sartorius stedim biotech

Complete Upstream Solutions
BIOSTAT® Bioreactor Systems | BioPAT® Tools

turning science into solutions

Fermentation Technologies and Upstream Solutions…

Sartorius Stedim Biotech is a leading provider of cutting-edge equipment and services for the development, quality assurance and production of biopharmaceuticals and vaccines. Its integrated solutions covering fermentation, filtration, purification, fluid management and media are supporting the biologics industry around the world to develop and produce drugs safely, timely and economically.

Sartorius Stedim Biotech offers the most complete range of equipment and consumables to flexibly support your upstream process requirements in cell culture and microbial fermentation. As the market leader in bioreactor and fluid management technologies, we are working with customers globally since more than 60 years to successfully turn their biological project pipeline into safe vaccines and medicines for patients. Based on our expertise in sterile filtration, liquid handling, bioreactor design, automation and engineering we have been able to develop completely single-use process solutions that meet the requirements of today and tomorrow.

Independently of your preference, we can provide you with a fully scaleable and interchangeable range of single-use or established glass and stainless steel bioreactor solutions. We understand that not every customer has the same needs, and requirements can change over time and as the product progresses through development. Our range of benchtop bioreactors supports effective and efficient development of your processes throughout all phases. A seamless transfer into pilot and production scale bioreactors – both for single-use and stainless steel solutions – is ensured by our thorough understanding of bioreactor design and scale-up principles, well thought through automation concepts and harmonised controller strategies for oxygen, pH, temperature and feed addition.

Overview BIOSTAT® Standard Bioreactor Systems

Benchtop Bioreactors Autoclavable	Vessel Size [L] Working Volume	Minimum Volume
BIOSTAT® Qplus	0.5	0.15
	1	0.4
BIOSTAT® Aplus	1	0.4
	2	0.6
	5	0.6
BIOSTAT® B	1	0.4
	2	0.6
	5	0.6
	10	5 | 1.5*
BIOSTAT® B-CDU II	0.5	0.15
	1	0.4
	2	0.6
	5	0.6
	10	5 | 1.5*

In-Situ Sterilizable Bioreactors	Vessel Size [L] Working Volume	Minimum Volume
BIOSTAT® Cplus	5	– | 1.6
	10	3.5 | 4.5**
	15	5.0 | 5.5**
	20	5.5 | 7.5**
	30	7 | 9**
BIOSTAT® D-DCU	10	2.5 | 3.5
	20	3.5 | 5.5
	30	5.4 | 6.4
	50	13 | 13
	100	24 | 24
	200	41 | 47

Single-Use Bioreactors	Vessel Size [L] Working Volume	Minimum Volume
BIOSTAT® RM	0.5	0.05
	1	0.1
	5	0.5
	10	1
	25	5
	50	10
	100	20
	300	60
BIOSTAT® STR	50	12.5
	200	50
	500	125
	1000	250

* depending on length of included sensors

** H:D 3:1 | 2:1

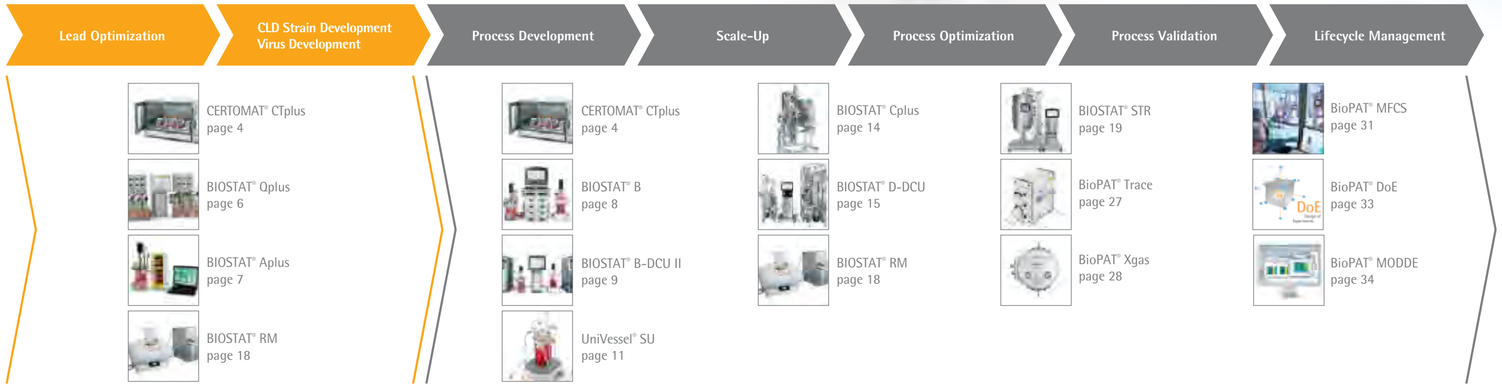
…for Process Development and Production

We are your partner for process development, scale-up and production. We understand your needs for efficient and effective R&D processes, process transfer, security of supply and service.

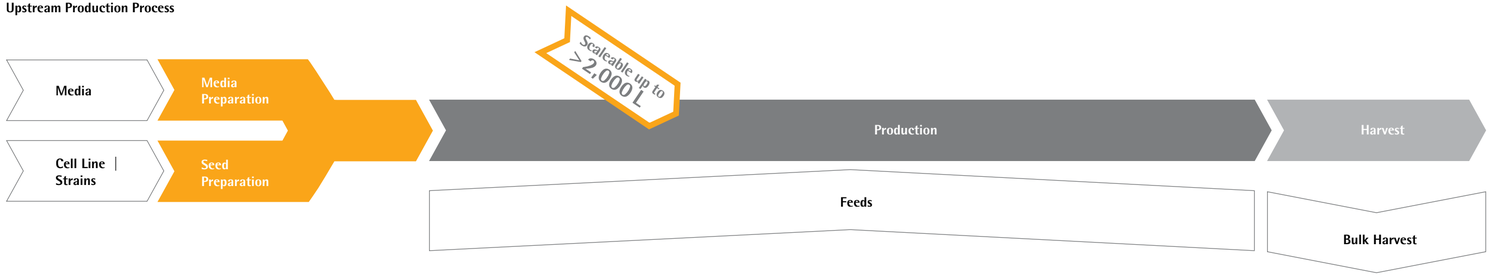
Unparalleled Range of Products for Upstream Processing

- Media preparation, filtration, storage and feed addition
- Virus and mycoplasma risk mitigation approaches
- Cell culture and microbial fermentation
- Harvest and cell removal
- Sterile connection and disconnection technologies
- Process monitoring and control tools
- Process optimization software
- Bio-analysers and sensor technology

Biopharma R&D Process



Upstream Production Process



Contents

CERTOMAT® CTplus

CO_2 Incubation Shaker – Specifically Designed for Cell Culture

Applications

- Cultivation of mammalian cells
- Clone propagation
- Clone selection
- Process optimization
- Seed train work

The CERTOMAT® CTplus has been specifically designed for cultivation of mammalian cells in shake flasks under stringent control of temperature, CO_2 concentration and humidity. A radically new design was chosen placing all components into their functional context.

Basic design principle for CERTOMAT® CTplus is encapsulation – incubation chamber, mechanical drive and control unit are strictly isolated from another. This prevents corrosion of the drive unit and other parts due to formation of carbonic acid in the incubation chamber. Separate heating systems for incubation chamber, doors and humidification pan effectively prevent any condensation.

Features	Benefits
Purpose-built incubation chamber	Low CO_2 consumption precise temperature control and very even temperature distribution
Encapsulated drive	Protect drive against humidity and CO_2 – reduced wear
Variable mass compensation	Reduced vibration of equipment – allows full shaker speed even when stacked
Water pan in front, no heat mat attached	Water pan can be readily removed, may be autoclaved for sterilization
Expandable for data exchange and process monitoring	Use the same SCADA software as for BIOSTAT® fermenters Measure dissolved oxygen and pH using additional SENSOLUX® intelligent tray

SENSOLUX®

The Intelligent Shaker Tray for Determination of pH and DO

Applications

- Cultivation of animal and human cells
- Clone selection
- Media optimization

The SENSOLUX® stand-alone version is an intelligent shaker tray with an integrated sensor system. It is applied for monitoring the pH value and the dissolved oxygen (DO) saturation during the cultivation of animal and human cells. For clone selection and media optimization, the online determination of pH and dissolved oxygen provides important information about the status of the culture.

Used in combination with the new single-use SENSOLUX® Erlenmeyer Flasks, it facilitates the easy, safe and highly informative online measurement of these crucial process parameters in incubation shakers.

Features	Benefits
Nine measurement points for both PH and DO are integrated	Nine samples treated in parallel
Single-use SENSOLUX® EF Erlenmeyer flasks are equipped with two pre-calibrated sensor patches	Reliable measurements with calibrated single-use flasks
SENSOLUX® EF available in four different sizes: 125 ml, 250 ml, 500 ml and 1000 ml, the flasks are delivered sterile, single packed and ready-to-use	Ready-to-use, one package per experiment, no calibration needed
Dedicated software for monitoring and visualization of measured parameters	Recording of data even without PC connection, various analyses enabled
Tray is compatible with a broad range of standard incubation shakers including the CERTOMAT® shaker family	Adapt SENSOLUX® to your incubation shaker

BIOSTAT® Qplus

The Multi Parallel Screening Tool

Applications

- Growth studies of microbial, mammalian, insect and plant cells
- Culture media optimization
- Clone screening
- Multivariate process optimization studies (DoE)
- Small scale protein and mAB expression

The BIOSTAT® Qplus is a Fermenter | Bioreactor designed for screening applications in early development and multivariate process optimization studies. Up to twelve culture vessels can be operated at the same time. Manual operation is reduced to a minimum.

The BIOSTAT® Qplus is available in a working volume range of 0.15 to 1 L.

Features	Benefits
Parallel & individual operation of up to 12 culture vessels	Reduced development effort Save valuable bench space
Application-driven pre-configured packages	Get going right away
Sanitary stainless steel housing	Reduced need for extensive cleaning
Group calibration of sensors	Reduced set-up time

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BIOSTAT® Aplus

Plug-in and Grow

Applications

- Microbial culture – growth of bacteria, yeast and funghi
- Cell culture – growth of animal, insect and plant cells
- Transition from shake or tissue culture flasks
- Small-scale protein expression

The BIOSTAT® Aplus is a compact, fermenter| bioreactor system specially designed for educational use and investigational R&D applications.

