



sartorius

# insight

Sartorius in Profile



## Laboratory

Faster Development of  
Novel Therapeutics

## Bioprocess

Innovative Technologies for  
Biopharmaceutical Production

## Corporate Values

Sustainability, Openness,  
Enjoyment



## MISSION

At Sartorius, we empower scientists and engineers to simplify and accelerate progress in life science and bioprocessing, enabling the development of new and better therapies and more affordable medicine.



## VISION

As pioneers, we are a magnet and dynamic platform for the leading experts in our field. We bring creative minds together for a common goal: technological breakthroughs that lead to better health for more people.

## Editorial



Dear Readers,

Many serious diseases, such as cancer, rheumatism and Alzheimer's, are still incurable or treatable only to a limited extent. Although global medical knowledge continues to expand at a rapid pace, the development of new drugs has become increasingly time-consuming and costly. It now takes an average of more than twelve years to progress from initial idea to market maturity at a cost of more than one billion euros.

Successes in the fight against certain cancers or autoimmune diseases have been achieved with biopharmaceutical drugs, such as monoclonal antibodies, which have rapidly evolved from a medical novelty into a dependable therapeutic. In the field of gene and cell therapy, recent breakthroughs promise further progress.

With innovative tools and technologies that cover key steps in drug development and production, Sartorius supports life science research and enables the biopharmaceutical industry to achieve relevant results faster, simplifying manufacturing and increasing the overall safety of production processes. In this way, we help to ensure that new scientific discoveries can be translated more quickly into effective patient care and that more people have access to better medicines.

The following pages describe how we do this, what motivates us and what our goals are.

Dr Joachim Kreuzburg  
Chairman of the Board

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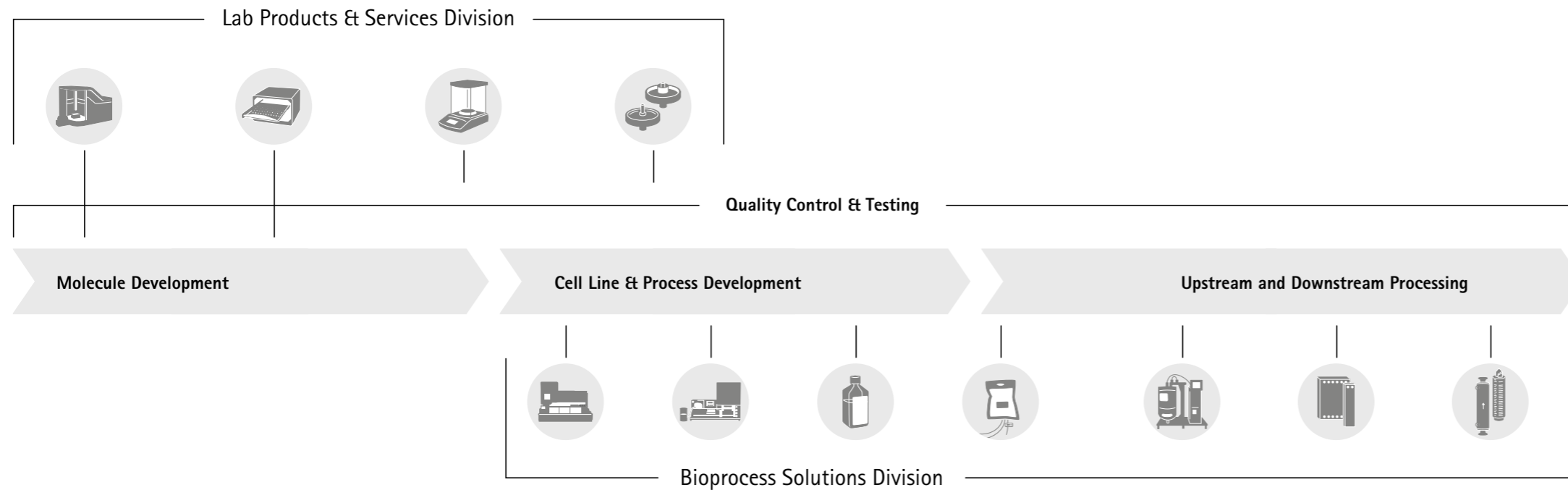
# Innovative Solutions for Better Medications

With its pioneering spirit and a profound understanding of customer requirements, Sartorius has evolved throughout its 150-year history into a key partner for biopharmaceutical research and the industry. Today, around 9,000 employees across the world are committed – day in, day out – to ensuring that customers can develop and manufacture new medications faster and more efficiently using our innovative tools and technologies.



