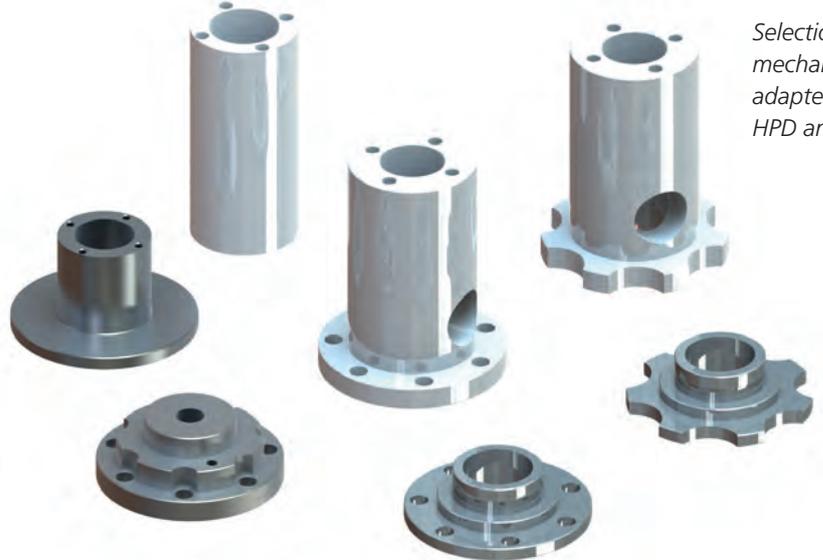
*Simple FHC 120x400
blanket mounted on
BactoVessel*



Two agitation methods

HPD drive

- Head-Plate-Drive (HPD) for CellVessel SUB offer coupling / adapter kits to Applikon, Biostat, DasGip, BJ, NBS, Solaris, Finesse, BBI-biotech, Diachrom and others
- Re-usable adapters easily attached to the OD30 mm centre bearing on the CellVessel head plate
- The system is most stable and required no extra mechanical support

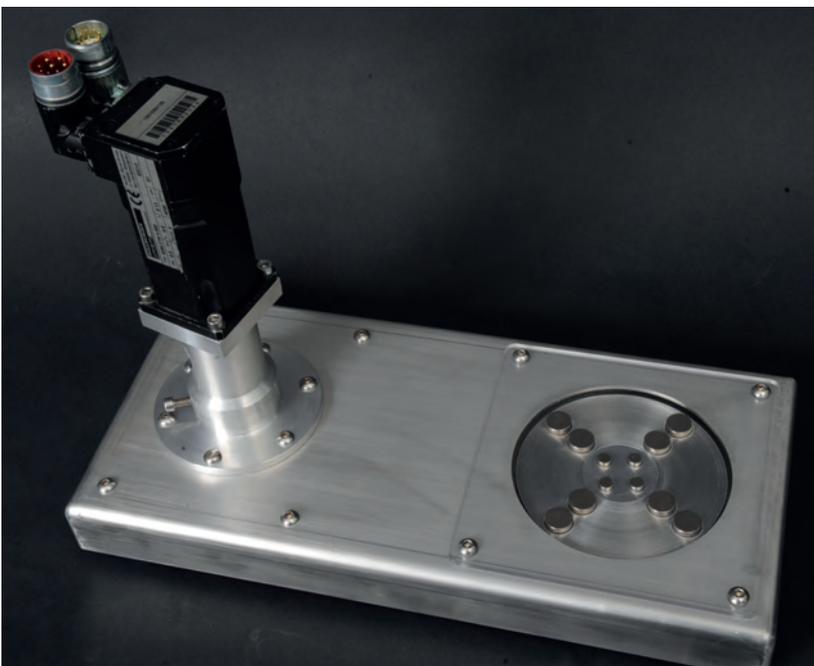


*Selection of
mechanical
adapters for
HPD and MST*

*Kollmorgen servo
motor on MST*

MST drive

- For CellTank, CellVessel SUB and BactoVessel SUF
- Magnetic-Stirrer-Table (MST) stainless steel construction featuring long life and silent running toothed polyurethane belt, two sealed double-row ball bearings, aluminium sprockets
- Rotor is equipped with 12 permanent magnets and able to transfer unlimited power off cause depending on the particular servo motor capacity
- Dim: 390x180x50 mm, weight is 5,7 kilo



Products

With our Configurator Tool we can help you design your SUB or SUF to your User-Requirement-Specification.

We supply you with CAD drawing and product code for your approval.

Basic CellVessel cultivation SUB kit and BactoVessel fermentation SUF kit sizes to select from

Vessel diameter, OD mm	110	130	150	200	250
Number of PG13.5 ports	7	7	9	10	12
Impeller diameter, OD mm	40/52	58	70	80/100	100/120
Vessel volume, ml					
225 mm + 30 mm = vessel height	2,100	3,000	4,100		
320		4,100	5,600	10,300	15,700
400		5,100	6,900	13,400	19,300
500			8,500	16,500	23,800
600			10,100	19,600	28,300

CellCompact continuously operating SUB kit

Part No.	Vessel, ml	Matrix, ml	Agitation methods	Cultivation of cell lines
33-0005	250	5	peristaltic pump	For expression or proliferation
33-0015	250	15	peristaltic pump	For expression or proliferation

CellTank continuously operating SUB

Part No.	Vessel, ml	Matrix, ml	Agitation methods	Cultivation of cell lines
34-0150	2,000	150	MST turn table	For expression of a product

CellReactor continuously operating SUB

Part No.	Vessel, ml	Matrix, ml	Agitation methods	Cultivation of cell lines
36-1500	5,500	1,500	MST turn table	For expression of a product

Io Process-Control-System CerCell / Solaris Biotechnology

Part No.	Vessels	Peri pump	Agitation methods	Process
60-0005	1	4	servo motor for HPD	Cultivation expression
60-0010	2	8	servo motor for HPD	Cultivation expression
60-0015	1	4	servo motor incl MST	Fermentation expression
60-0020	2	8	servo motor incl MST	Fermentation expression
60-0025	2	4	servo motor incl MST	Continues expression CellCompact
60-0030	1	8	servo motor incl MST	Continues expression CellCompact
60-0035	1	8	servo motor incl MST	Continues expression CellCompact



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