The BIOSTAT® Aplus is available with interchangeable 1 L, 2 L, or 5 L single-wall glass culture vessels. Alternatively a single-use 2 L polycarbonate culture vessel can be connected for cell culture applications.

Features	Benefits
Pre-defined packages for microbial or cell culture applications	Fully-functional fermenter	bioreactor for small budgets
Plug & play connections and installation video	Easy set-up especially for inexperienced users
Intuitive operation via laptop PC	Well-known Windows-based operation principle for easy navigation
Compact housing design	Fast set-up and dismantling

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BIOSTAT® B

The Gold Standard of Benchtop Bioreactors

reddot design award
winner 2013

Applications

- Production of and process development for vaccines, recombinant proteins and monoclonal antibodies
- Seed production in small scale
- Low-shear cell culture of sensitive organisms
- Production scale-down for process optimization

The BIOSTAT® B is a fermenter | bioreactor which has been developed specifically for the varied requirements of biotechnological and biopharmaceutical research and development. With multiple thousand installations worldwide the BIOSTAT® B is the market leading benchtop system for research applications.

Single or Twin versions are available with single-wall or jacketed glass culture vessels in the range of 1 L, 2 L, 5 L and 10 L. Alternatively a 2 L single-use polycarbonate vessel may be connected for cell culture applications.

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Features	Benefits
Single or Twin set-up for control of one or two culture vessels with the same control tower	Saves valuable bench space in the development lab
Up to four mass flow controllers and possibility to switch gas flow from sparger to headspace gassing via touch key	Maximum flexibility to match a broad range of daily-changing application requirements
Stainless steel housing and storage dish	Easy cleaning, additional storage space for a tidy workplace
Equipotential bonding	Increased measurement safety and control of your process according to the latest standards

BIOSTAT® B-DCU II

Fully Flexible for Advanced Process Development

Applications

- Microbial, insect and mammalian cell culture
- Suspension and microcarrier culture
- Process development
- Process optimization
- Critical process parameter ranges (process validation)

The BIOSTAT® B-DCU II is designed to meet demanding requirements in process development and validation. The unique space-saving tower design allows the integration of up to six supply towers | vessel combinations together with the DCU control tower into a multiparallel bioreactor system occupying less than 3 meters of bench space.

The BIOSTAT® B-DCU II can be combined with our stirred glass vessels (UniVessel®) or single-use vessels (UniVessel SU®). The volumes for our UniVessel® range from 0.5 L to1 L, 2 L and 5 L up to 10 L. The UniVessel SU® is available as a 2 L polycarbonate vessel.

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Features	Benefits
Independent process control for up to six culture vessels	Saves valuable bench space
Superior gas mixing with up to six Rotameters and Mass Flow Controllers	Fully flexible gassing strategy to meet your cells gassing requirements
Up to six integrated peristaltic pumps with choices for fixed and analogue speed pumps	For more working space on your laboratory bench
Interchangeable operation with glass or single-use culture vessels	No more bottlenecks during capacity peaks
Non-invasive optical pH and DO single-use measurement when operated with the Univessel SU	Reduced time for bioreactor set-up and change-over

UniVessel®

Multi-Purpose Glass Culture Vessel

Applications

- Microbial fermentation (bacteria, yeast, funghi)
- Suspension cell culture (mammalian, plant, insect)
- Adherent cell culture with micro carriers
- Process development and Process optimization
- Scale-up and scale-down experiments
- Production process control
- Seed production

The UniVessel® glass culture vessels are specially tailored to the needs of biopharmaceutical process development applications, for e.g. monoclonal antibodies, recombinant proteins and bacterial or cell-derived vaccines.

They have been developed with over 40 years of experience in sterile and scaleable design. All vessels are made of borosilicate glass with a stainless steel head plate and can be configured according to individual needs. They have a round bottom design for optimal mixing at low agitation rates.

Set-up Examples

- Microbial culture with Rushton impellers, baffles, inoculation ports and ring sparger
- Cell culture with 3-blade segment impellers, microsparger, dip tubes for gentle inoculation
- Continuous cultivation with integrated spinfilters for cell retention in perfusion applications
- Aeration basket for gently aeration of shear-sensitive organisms
- Anti-foam disc for mechanical foam destruction eliminating the need for anti-foam agents

Features	Benefits
0,5, 1, 2, 5, 10 L WV	Flexible changes between vessel sizes without extra investments on the controller
Fit to all BIOSTAT® Aplus, B, B-DCU I/ II and Qplus controllers	Decrease your investment on new controllers by using existing UniVessel®
Developed with more than 40 years experience in biopharma applications	Largest installation base in the market with numerous publications on scalability and reproducibility
	Long equipment lifetime (~ 10 years)

UniVessel® SU

Single-Use Bioreactor, Proven Design, Ready for the Future

Applications

- Mammalian and insect cell culture
- Suspension and microcarrier cultures
- Process development
- Process optimization
- Critical process parameter ranges (process validation)

The UniVessel® SU is a stirred tank single-use bioreactor with a working volume range of 0.6 to 2 L. It combines the proven, scaleable design of glass bioreactors and the fast turnaround of single-use systems. UniVessel® SU is compatible with your controller and can be used interchangeably with glass vessels to help you efficiently manage peak workloads despite challenging timelines. Since you discard the complete vessel after one use, you no longer have to bother with the hassle of cleaning, autoclaving and reinstallation.

Features	Benefits
Completely single-use from vessel to sensor	Achieve turnaround in less than an hour
Compatible with your existing bioreactor controller	Utilize your existing controller with state of the art single-use technology vessels and sensors, no additional investment into new controller needed
Proven and scaleable design	Comparable results to glass, stainless steel and large scale SU bioreactors
Interchangeable with glass vessels	Utilize your existing bioreactor controller for both multi-use and single-use culture vessels
Single-use sensors	Reduced time for bioreactor set-up and change-over

Foam Disc for Installation on Stirrer Shaft

In fermentation applications high oxygen transfer rates are achieved through high gassing and agitation rates. This in turn often results in exessive foaming of the media.

The foam disc, a mechanical foam destroyer, solves the foam problem where it starts, directly at the liquid surface. The foam disc is installed on the stirrer shaft, which makes retrofitting fast and easy. It is a two layer disc with four sections. Its lower layer has downwards positioned slots and paddles for foam skimming. The foam disk is available for all autoclavable culture vessels.

The rising foam enters the foam disc at the bottom side through four self-priming ports. With the rotation of the disc the foam is spun against the reactor wall causing the gas and liquid to separate into two phases. While the lighter gas phase leaves the reactor through the air exhaust the liquid phase drops back into the medium.

Flexible Adapter for Exhaust Cooler

Typically the exhaust cooler and its fittings are the highest point of the culture vessel. They have to be arranged vertically in order to cause the condensate to flow back into the vessel. However, in case of small autoclaves, the height of the fully equipped UniVessel® can be challenging.

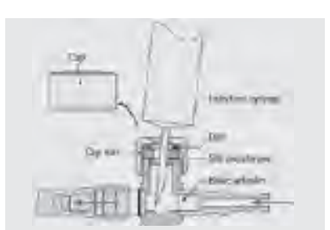
Using a flexible adapter reduces height requirements in the autoclave. The adapter gets installed between the exhaust cooler and its top plate port at the culture vessel. After autoclaving, the adapter stays between the exhaust cooler and the culture vessel. The exhaust cooler will be fixed along a holding bar at the vessel to stand upright.

STT Connectors

STT quick connect couplings enable aseptic connection of additional containers, external cell retention devices, harvest lines and the like. They can be used to achieve fast and secure hose connections to link multiple vessels. Connections can be made aseptically to transfer inoculum, supplying corrective agents or harvesting culture media. Furthermore, they are applied for the supply of liquids to a culture vessel or removal of samples.

Components:
- Female connector, with holder for a slotted membrane, slotted membrane, a tube connector and a blind closure for autoclaving.
- Male connector, with integrated tube connector and a sterile cap for autoclaving.
- The STT Quick Coupling can be connected to tubing of size ID Ø = 1.6 .. 2 mm and 3.2 .. 5 mm.

Bypass Sampler



The by-pass sampler allows for sample removal from and additions to the culture vessel in a closed bypass loop, which offers the benefit of sampling without dead volumes. It can also be used for introducing small volumes of additives which shall be fed to the culture.

The membrane holder contains a self-closing membrane which can be pierced, e.g. with an injection syringe. The bypass sampler loop is created by connecting its tubing assembly to a peristaltic pump.

Spinfilter

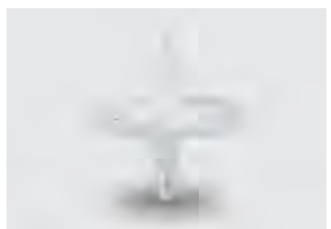
The purpose of the spinfilter in continuous perfusion processes is cellfree removal (harvesting) of culture supernatants from the culture vessel. The spinfilter allows cells to be cultivated permanently without the need to remove the production organism from the culture vessel. Together with the precise level control of our BIOSTAT® controllers, either by level sensor or a gravimetric level controller, an optimal media exchange with a constant culture volume can be achieved.

The spinfilter is mounted on the stirrer shaft inside the bioreactor vessel. Together with a 3-blade segment impeller and a draft tube a tangential flow along the filter meshes is assured. Mesh sizes for our autoclavable stainless steel spinfilters range from 10, 20, 40 up to 75 µm and are available for 2 L, 5 L and 10 L UniVessel® glass. The spinfilter is applicable especially for adherent growing cells on microcarriers since it has no effect on the cultivation parameters, such as e.g. temperature differences due to the use of external devices or cell stress caused by peristaltic pumps.

Manual Sampler

The manual sampler contains a sampling tube, a syringe with 0.2 µm filter and the clamp holder to fasten the support rod of the culture vessel. The cover of the sampling tube has 3 hose nozzles for the sampling tube from the culture vessel, for the sampling outlet, and for the syringe. The sterile filter on the syringe prevents non-sterile air from entering the sampling chamber. Samples are taken by pulling the media through a harvest pipe in the culture vessel into the sampling chamber by means of underpressure generated by the syringe. After closing the vessel line and opening the sampling line, the sample can be pushed through the sampling chamber dip tube and out of the sampling chamber into an external container.