Sartorius offers intelligent technologies to ensure that complex work and production processes are efficient and safe.

## Two Strong Divisions to Serve the Biopharma Market



Whether cancer, Alzheimer's, or rheumatism: many serious diseases are still not curable or can only be treated to a limited extent. Biopharmaceuticals are playing an increasingly important role in fighting these conditions. Such drugs are active compounds that are produced using living cells in complex research and production processes. Since the first biopharmaceutical, human insulin, was launched onto the market about 30 years ago, the industry

has been evolving at an exceptionally fast pace. In 2018, for example, seven of the world's best-selling medical drugs were biologics; in the same year, biotechnologically produced active ingredients accounted for approximately one third of all the newly approved drugs in the USA. Sartorius has been contributing to this progress with innovative tools and technologies that ensure more efficient processes at all levels, from research and development to commercial-scale production. As a result, Sartorius helps more people gain access to affordable medicines.

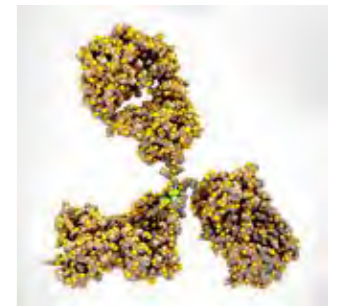
### Technologies for Every Phase of the Value-Added Chain

From an early stage, Sartorius identified the potential of the biopharma sector and subsequently aligned its product and service portfolio to this industry's requirements. Founded in 1870 as a precision engineering workshop for analytical balances, today's Sartorius Group is positioned as a strategic partner of biopharmaceutical research and the industry.

The Sartorius Group supports its customers every step of the way from initial idea to the market readiness of a new medication – a long, labor-intensive and expensive journey. On average, only one in 10,000 drug candidates actually makes it to the pharmacy counter. Until then, it usually takes more than a decade, with costs tallying up to substantially more than one billion euros being the rule rather than the exception.

As biopharmaceuticals are many times more expensive to produce than chemically manufactured medications, this puts mounting pressure on healthcare systems – and thus also on the pharma sector, which is compelled to design its workflows and manufacturing operations as efficiently as possible. What's more, as original drugs go off-patent, generic versions, so-called biosimilars, are increasingly entering the market. These are much faster and less expensive to manufacture than the original medicines.

## BACKGROUND



Biopharmaceutical active ingredient

## What are Biopharmaceuticals?

"Classic", chemically manufactured drugs are based on small molecules of only a few atoms. The situation is different with biopharmaceutical active ingredients. They are produced using living organisms – such as bacteria, yeasts or mammalian cells – and consist of very large molecules with up to 20,000 atoms. Therefore, they cannot be administered as tablets, but only by injection or infusion.

Their advantages: biopharmaceuticals only bind to very specific cell receptors and thus intervene more specifically than other drugs in the body's own processes. In particular, they open up new therapeutic options for patients with severe or rare diseases and are promising candidates in the fight against cancer.

## Share of biopharmaceuticals in the ten top-selling drugs

1 out of 10 | 2000



7 out of 10 | 2018



With its solutions available throughout the entire biopharmaceutical industry's value chain, Sartorius empowers its customers to accelerate drug discovery and development and make production more efficient. Its premium laboratory instruments take exacting benchtop routines to a whole new level of ease and accuracy; innovative bioanalytic technologies ensure the faster screening of drug candidates; highly automated microbioreactors help to determine the optimal growth conditions for cell cultures in parallel experimental series; and a broad portfolio of scalable single-use products, such as bioreactors, filters and bags, is available for the actual manufacture and purification of pharmaceuticals.

Compared with stainless steel systems, these single-use solutions have many advantages, particularly for production batches of up to 2,000 L. They are faster to install, require a much lower capital outlay, can be readily adapted to accommodate new production processes and are even more environmentally friendly than stainless steel systems; single-use products eliminate the need for highly complicated, labor-intensive and expensive cleaning procedures after every production run. At the same time, single-use systems minimize the risk of contamination by bacteria, fungi and viruses, which can sometimes survive even the most thorough cleaning protocols.

With its solutions available throughout the entire biopharmaceutical industry's value chain, Sartorius empowers its customers to accelerate drug discovery and development and make production more efficient.