Midisart® 2000
Ready-to-use Filter for Sterilizing Gases and Venting



Midisart® 2000 filtration units are ideal tools in biotechnology, the pharmaceutical industry, research institutes and anywhere else you need sterile vents, bioisolation or sterile air and gases. It's extremely hydrophobic PTFE membrane prevents you of water blockage caused by high humidity air streams even after prolonged time of use (> 14 days). An extended flow rate performance allows high air flow rates at low differential pressure for economic filter sizing. Our broad variety of connectors offered, ranging from hose barb to tri-clamp connection, enables you to easily and flexibly connect our filters to fermenters, bioreactors and vessels.

BIOSTAT® Cplus

Convenience from Research to Small Scale Production

Applications

- Microbial and cell culture
- Suspension and microcarrier cultures
- Process development and scale-up
- Seed production
- Protein supply for research and development

Academic and industrial research, process development and small scale production need a scaleable, reliable industrial Sterilizable- In-Place (SIP) fermenter | bioreactor system with no room for compromises. The BIOSTAT® Cplus fulfills these requirements with state-of-the-art technology and design.

The BIOSTAT® Cplus comes as a floor standing version, available with culture vessels from 10 L – 30 L working volume. A benchtop version is available with culture vessel providing 5 L working volume.

Features	Benefits
Complete sanitary stainless steel design	Easy to clean
Closed loop temperature control system with choice of steam or electrical heating	Highly precise temperature control which matches your laboratory infrastructure
Automatic SIP sequence	Minimized manual operation
Open frame piping skid	Easy access during operation and maintenance
Casters for skid available	Easy handling of the system

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BIOSTAT® D-DCU

Your “Fast Lane” to Production

German Design Award
SPECIAL MENTION

product design award
2012

Applications

- Microbial and cell culture
- Suspension and microcarrier cultures
- Process development
- Seed production
- Production

The BIOSTAT® D-DCU incorporates many desirable and advanced features to fulfill virtually any demand for modern bioprocess applications. Furthermore, the BIOSTAT® D-DCU is designed to interface single-use storage bags for media addition and harvest as well as single-use sampling systems.

Due to the modular design, various configurations are available, from basic to fully-featured, the system offers an excellent solution for every budget and every need. Available vessel working volumes of 10 L, 20 L, 30 L, 50 L, 100 L and 200 L fulfill each process requirement.

Features	Benefits
Single or Twin configuration	Saves valuable space
Automatic Sterilization in Place (SIP) and Cleaning in Place (CIP) sequences	Minimized manual operation, effective use of laboratory resources
Powerful industrial rated DCU control system	Reliable and flexible to grow with your needs
Fully configurable from basic batch set-up to sophisticated configurations supporting advanced gassing and feeding strategies	Fits to almost every budget and process requirement
Gear free low noise agitation system	For silent operation even at high agitation speed

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Resterilizable Addition Port

Addition port (AP) kits are intended for resterilizable connections of containers with corrective agents, feeds and media or for connection of smaller scale fementors | bioreactors to inoculate the culture vessel. Furthermore, the AP can be resterilized and reused during the fermentation process. The AP is available in two versions; a) for a 19 mm lid port and b) for a 25 mm side port. When equipped with a dip tube it can be used for harvest or for additions below the liquid surface.

Benefits:
- No open flames needed for aseptic connection
- Re-usable during process
- Different adjacent addtions via a single port

SACOVA

The SACOVA is an addition valve designed to add sterile liquid to an in-situ sterilizable fermenter or bioreactor. The SACOVA is easily removable from the culture vessel for autoclaving together with the connected addition bottle or thermoweldable tubing, for later on connection to a single-use bag. After autoclaving the SACOVA is then inserted in a vessel lid or side port and then sterilized together with the culture vessel. After sterilization the SACOVA is ready to use. In this way, the SACOVA is an easy, safe and inexpensive alternative for making a sterile additions to the culture vessel.

Benefits:
- No open flames need for aseptic connection
- Safe handling due to needle free operation
- 3-channel version for multiple additions in a single port

Sampling Valves

Sampling valves are intended for aseptic sampling of the culture vessel. Two different versions are available, the SVC 25 and the Keofit W9. Both sampling valves are resterilizable and reusable during the fermentation process. At the BIOSTAT® D-DCU, the sterilization of the sampling valve can be either manual or fully automatic. The SVC25 fits into a 25 mm side port, the Keofit W9 is designed to fit into a sanitary flange: Both sampling valves can be supplied for sampling into an open bottle or into a contained sampling bottle.

Benefits:
- Precise dosing of sampling volume
- No dead volume, representative sample
- Resterilizable
- Safe

Spinfilter

The purpose of the spinfilter in continuous perfusion processes is cellfree removal (harvesting) of culture supernatant from the culture vessel. The spinfilter allows cells to be cultivated in continuously. Together with the precise level control of our BIOSTAT® controllers, either by level sensor or a gravimetric level controller, an optimal media exchange rate with a constant culture volume can be achieved. The spinfilter is mounted on the stirrer shaft inside the bioreactor vessel.

Containment Sampling Kits

The containment sampling kit is available for the sampling valve SVC 25 and Keofit W9. The kit is designed to take an aseptic and aerosol free sample out of the culture vessel. It consists of an autoclavable silicone jacketed glass bottle, a stainless steel lid with venting filter and diaphragm valve as well as a condensate line. At the BIOSTAT® D-DCU the sterilization of the containment sampling kit can be either manual or fully automatic.

Benefits:
- Aseptic sampling
- Aerosol free sampling
- Safe silicone jacketed sampling bottle

3-Fold Weighing System

The 3-fold weighting system provides 3 balance functionalities with no additional space requirement – mounted on the Control Tower. Glass bottles of 2 L or bags up to 5 L can be used. In combination with a feeding pump and a DCU Gravimetric Feed Control loop highly precise media feedings can be added. The 3-fold weighing system is available for the BIOSTAT® D-DCU.

Benefits:
- No additional space requirement
- Holder for glass bottles or bags available
- Operated via DCU, no additional operating panel

Sartofluor® Minicartridges for Sterile Gas Filtration

Sartofluor® Minicartridges 0.2 µm rated are filter elements for sterilizing grade filtration of air and gases in the pharma | biotech industry. Their unique hydrophobic PTFE membrane is ideally suited for particle removal and sterilizing grade filtration of air and gases. The membrane also prevents your filter of water blockage caused by high humidity air streams even after prolonged time of use (> 14 days). Our high quality standards underlined by validations to HMA & ASTM F-838 05 guideline, as well as individual integrity testing during production ensure highest prevention of microbiological contaminations.

BIOSTAT® RM

Proven Rocking Motion Single-Use Bioreactor

Applications

- Cultivation of shear sensitive cells such as mammalian, insect and plant cells
- Frequently used for stem cell cultivation
- Microorganisms for low to medium density cultivation
- Seed expansion for large scale bioreactors
- Protein supply for research and development

The BIOSTAT® RM is the new generation of single-use bioreactors utilizing rocking motion for mixing with low shear. The BIOSTAT® RM is available in different packages. Basic packages consist of the stand alone rocker and a basic bag which provides all necessary tubes, connectors and filters for easy and simple cultivation. This can be combined and expanded with the powerful DCU for full feedback control for batch, fedbatch and perfusion process.

The single-use CultiBag RM, which forms the cultivation chamber, is mounted on the rocker platform and contains the medium and the cells. Due to the wave in the bag, generated by the moving platform, the media surface is renewed constantly, providing bubble-free aeration at low shear rates.

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Features	Benefits
Single-use bioreactor with wave-induced mixing	No more sterilization or cleaning in place
Available in scaleable working volumes from 0.1 L to 300 L	Validation, maintenance and overhead costs are reduced
Three different packages available (basic, optical, perfusion)	Great flexibility in cultivation volume and process strategies
Integrated Air / CO_2 module (option) for basic rocker	Matches exactly your specific process requirements, from cost effective seed production to high end perfusion applications
Pre-calibrated precise optical pH and DO sensors	
Possibility to work with fixed percentage of CO_2 (“incubator style”)	Easy to use and cost effective

BIOSTAT® STR

True Scaleability in Single-Use

Applications

- Suspension and microcarrier cultures
- Cultivation of mammalian and insect cell types
- Process development
- Process scale-up
- Pilot scale production
- Seed cultivation for large scale bioreactors
- Production

The BIOSTAT® STR is a fully scaleable single-use bioreactor with a conventional design. The system is comprised of a stainless steel support housing, a single-use bioreactor chamber and a superior control system utilizing single-use or conventional sensors. It’s advanced control platform offers an excellent solution for every budget and every process requirement.

The single-use cultivation vessel CultiBag STR, has a classical stirred tank design, making transition from traditional stainless steel to single-use as easy as possible. Set-up is simple and hassle free. The bag is available in a working volume range of 12.5 L to 1,000 L. It’s vertically positioned stirrer is pre-installed inside the bag and contains two impellers.

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Features	Benefits
Only single-use bioreactor consequently based on conventional stirred tank bioreactor design	Easy process transfer from or to conventional glass or stainless steel bioreactors
Available in 50 L, 200 L, 500 L and 1,000 L size with 1:4 turndown ratio	Suits your specific process needs
Pressure control system and exhaust cooler	Eliminates risk of bag overpressure during operation
Overlay & sparger aeration with ring-, micro- or combi-sparger	Efficient oxygen transfer and CO_2 removal even in high cell density processes
Advanced agitation system with the choice between 6-blade disk and 3-blade segment impellers	Excellent mixing even for difficult applications such as microcarrier cultivations
	Excellent cell growth and titers

CultiBag ORB

Single-Use Cultivation Chamber

The CultiBag ORB is a single-use cultivation chamber optimized for cell culture. The culture system has a working volume of 50 L – 200 L. The CultiBag ORB is named after its innovative orbital shaking principle which ensures efficient mixing and oxygen transfer combined with ease of use.

Every bag is equipped with single-use optical sensors for pH and DO. The sensors are pre-calibrated and supplied with calibration parameters.

The CultiBag ORB bags are designed for use in the Kühner OrbShake bioreactor.

Applications

- Mammalian cells
- Insect cells
- Plant cells
- Microorganisms

Features	Benefits
Orbital shaking technology with surface aeration	Efficient mixing and high oxygen transfer capabilities
No need for internal mixing and sparging devices	Economical alternative to stirred single-use bioreactors
Dip tube	Gentle feeding without sheer stress
Needle-free sampling ports	Easy and convenient aseptic sampling without the risk of contamination

Exhaust Cooler

The exhaust cooler is a single-use device for the BIOSTAT® STR. It is mounted by means of a sterile connector between the bag and the exhaust filter. Humidity is removed from the exhaust gas, thereby efficiently protecting the exhaust filter from blockage. The condensate can be returned to the bag.

Hydrocyclone

Application

- Mammalian Cell Retention

Device for single-use and multi-use Bioreactors.

In fed batch mode, media and other nutrients are added to the culture and the product is only harvested at the end of the run. This approach is well characterized, reliable and produces higher yields than simple batch processes. However, there are some disadvantages such as waste product accumulation, nutrients may become exhausted and the product may be degraded prior to harvest due to the long residence time in the bioreactor. Perfusion mode is an alternative processes methodology which eliminates the disadvantages of fed-batch processes and further increases the volumetric productivity. In perfusion mode, the cells are retained in the bioreactor while medium is continuously exchanged and therefore the product is harvested throughout the entire culture period. Investment costs are lower as smaller upstream equipment is required. The key to successful perfusion operation is an efficient and scaleable cell retention device such as the Hydrocyclone. Until now, Hydrocyclones have been used in biotechnology primarily for yeast separation. A new Hydrocyclone has been developed for the retention of mammalian cells.

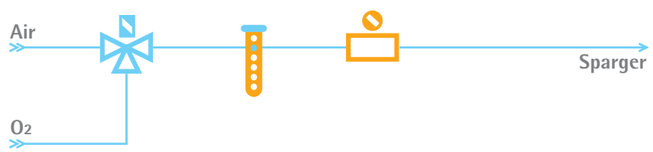
Design
The Hydrocyclone is a simple device with small dimensions and no moving parts. Furthermore, the disposable design of the Hydrocyclone eliminates cleaning requirements and cleaning validation.

Overview Gassing Strategies

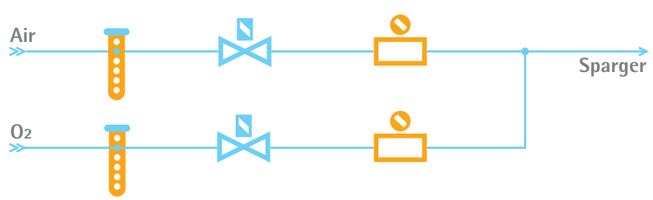
O_2-Enrichement

The O_2-Enrichment gassing strategy uses, as shown in the schematics, a 3/2-way solenoid valve to select either Air or O_2 flow to the sparger. A flow meter visually indicates and controls the sparger flow rate. O_2 is pulsed via a solenoid valve, sparging only when required to maintain the dissolved oxygen (DO) setpoint.
Air is not provided at this time. Mass flow controllers can be integrated to measure and control the total gas flow rate via manual adjustment or automatically in conjunction with the controller.

BIOSTAT® Cplus



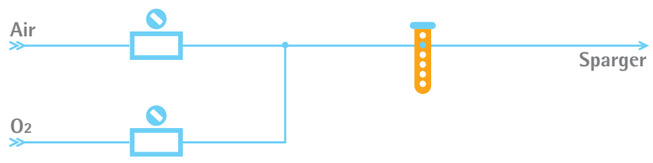
BIOSTAT® B



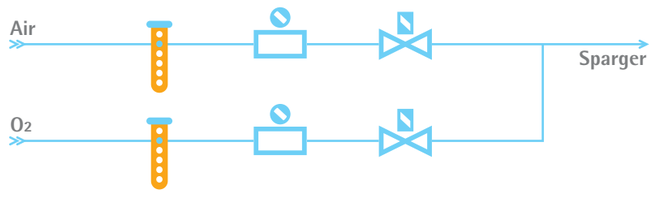
Gas Flow Ratio

The Gas Flow Ratio Control gassing strategy utilizes two flow paths, each of them with the option of using mass flow controllers, one for Air and one for O_2 flow. Flow meters visually indicate the flow of Air and O_2. Both mass flow controllers can be operated manually or automatically in conjunction with the DO controller.

BIOSTAT® Cplus



BIOSTAT® B-DCU II, D-DCU



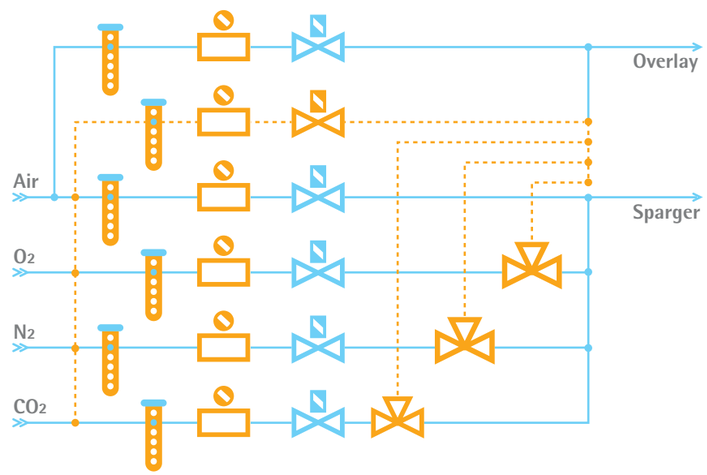
Legend

Described options might vary depending on the particular system configuration.
Additionally, the pictures only show system-dependent gassing structures.

Advanced Additive Flow

The Additive Flow gassing strategy allows individual flow rate control for Air, N_2, O_2 and CO_2. With the Advanced Additive Flow gassing strategy it is furthermore system-dependent possible to direct Air, O_2, N_2 and CO_2 to the sparger. Air is routed to overlay. Flow meters visually indicate the flow rate for each gas. One additional gas flow path can be added to sparger or overlay outlet for some systems. Depending on the bioreactor system mass flow controllers can be installed for each gas flow path as well as gas switching between overlay and sparger is available.

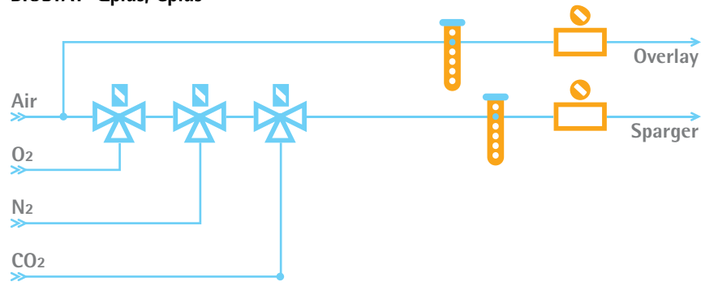
BIOSTAT® B-DCU II, D-DCU



Exclusive Flow

The Exclusive Flow module uses a series of 3-way solenoid valves to select either Air, O_2, N_2 or CO_2 for sparger gassing. Flow meters for sparger and overlay visually indicate the flow rate of the selected gas. Optional mass flow controllers are available for sparger and overlay total flow control.

BIOSTAT® Qplus, Cplus



Product Selector Tool for Fermenters | Bioreactors

Product	Application											
	Early Protein Supply		Screening		Process development / Optimization / Validation		Seed Production		Production	
	CC	MO	CC	MO	CC	MO	CC	MO	CC	MO
CERTOMAT® CTplus	●		◇		○		◇			
SENSOLUX®			◇		●		●			
BIOSTAT® Qplus	●	●	◇	◇	●	◇				
BIOSTAT® Aplus	◇	◇			○	○				
BIOSTAT® B	◇	◇			●	◇	●	◇		
BIOSTAT® B-DCU II			●	●	◇	◇	◇	●	○	○
BIOSTAT® Cplus	◇	◇			●	◇	●	◇		
BIOSTAT® D-DCU	●	●			◇	◇	◇	◇	◇	◇
BIOSTAT® RM	◇	○					◇	●	○	○
BIOSTAT® STR	●	○			◇	○	◇	○	◇	○

◇ optimized for ● suitable for ○ applicable for selected applications

Process Analytical Technology (PAT) Solutions

Risk is Inverse to Process Understanding

Conventional biopharmaceutical manufacturing is characterized by fixed, validated process steps and extensive lab testing procedures.

The FDA Guidance on Process Analytical Technology (PAT) recommends the use of potential for improving pharmaceutical development, manufacturing, and quality assurance through innovation in product and process development, process analysis and process control. PAT is much more than just one sensor integrated into a process. It is a risk-based strategy for designing, analyzing and controlling manufacturing processes. The Critical Process Parameters (CPPs) are identified in line with the definition of the Critical Quality Attributes (CQAs) of intermediates or final products. Process Analytical Technology offers a number of tools for defining, measuring and controlling these CPPs in Biopharmaceutical Manufacturing. Process understanding based on PAT intrinsically results in safety of patients, regulatory compliance and process economics.

Sartorius provides you with tailored PAT solutions that ensure product quality, cost savings and ease of documentation.

Process Analyzers & Sensors

- Process analyzers are indispensable tools within the PAT framework for monitoring critical process parameters (CPPs).
  CPPs are identified by risk analysis during process development. These should be monitored and controlled to reach a specified product quality in an effective and reproducible manner. Depending on the criticality of a process step, instant intervention is essential to keep the process parameters within defined ranges. Inline and online analyzers provide real-time data for advanced process control, which results in process economics and product safety.
  Moreover, where required by regulatory authorities or process criticality, thorough 100 %-monitoring of process parameters with subsequent documentation ensures compliance, makes tech-transfers verifiable and is establishing trust.

- Sartorius provides a comprehensive range of process analyzers & sensors for your process needs.
- Innovative, tailored analytical solutions
- Multivariate process monitoring
- Chemical, physical and microbiological parameters
- Enabling real-time monitoring and control
- Ensuring consistent process and product quality

BioPAT® Trace

Online Glucose | Lactate Measurement

The BioPAT® Trace analysis system is used for simultaneous online monitoring of glucose and lactate in laboratory or industrial cultivations of microorganisms and cell lines.

The BioPAT® Trace ensures a high degree of measurement and process reliability due to its utilization of a reusable analyzer in combination with single-use sensors and fluidic elements.

Applications

- Measurement of nutrients during cell culture and microbial fermentation
- Control of feeding strategies
- Usable in each step from cell line development up to production

Features	Benefits
Simultaneous online measurement of glucose and lactate	Reducing manual effort associated with sampling
Fully automated, self calibrating	After setup no additional work is necessary
Modes: Filtration, Dialysis, Sampling	Different sampling modes allow the connection to all sizes of culture vessels
Unique dialysis mode for small volume bioreactors	Fully automated nutrient measurement and control of small bioreactor systems
Fully disposable sensor & fluidics set	No maintanance is necessary

BioPAT® Xgas

Advanced Off-Gas Analysis for Monitoring and Control of Fermentation Processes

Applications

- Enabling advanced and automated control strategies: harvest initiation, support for gas mixing strategies or the addition of feed and induction media
- Process control tool in line with PAT concept by linking off-gas values to critical process parameters
- Providing key parameters for process development and scale-up

With the BioPAT®Xgas, you can monitor and control bioprocesses in real-time. The BioPAT®Xgas is a combined O_2 – CO_2 sensor featuring automatic compensation of humidity and pressure. The O_2 concentration can be measured in a range of 1 – 50% and the CO_2 concentration in a range of 0 – 10%. The BioPAT®Xgas is directly integrated into the exhaust gas line of a bioreactor.

The online off-gas analysis provides real-time insights into the metabolic processes of the culture and allows the user to optimize yields and processes. The measurement of O_2 and CO_2 provides data on biomass production, substrate consumption and product formation rates.

Features	Benefits
Standardized integration into Sartorius bioreactors and automation systems	Event based control enabled by real time determination of key off-gas parameters
Parallel and continuous determination of O_2 and CO_2 with one sensor	Immediate detection of small changes by 100 % off-gas monitoring of every single bioreactor
Automatic moisture and pressure compensation	Process reliability ensured by high measurement accuracy at varying humidity and pressure
Compact design	Integration into small lab bioreactors as well as large production-scale fermenters
Status display and calibration buttons directly on the BioPAT®Xgas	Easy operation

BioPAT® Spectro

NIR Spectroscopy for Bioprocess Monitoring & Control

Applications

- Real-time monitoring of fermentation processes
- Golden batch comparison
- Cell growth and viability monitoring
- Nutrients and metabolites monitoring
- Media quality fingerprinting

The BioPAT® Spectro system has been designed especially for the use on production scale stainless steel bioreactors. The system is connected to the fermenter via a standard Ingold port and allows monitoring of the fermentation or cultivation process. It is possible to compare the actual running batch to a defined golden batch, by means of process trajectory monitoring. The use of process trajectories allow for simple monitoring of changes in the process – in real-time – providing significant benefits over offline sampling techniques. In addition to monitoring target analytes, cell parameters are measureable.

Our BioPAT® Spectro is the first system which is completely free of fibers – a so called "Free Beam" spectrometer. With this configuration and the use of diode array technology, the BioPAT® Spectro is robust to shocks. The free beam design enables our system as the first in the market to really monitor cell parameters such as cell growth and viability – due to the larger spot size and minimal light loss. Moreover, the use of free beam optics in combination with our novel detection algorithm enables the control of window fouling. The system will automatically determine whether the results are still valid or not and set an alarm signal once window fouling is detected. The BioPAT® Spectro is best suited for use in the late clinical phase, in pilot and commercial production scale as the comparison of batches is feasible in this phase of the drug development process.

Features	Benefits
Process trajectories for real time fermentation monitoring	Early detection of process deviations
	Help saving batches
	Allow fast restart
Golden batch comparison	Compare running batches with known batch quality and set alarm signals faster than with the help of routine analysis
Cell growth and viability monitoring	Direct feed back of cell parameters without sampling
Nutrients and metabolites monitoring	Monitoring of the nutrients and metabolites for visualizing the correct process trend
Media quality fingerprinting	Assuring the right quality of the used media by comparing media quality before and after sterilization

Process Control & Software Tools

Stable and robust processes require sophisticated control of critical process parameters (CPPs) based on reliable data acquisition, storage and evaluation capabilities. State-of-the-art process control prevents or mitigates risks of producing faulty batches and represents a further step towards knowledge- and risk-based production of biopharmaceutical products.

Combined with process analyzers, process control & software tools provide an excellent approach for prospective quality assurance. Regarding the variability of input materials and production conditions, these software tools keep the CPPs within a proven operating range or design space, resulting in an overall increased process reproducibility and consistent high product quality.

BioPAT® DCU
Local Touch Control Unit

The Sartorius Digital Control Unit (DCU) is the central part of our local process control offering for the BIOSTAT® bioreactor systems. Key design principles for its human machine interface are "intuitive use". By grouping process parameters, controls and alarms around a process diagram, user actions are effectively directed through the menu. Touchable with gloves the user can interact with the bioreactor local control in an easy understandable manner, which reduces time to get acquainted with the instrument to a minimum. Furthermore, the same operation procedures are used from benchtop to production, from upstream to downstream which eliminates expensive user trainings, one does it all.

Besides process parameter monitoring, alarming and control loops, the DCU is equipped with guided calibration procedures for pH and DO probes and enables feeding strategies based on automated sequences.

Compared with an engineered system the BioPAT® DCU offers an unmatched price-performance-ratio, covering broad standard and advanced functionality, ready-to-use. Increased operational efficiency can also be achieved in related process steps like media preparation or cell harvest where the BioPAT® DCU serves as local control unit for our FlexAct® unit operations (e.g. FlexAct® MP and FlexAct® CH).

Besides the BioPAT® DCU offers a plug-and-play interface to the Sartorius BioPAT® MFCS SCADA Software to enable supervisory bioprocess control and data acquisition (page 31).

Applications

- Process-near visualization and control of process state and parameters
- Reliable monitoring and control from
  - upstream to downstream
  - small-scale to large-scale
  - single-use to resuable applications

Features	Benefits
Common user interface, easy to comprehend and ready-to-use	Fast implementation into daily working routine, reduced training efforts
Process parameter monitoring, alarming and control loops	Batch-to-batch consistency enabled by fully automated sequences
Guided calibration procedures for pH and DO probes, open interfaces for advanced analytics	One central device for local bioprocess monitoring and advanced control
Generic automation platform for different scales, implemented in all Sartorius unit operations	Faster upscaling and tech transfer through consistent use of recipes and control strategies
Plug and play connection to Sartorius SCADA system BioPAT® MFCS	Reduced engineering efforts and faster time-to-market
Standardized basic and advanced functionality options for process monitoring and control	Unmatched price-performance-ratio

BioPAT® MFCS
SCADA Software for Reliable Data Acquisition, Monitoring and Control

Microsoft Partner
Independent Software Vendor (ISV)

BioPAT® MFCS is the world standard software for supervisory bioprocess control and data acquisition. Based on over 25 years of experience and more than 5,000 installations, the latest release of BioPAT® MFCS provides various solutions to meet your particular requirements.

BioPAT® MFCS is provided in two versions. BioPAT® MFCS/DA is designed as a "plug & play" tool and ideally suited for capturing, storing and visualizing process data in a R&D environment. In contrast BioPAT® MFCS/win is a feature-rich, GAMP category 4 software package capable of supporting the most demanding research or production environment.

BioPAT® MFCS/win features modules for
- S88 Recipe Control (page 32)
- Design of Experiments (page 33)
- 21 CFR Part 11 compliance
- Secure integration to corporate networks
- Flexible device connectivity using OPC

Applications

Reliable data acquisition, monitoring and control for
- upstream and downstream unit operations
- from shake flask to large-scale bioreactors
- single-use to reusable bioreactors

Features	Benefits
Scalable software for almost all bioprocess applications	Reduced training efforts and improved data consistency
Fully user configurable and upgradeable with specific modules	Unique customization level and flexible investment costs
Proven record over 25 years of software development	Reliable and robust system performance
Installation, configuration, validation & engineering services	Technologically and economically optimized solutions
Central platform for real-time data and historians of Process, Analytical and Sampling Data	Full transparency and accessibility for advanced process control and understanding

BioPAT® MFCS/win Recipe (S88) Control Module

Advanced Automation and Robust Processes

Applications

- Event detection, which means the identification of process states based on inline, online or atline measurements
- Control of advanced feeding strategies for fed-batch bioreactors
- Implementation of recurrent events based on loops and jumps

Besides the core functionality of a real SCADA system for bioprocess applications, BioPAT® MFCS/win offers a number of additional software modules for adaptation to individual requirements and thus provides customization options to fine tune your bioprocess management. BioPAT® MFCS/win and additional modules were strictly developed according to the software lifecycle concept and are compatible with the latest off-the-shelf hardware and software technology.

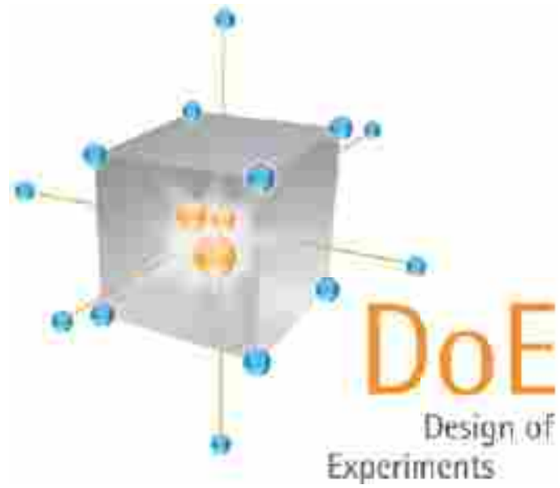
The unique Recipe Control (S88) Module allows you to realize automation strategies for batch, fed-batch and continuous processes inline with Quality by Design (QbD) principles. With its condition allogic and the direct translation of biopharmaceutical unit operations into S88 phases, the Recipe Control Module supports your automation strategy to reduce variability and increase batch-to-batch consistency.

As S88 provides a common language for process design and specification, an early recipe development enables the implementation of an operator independent and robust process control strategy across development and commercial manufacturing.

Features	Benefits
Recipe structure with common terminology	Standardized approach for simplified and derisked transfer of processes from development to production and between different sites
Event-based control, 21CFR 11 compliant	Advanced control strategies with global regulatory acceptance
Easy graphical programming with a new recipe editor	Application-oriented automation with customized recipes

BioPAT® MFCS/win DoE Module

Optimized Bioprocess Parameters



Applications

- Screening, optimization and robustness testing of basic process state variables and control parameters

The new DoE module provides an interface between BioPAT® MFCS/win and the professional DoE Software MODDE. Jointly developed with UMETRICS AB, a market leader in software products for Multivariate Data Analysis (MVA) and Design of Experiments, new opportunities are arising for PAT based bioprocess optimization.

Covering all advantages of MODDE, the unique DoE module not only provides an easy start to any designed experiments, but first and foremost represents a valuable tool for bridging the gap between a fast and at the same time reliable experimental workflow.

In addition to the Recipe Control (S88) Module and the DoE Module, BioPAT® MFCS/win features modules for
- 21 CFR Part 11 compliance
- Secure integration to corporate networks
- Flexible device connectivity using standardized OPC technology
- Enhanced data logging & historical archiving features
- Distributed alarming & transmission to multimedia devices.

Features	Benefits
DoE transfer from lab to pilot plant for process parameters	Lean and efficient workflow optimization
Automatic design setup, data transfer and S88 recipe configuration	No typing errors and hence no odd anomalies making statistical analyses difficult
Seamless integration of existing control strategies	Significant time savings by use of prior knowledge

BioPAT® MODDE

DoE - The Efficient Way of Bioprocess Optimization

MODDE

Applications

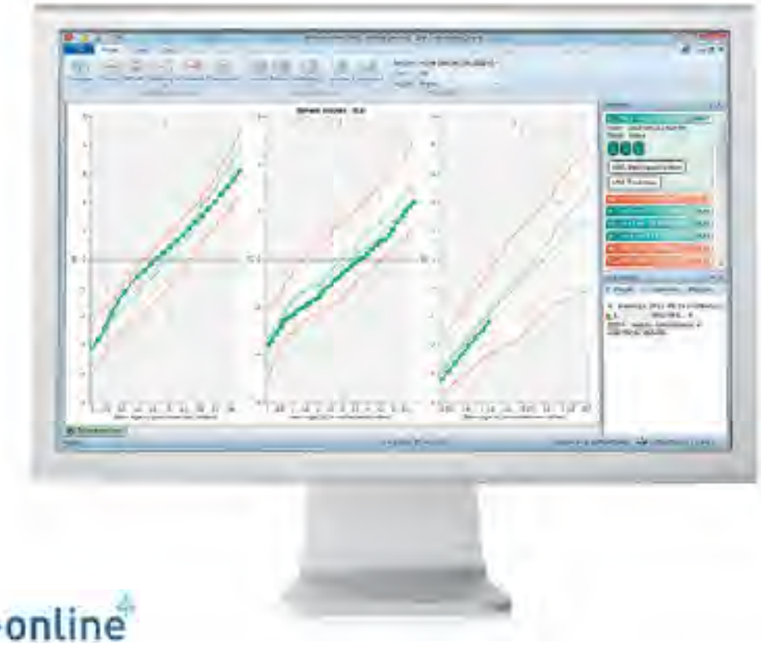
- Optimization of growth and production culture media
- Screening and Optimization of basic process state variables and control parameters including feeding strategies
- Design space estimation (DSE) and validation

MODDE is a state-of-the-art design of experiments software package that is used by scientists, engineers, and statisticians alike to help understand complex processes and products. MODDE enables rapid process optimization with a reduced number of experiments. Use the 21 CFR Part 11 compliant MODDE software to speed up your development work, to increase productivity and elucidate primary effects and interactions of potential critical process parameters (CPPs) and critical quality attributes (CQAs).

Features	Benefits
Visual user guidance with a multitude of automated functions	Tool for beginners and experienced users
User-friendly design and analysis wizard	Easy setup and reliable data evaluation of experiments
Graphically oriented result presentation and reports	Decision-making based on statistically verified statements

BioPAT® SIMCA & SIMCA-online

MVA – Discover Hidden Process Information



SIMCA

SIMCA-online

Applications

- Early fault detection
- Real-Time Release (RTR) testing
- Real-Time Multivariate Statistical Process Monitoring (RT-MSPM)
- Classification and process predictions

For many years SIMCA has been the standard tool for scientists, engineers, researchers, product developers and others coping with large amounts of data. SIMCA enables you to effectively explore your data, analyze your process and interpret the results. Use SIMCA to transform data into information, allowing you to make decisions - quickly and with confidence.

Massive amounts of data containing obvious as well as hidden information are generated every day in process environments. SIMCA-online uncovers the hidden secrets of your processes. It is a highly efficient software for real-time process monitoring and control as well as predictive analytics and soft sensor models based on process parameters and spectral data.

Features	Benefits
Easy interpretation and analysis of large process data sets	Improved process performance resulting in e.g. yield increase or impurity reduction
Early detection of process deviations with guidance to potential root cause	Faster troubleshooting reduces the risk for costly shutdown periods
Process trajectories for real-time fermentation monitoring	Enhanced process safety by easy understandable graphics
Summary of all kind of process information in one data model	Control and assurance of overall process and product quality

Sartoguard PES

Membrane Filter for Bioburden Reduction and Prefiltration

Applications

- Prefiltration of serum free culture media and chemically defined cell culture media
- Prefiltration of buffers

Sartoguard PES filter cartridges are especially designed for effective bioburden control and reliable removal of particles from a broad range of fluid streams.

They provide the finest, most efficient and reliable performance for critical prefiltration applications.

They are designed to protect sterile downstream processes and extent the lifetime of more expensive sterilizing grade and Mycoplasma retentive final filters.

Their efficiency allows downsizing of filtration systems and cost saving in applications where the use of validated sterilizing grade filters is not required, but reliable bioburden and turbidity reduction is.

Features	Benefits
High dirt holding capacity and flow rates	Optimal protection of sterilizing grade and Mycoplasma retentive filters to minimize filtration costs
Individually integrity tested during production and on-side integrity testable	Highest security and reliability during use
Broad variety of sizes and formats available ranging from cartridges, T-style MaxiCaps to MidiCaps and small scale capsules	Easy and flexible integration into any filtration process independent from the batch size

Sartoguard GF

Integrated Glass Fiber Material for Outstanding Performance

Applications

- Protection of more expensive Mycoplasma retentive and sterilizing grade filters specifically for soy, yeast or serum supplemented cell culture media
- Prefiltration of clarified cell culture harvest in front of sterilizing grade filters
- Prefiltration in buffer preparation

The Sartoguard GF filter elements combine the depth filter characteristics of glass fiber material with the advantages of a heterogeneous PES double membrane.

They combine the defined retention performance for particles and microorganisms of membrane filters with the high total throughput capacity in the depth of the fibrous material.

They are ideally suited for effective retention of particles, colloids and lipids which block more expensive sterilizing grade or Mycoplasma retentive membrane filters quickly.

Features	Benefits
Combination of PES membranes and glassfiber fleeces to remove effectively bioburden, colloids and lipids from the fluid stream	Prevents premature blocking of more expensive final sterilizing grade and Mycoplasma retentive filters and reduces filtration costs in media and buffer preparation significantly
Individually integrity tested during production and on-side integrity testable	Highest security and reliability during use
Broad variety of sizes and formats available ranging from cartridges, T-style MaxiCaps to MidiCaps and small scale capsules	Easy and flexible integration to your filtration process independent from batch sizes

Sartoguard NF

Introducing Nanofleece Technology to Liquid Filtration

Applications

- Protection of more expensive Mycoplasma retentive and sterilizing grade filters specifically for chemically defined cell culture media
- Prefiltration in buffer preparation

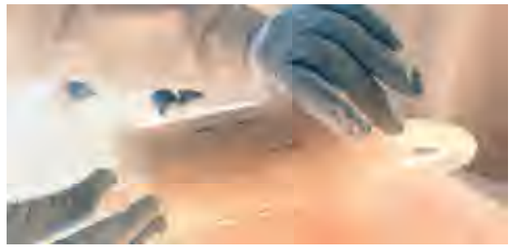
The Sartoguart NF filter elements introduce the Nanofleece technology to liquid filtration.

The unique triple layer construction of PES Nanofleece with heterogeneous PES membrane double layer, is the perfect combination of total throughput, flow rate and protection of your sterile processes.

Features	Benefits
Combination of PES membranes and Nanofleece technology for removal of bioburden and particulate matter from the fluid stream	Optimal protection of more expensive sterilizing grade and Mycoplasma retentive filters to minimize filtration costs in media and buffer preparation
All filter active materials made from PES provides small extractables footprint and low unspecific adsorption for growth factors	Optimal cell growth
T-style MaxiCaps and MidiCaps are gamma irradiatable up to 50 kGy	Flexible integration into single use processing solutions

Sartopore® XL Family

Innovative Filtration Solutions for Cell Culture Processes



Applications

- Sterilizing grade filtration and reliable Mycoplasma removal of different cell culture media

The Sartopore® XL Family is especially designed for sterilizing grade filtration and Mycoplasma removal in special applications of cell culture processes.
The unique heterogeneous double layer PES membrane combination is specially adapted to deal with the broad variety of contaminants in up- and downstream processing of biotech applications.

The PES membrane of Sartopore® filters provides broad chemical compatibility from pH 1 to pH 14 and low extractable levels.

Sartopore® 2 XLG and XLI filter cartridges are fully validated as sterilizing grade filters according to HIMA and ASTM F-838-05 guidelines. Both version differ in the pore size combination of the PES double layer (0.35/0.2 µm for XLI and 0.8/0.2 µm for XLG).

Sartopore® 2 XLM filters use double-layer PES membranes with pore size combination of 0.2/0.1 µm. They are validated for sterilizing grade filtration according to ASTM F 838-05 standard and for reliable Mycoplasma retention with a LRV of 7/cm2 filtration area. They provide the highest security level to avoid unwanted microbial contamination.

Features	Benefits
Combination of different prefilter membranes with 0.1 µm and 0.2 µm final filter membranes	Assures minimized filtration costs for supplemented media (soy, yeast, serum etc.) as well as for chemically defined media
Low unspecific protein binding	High growth rate of cells
Secure retention of Mycoplasma due to high LRV of 7/cm² filtration area for Acholeplasma laidlawii by Sartopore® 2 XLM 0.1 µm	Avoids contamination of the cell culture process by Mycoplasma
Available in a broad range of sizes and formats to provide linear scale-up from R&D to process scale	Identical filtration solution in all scales of the media preparation process

FlexAct® MP

Disposable Solution for Media Preparation

The FlexAct® MP is a standardized configurable disposable solution for convenient media preparation in biopharmaceutical processes.

Combined with a Flexel® for Magnetic Mixer and Palletank®, the multifunctional Central Operating Module enables the user to install, operate and monitor a fully single-use unit operation.

Applications

The FlexAct® MP is available from 50 L to 1,000 L media preparation. This covers the typical needs of process development, scale-up and production. The integrated control unit allows end-users to perform other tasks during media preparation.

Features	Benefits
Multifunctional Central Operating Module	Operator friendly
Tailored bag configurations	Flexible media supply
50 – 1,000 L working volumes	Fully scaleable
Quick system set-up	Increased efficiency
Integrated disposable sensors (p, pH, T)	Enables monitoring
Bidirectional operation	Highly flexible

Microsart® AMP Mycoplasma

Real-Time PCR for Detection of Mycoplasma Contaminations

Rapid real-time PCR kits for the detection of Mycoplasma contaminations in cell culture media, in mammalian cell cultures and cell culture supernatants, or cell-culture derived biologicals for lot release.

The Microsart® AMP Mycoplasma enables a reliable and sensitive detection of Mycoplasma DNA. The test procedure is successfully validated for sensitivity, specificity and robustness according to EP 2.6.7. The volume range of up to 18 ml ensures highest sensitivity.

The kit contains all essential components in a function tested ready-to-use master mix including the polymerase.

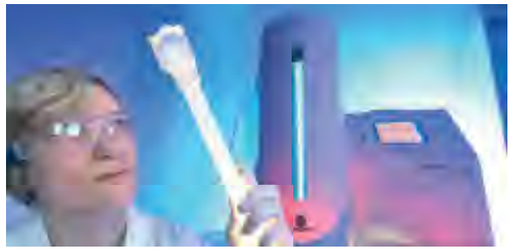
Applications

- Specifically designed for microbiological QC labs or contract labs performing Mycoplasma contamination in-process controls and | or lot release testing according to EP 2.6.7.
- Used for direct detection of Mollicutes in cell cultures, cell culture media components and derived biologicals

Features	Benefits
Kit based on RT-PCR technology	Easy-to-use
	Fast result
Qualified according to EP 2.6.7	Easy implementation for in-process and lot release testing
No specific hardware requirements	No additional costs
Flexible sample volumes from 200 µl to 18 ml	The level of security can be adapted to the needs

UVivatec®

Viral Risk Mitigation Starts in the Upstream Process



Applications

Inactivation of (putative) viruses in:

- Cell culture media
- Vaccines
- Blood & plasma products
- Large molecules (> 200 kDa)
- Proteins|enzymes derived from tissue extracts

Viurs inactivation based on UV-C irradiation
Inactivation of viruses using the UVivatec® technology is based on nucleic acid damage caused by UV-C irradiation. The novel helical inactivation chamber design provides uniform irradiation through efficient radial mixing based on Dean vortices.

UVivatec® shows efficient (> 4 log) inactivation of both small non-enveloped viruses (20 nm) e.g. PPV, MVM and larger enveloped viruses (> 50 nm) e.g. MuLV from biopharmaceutical feed streams by UV-C irradiation (254 nm) while maintaining product integrity.

Features	Benefits
Inactivation based on UV-C irradiation (254 nm)	Targets all viruses, specifically efficient against small non-enveloped viruses (e.g. Parvoviruses)
Novel helical module desgin with optimized hydrodynamic properties	Uniform irradiation through efficient radial mixing based on Dean vortices
	Narrow residence time distribution
	Effective inactivation with minimal impact on product integrity
Disposable modules	Quick & easy to install and maintain
UV-C dose concept	Reliable scalability

Virosart®

Applications

Virus removal in:

- Cell culture media
- Monoclonal antibodies
- Hydrophilic recombinant proteins

Virus removal based on size exclusion
The 20 nm PESU virus filter for the robust and efficient removal of small non-enveloped and large enveloped viruses. Virosart® CPV provides highest virus safety for the biopharmaceutical product. This filter retains more than 4 log10 of small non-enveloped viruses (e.g. PPV, MVM) and more than 6 log10 of large enveloped viruses (e.g. MuL).

Features	Benefits
Homogenous double layer high performance PES membrane	Robust & efficient virus retention (> 4log PPV & > 6log for MLV)
	Clearance not affected by throughput or flow decay
	Capacities up to > 1,000 L/m² for chemical defined media
Plug & Play: Standard Fittings	No special equipment | holders needed
Fast & Easy set up | wetting with water & IT	No need for pre-flush with e.g. alcohol

Flexboy® Bags | Flexboy® Tray and Rack System

Flexboy® Bags are designed for preparation, storage and transport of biopharmaceutical solutions, intermediates and final bulk products. They provide a single-use alternative to traditional glass, stainless steel and rigid plastic carboys in a large variety of applications.

Flexboy® Bags are available in bag chamber volumes between 5 ml and 50 L. They are supplied sterilised and ready to use. Multiple configurations, including thermoweldable TPE tubing, are provided for maximum process flexibility.

The Flexboy® Tray and Rack Systems are designed to facilitate handling of both individual and manifold Flexboy® single-use Bioprocessing Bags (5 L – 20 L) within biopharmaceutical manufacturing processes.

Applications

- Buffers and media sterile filtration and storage
- Bulk harvest
- Product pooling
- Fraction collection
- Sample collection
- Bulk intermediate hold
- Final product transport

Applications

- Buffer and Media storage
- Bulk harvest
- Product pooling
- Fraction collection
- Sample collection
- Bulk intermediate hold
- Final product transport

Features	Benefits
Multiple manufacturing sites	High security of supply
100 % integrity testing of bag and immediate connection	Process safety and integrity
All connections extensively qualified	Safe and robust
Full compliance with ISO11137	Highest sterility assurance level
Standard design	Most designs available from stock

Features	Benefits
Integrated wheels	Facilitated manoeuvrability within the facility
Modular rack accommodate up to 20 trays	Flexible
Dedicated area for storage of pump tubing filters	Easy to use

Flexel® Bags | Palletank® In-Process Fluid Handling

3D Bioprocessing Bags for Palletank®

Flexel® 3D Bioprocessing Bags ranging from 5 L to 3,000 L are three dimensional single-use bags made of S40 film, supplied pre-assembled with tubes, clamps, filters, sensors and connectors, sterilized and ready to use in standard, configurable and custom configurations. The Flexel® 3D Bioprocessing Bag range offers safe, robust, reliable and sterile single-use solutions for processing, storage and transport of large volume biopharmaceutical fluids providing a cost effective alternative to traditional stainless steel vessels.

The Palletank® for in-process fluid handling are specifically developed for users who wish to leave the containers in close proximity to process equipment. Palletank® and Flexel® 3D bags for in-process fluid handling are available in 200 L, 500 L, 1,000 L, 1,500 L, 2,000 L, 2,500 L and 3,000 L volumes. The Flexel® 3D Bags are manufactured according to a patented design that precisely fits the Palletank®.

Applications

- Buffer preparation
- Contained collection of downstream processing intermediates
- Media feeds and harvesting of cell cultures
- Media preparation
- Harvest
- Formulation and final filling

Applications

- In-process intermediate and bulk product hold
- Storage and distribution of media and buffers
- Solution distribution in Flexel® 3D Bag manifold
- Waste collection
- Feed & harvest from bioreactor

Features	Benefits
Multi-layer film	Strong structure with low gas permeability, high chemical resistance and high cleanliness
Same film for all volumes	Scale up from 5 L to up to 3,000 L
Extensive standard range available on the shelf	Instant delivery time
Multiple design options available in our Configurator	Flexible design and fast delivery time
High sensitivity supplier integrity testing available	Enhanced Quality Assurance
Flexel® Validation Guide and Extractables Guide	Facilitated validation and regulatory approval

Features	Benefits
Continuous processing without movement of the containers	Easy operation
Double hinged front door with safety latches	Easy access
Lifting system for large size containers	Optimal bag unfolding and filling

BioWelder® TC

Sterile Connections and Disconnections

reddot design award
winner 2013

The BioWelder® TC is a fully automated device for connecting thermoplastic tubing in a sterile welding operation. This new innovating technology allows sterile connection of liquid filled tubing up to 1 inch outer diameter.

Applications

The BioWelder® TC is used to connect thermoplastic tubing used on disposable bags or bag assemblies within all biopharmaceutical manufacturing processes. BioWelder® TC can weld either dry or liquid-filled tubing in non classified and classified environment while maintaining product sterility.

Features	Benefits
Liquid filled tubing from 5/8" to 1" OD	Flexible, multiple additions via the same tubing line
Fully automated device	Easy to use
Standard programs	Ready to use for C-Flex®, PharmaPure®, AdvantaFlex®, SaniPure® and PharMed® tubing
New design (including holder | blade)	Ergonomic
Extensively qualified	Safe and robust connections
Short welding time	Fast connections

BioSealer®

The BioSealer® is a fully automated device, designed to produce permanent and consistant leak free seals on thermoplastic tubing. There is no need of any laminar flow cabinet or similar environment to disconnect tubes from disposable bag assemblies (Gammasart BioSystems®) in a sterile manner.

Applications

The BioSealer® is used to disconnect thermoplastic tubing on disposable bag assemblies used in biopharmaceutical manufacturing processes. Individual bags or bag assemblies can be disconnected in a non sterile environment by maintaining sterility of the product.

Features	Benefits
Seals tubing between 1/4" - 3/4" OD	Automated and reproducible disconnection
Sealing times between 1 and 4 Minutes	Ready to start immediately
Programmable for several thermoplastic tubing	Easy adaption to various space requirements due to removable sealing head

Opta® SFT | Clipster® Aseptic Disconnector

Sterile Connections and Disconnections

Opta® SFT Sterile Connectors are used to create a sterile fluid path between two presterilized components in classified as well as non classified production environments Opta® SFT Sterile Connectors are quick and easy to use, and are backed by extensive validation work and 100 % in house integrity testing.

Applications

All operations in Up- and Downstream Processing that are using single-use or hybrid equipment.

Features	Benefits
Male and female connector couplings sealed with sterilizing grade membrane	Sterile fluid transfer in non classified & classified environments
Male and female connector couplings	Prevent mistaken connections
Sterilizable by Gamma irradiation & autoclave	Flexible implementation of Hybrid single-use and multiple use technologies
100 % integrity tested	Highest security
Claimed size equivalent to tubing ID size	No flow restriction
3-step operation	Easy, robust, repeatable operation
All hose barb connections intensively qualified (SFT-I only)	Safe and robust tubing connections

The Clipster® Aseptic Disconnector is a single-use device developed by Sartorius Stedim Biotech that completes our range of products by performing aseptic disconnections of tubing. The Clipster® Aseptic Disconnector may be sold as a stand alone product or preassembled on our Fluid Management bag assemblies. The Clipster® Aseptic Disconnector is safe, quick and easy to use. The disconnection is performed with a hand-held tool which ensures easy execution in various space requirements.

Applications

The Clipster® Aseptic Disconnector is used after a fluid transfer to disconnect single-use transfer lines and bag assemblies used in biopharmaceutical applications. The Clipster® Aseptic Disconnector allows aseptic disconnection in non classified and classified environments while maintaining product sterility. It can be applied to multiple types and sizes of tubing.

Features	Benefits
Mechanical disconnection	Could be performed on platinum cured silicone and TPE tubings
Error proof design	Prevents mistakes
4-step operation	Easy, quick, robust and repeatable
Intensively qualified	Safe and robust
Available as stand alone product or preassembled	Flexible
Hand-held tool	Easy to use
3 Clipster® sizes	Compatible with 5 tubing dimensions

TuFlux® SIL Silicone Tubing

TuFlux® SIL is designed to facilitate fluid transfer in the biopharmaceutical manufacturing processes. TuFlux® SIL is a highly resistant platinum cured silicone tubing manufactured by Raumedic.

TuFlux® SIL is available today in 7 different dimensions from 1/8" (3.2 mm) to 3/4" (19.1 mm) for the internal dimensions and a wall thickness from 1.6 to 4.8 mm.

Applications

TuFlux® SIL is designed to be used in many pharmaceutical and biopharmaceutical applications such as:

- Media and buffer processing
- Filtration
- Fermentation
- Cell harvest

Features	Benefits
Low extractable profile and unique Validation Guide for TuFlux® SIL available	Support validation of TuFlux® SIL in a process
Shore hardness A 60	Very good rupture strength in peristaltic pumps and reduced kink effect
Platinum Cured Silicone	Resistant against weak acids and bases and extraordinary heat and cold resistance
Translucent	Visual contact with the fluid
Printing of ID and OD dimensions on the tubing	Facilitates tubing identification
Coils wrapped in double PE-bags	Tubing protected and easy to introduce in clean room
"Low-Tack" significantly reduced surface friction	Easier handling with gloves

Overview Biopharma Upstream Production Process

Cell Bank

Seed Expansion

Production

Cell Removal

Media Preparation

Medium, Feeds

BioPAT® MFCS

FlexAct® MP

Sartopore® 2

Sartopore® 2 XLM

Sartopore® 2 XLG

Sartopore® 2 XLI

Sartoguard GF

Sartoguard NF

Virosart® CPV

Flexboy® Bags

Flexel® Bags

TuFlux® SIL Silicone Tubing

Flexboy® Bags

Flexel® Bags

TuFlux® SIL Silicone Tubing

Microsart® AMP Mycoplasma

CERTOMAT® CTplus

BIOSTAT® B

BIOSTAT® RM

UniVessel® SU

BioPAT® MFCS

Midisart®

BioWelder® TC

BioSealer®

TuFlux® SIL Silicone Tubing

BIOSTAT® STR

BIOSTAT® D-DCU

BioPAT® Spectro

BioPAT® Trace

BioPAT® MFCS

BioPAT® SIMCA-online

BioWelder® TC

BioSealer®

Midisart®

TuFlux® SIL Silicone Tubing

Sartofluor® Minicartridges

Sartopore® 2

Sartopore® 2 XLG

BioWelder® TC

BioSealer®

TuFlux® SIL Silicone Tubing

Microsart® AMP Mycoplasma

Sales and Service Contacts

For further contacts, visit www.sartorius-stedim.com

Europe

Germany
Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen
Phone +49.551.308.0
Fax +49.551.308.3289

Sartorius Stedim Systems GmbH
Robert-Bosch-Strasse 5 – 7
34302 Guxhagen
Phone +49.5665.407.0
Fax +49.5665.407.2200

France
Sartorius Stedim Biotech S.A.
ZI Les Paluds
Avenue de Jouques – CS 91051
13781 Aubagne Cedex
Phone +33.442.845600
Fax +33.442.845619

Sartorius Stedim France SAS
ZI Les Paluds
Avenue de Jouques – CS 71058
13781 Aubagne Cedex
Phone +33.442.845600
Fax +33.442.846545

Austria
Sartorius Stedim Austria GmbH
Franzosengraben 12
1030 Vienna
Phone +43.1.7965763.18
Fax +43.1.796576344

Belgium
Sartorius Stedim Belgium N.V.
Leuvensesteenweg, 248/B
1800 Vilvoorde
Phone +32.2.756.06.80
Fax +32.2.756.06.81

Hungary
Sartorius Stedim Hungária Kft.
Kagyló u. 5
2092 Budakeszi
Phone +36.23.457.227
Fax +36.23.457.147

Italy
Sartorius Stedim Italy S.p.A.
Via dell'Antella, 76/A
50012 Antella-Bagno a Ripoli (FI)
Phone +39.055.63.40.41
Fax +39.055.63.40.526

Netherlands
Sartorius Stedim Netherlands B.V.
Edisonbaan 24
3439 MN Nieuwegein
Phone +31.30.6025080
Fax +31.30.6025099

Poland
Sartorius Stedim Poland Sp. z o.o.
ul. Wrzesinska 70
62-025 Kostrzyn
Phone +48.61.647.38.40
Fax +48.61.879.25.04

Russian Federation
LLC "Sartorius ICR"
Uralskaya str. 4, Lit. B
199155, Saint-Petersburg
Phone +7.812.327.5.327
Fax +7.812.327.5.323

Scandinavia
Sartorius Stedim Nordic A/S
Hoerskaetten 6D, 1.
2630 Taastrup, Denmark
Phone +45.7023.4400
Fax +45.4630.4030

Spain
Sartorius Stedim Spain SA
C/Isabel Colbrand 10,
Oficina 70
Polígono Industrial de Fuencarral
28050 Madrid
Phone +34.90.2110935
Fax +34.91.3589623

Switzerland
Sartorius Stedim Switzerland AG
Ringstrasse 24 a
8317 Tagelswangen
Phone +41.52.354.36.36
Fax +41.52.354.36.46

U.K.
Sartorius Stedim UK Ltd.
Longmead Business Centre
Blenheim Road, Epsom
Surrey KT19 9 QQ
Phone +44.1372.737159
Fax +44.1372.726171

America

USA
Sartorius Stedim North America Inc.
5 Orville Drive, Suite 200
Bohemia, NY 11716
Toll-Free +1.800.368.7178
Fax +1.631.254.4253

Argentina
Sartorius Argentina S.A.
Int. A. Ávalos 4251
B1605ECS Munro
Buenos Aires
Phone +54.11.4721.0505
Fax +54.11.4762.2333

Brazil
Sartorius do Brasil Ltda
Av. Dom Pedro I, 241
Bairro Vila Pires
Santo André
São Paulo
Cep 09110-001
Phone +55.11.4451.6226
Fax +55.11.4451.4369

Mexico
Sartorius de México S.A. de C.V.
Circuito Circunvalación Poniente
No. 149
Ciudad Satélite
53100, Estado de México
México
Phone +52.5555.62.1102
Fax +52.5555.62.2942

Asia | Pacific

Australia
Sartorius Stedim Australia Pty. Ltd.
Unit 5, 7-11 Rodeo Drive
Dandenong South Vic 3175
Phone +61.3.8762.1800
Fax +61.3.8762.1828

China
Sartorius Stedim Biotech (Beijing)
Co. Ltd.
Airport Industrial Zone B
No. 33 Yu'an Road
Beijing 101300, Shunyi District
Phone +86.10.80426516
Fax +86.10.80426580

Sartorius Stedim Biotech (Beijing)
Co. Ltd.
Shanghai Branch office
Room 618, Tower 1, German Centre,
Shanghai, PRC., 201203
Phone +86.21.28986393
Fax +86.21.28986392.11

Sartorius Stedim Biotech (Beijing)
Co. Ltd.
Guangzhou representative office
Room 704, Broadway Plaza,
No. 233–234 Dong Feng West Road
Guangzhou 510180
Phone +86.20.8351.7921
Fax +86.20.8351.7931

India
Sartorius Stedim India Pvt. Ltd.
#69/2-69/3, NH 48 Jakkasandra
Nelamangala Tq
562 123 Bangalore, India
Phone +91.80.4350.5250
Fax +91.80.4350.5253

Japan
Sartorius Stedim Japan K.K.
Kiba Park Bldg
5-11-13 Kiba
Koto-ku
Tokyo 135-0042
Phone +81.3.5639.9981
Fax +81.3.5639.9983

Malaysia
Sartorius Stedim Malaysia Sdn. Bhd.
Lot L3-E-3B, Enterprise 4
Technology Park Malaysia
Bukit Jalil
57000 Kuala Lumpur, Malaysia
Phone +60.3.8996.0622
Fax +60.3.8996.0755

Singapore
Sartorius Stedim Singapore Pte. Ltd.
1 Science Park Road,
The Capricorn, #05-08A,
Singapore Science Park II
Singapore 117528
Phone +65.6872.3966
Fax +65.6778.2494

South Korea
Sartorius Korea Biotech Co., Ltd.
8th Floor, Solid Space B/D,
PanGyoYeok-Ro 220, BunDang-Gu
SeongNam-Si, GyeongGi-Do, 463-400
Phone +82.31.622.5700
Fax +82.31.622.5799

www.sartorius-stedim.com

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