**A History of Success with a Future Ahead**

The ongoing growth of the Sartorius Group shows that the company, along with its product offering, continues to keep pace with the qualitatively and quantitatively increasing needs of a demanding customer group. In recent years, Sartorius has been able to raise its sales revenue by an average of 10% annually. In many product categories, the Group is among the global market leaders. Sartorius aims to more than double its sales revenue from €1.6 billion, as reported in 2018, to €4.0 billion by 2025. In addition to organic growth, especially in the Asian and American markets, acquisitions are expected to contribute to the company's positive development. The major aim of these acquisitions is to further increase customer benefits with complementary additions to the company's product portfolio. The current focus is on solutions for digitalization and automation that can help biopharmaceutical research and the industry to achieve additional efficiency gains.

**Strong Company Values**

To remain one of the innovation leaders, Sartorius needs one thing in particular: staff members who identify with the mission and values of our company. Sustainability, openness and enjoyment are prerequisites for the constant development of even better solutions for our customers that will ultimately benefit patients. In addition to the expertise and commitment of its own employees, Sartorius relies on a mutually advantageous exchange of ideas with industry experts at business incubators, universities and start-ups by entering into collaborative partnerships and by setting up or joining network platforms. As the initiator of the Life Science Factory, an independent non-profit enterprise based in Göttingen, Germany, Sartorius is actively supporting prospective scientific entrepreneurs and young companies willing to take their first steps outside of academic institutions.

The biopharma sector, which is still quite young compared with traditional pharmaceutical manufacturing, will continue to develop in a dynamic way and, with its new therapeutic approaches, give new hope to millions of people. Sartorius will play an integral part in helping to further drive progress in this direction. ●



**1** Sartorius has its roots in weighing technology. Today, the company is an important partner for biopharmaceutical research and the industry.

**2** Sartorius generates about a third of its sales revenue with membrane-based products. The filtration portfolio is among the most comprehensive in the industry.

**3** Sterile single-use bags for cell culture processes and the storage and transfer of liquids are a safe, cost-effective alternative to glass and stainless steel. Sartorius is one of the world's leading technology providers in this field.

# People at Sartorius

Around 9,000 people at Sartorius dedicate their expertise and are fully committed – day in, day out – to empowering researchers and engineers to make faster progress in the life sciences and in bioprocessing.

**S**artorius attracts people with positive personalities who appreciate ample freedom and quick decision making, and who want to set big things in motion in the exciting life science sector. Because, as unique as each individual is, they all share a common goal: better health for more people.

#### **Moving Ahead and Making a Real Difference**

Ever since its inception, a pioneering spirit, out-of-the-box thinking and creativity have been driving Sartorius – and its success – forward. With groundbreaking technologies, a strong brand and long-term relationships with customers and partners, Sartorius has been actively shaping its markets. Those who work at our company strive to move things forward and set trends. We look for people who share these ambitions and enjoy making a difference with their own efforts and activities.

#### **Growing and Going Forward**

Only those who are willing to step outside their comfort zone can grow professionally and personally. At Sartorius, employees have the opportunity to proactively drive their careers forward in a dynamically

growing company and, ultimately, advance their development in a variety of geographies while staying with us. As a globally operating group, with approximately 60 production sites and sales offices, Sartorius is at home around the world.

#### **Strong Individuals, Great Team Spirit**

Sartorius is proud that it employs people from nearly 80 nations – many of them experienced specialists who are among the best and brightest in their fields. They appreciate diversity and constructive dialogue with their co-workers who have different cultural backgrounds or may even share different opinions. Not only does the company benefit from the results of this exchange, but so does each individual. This is why promoting team spirit and recognizing individual achievements is a given for Sartorius. ●

In Yauco, Puerto Rico, Sartorius' 500 employees produce membrane filters and single-use bags for the American market. Ramon Ramirez works as a plant operator in filter cartridge production.



In Bangalore, India, about 400 Sartorius employees produce stainless steel bioreactors, components and filters. As Senior Project Engineer in the Integrated Solutions division, Kavitha Gowda is responsible for project management and the on-time delivery of customer-specific production systems.



#### Sandra Mei

Responsible for human resources management since 2013 in eight Asian countries

**Growing with your tasks** "I can handle it, is what I thought when I was assigned responsibility for five additional Asian countries. Before that, I had spent three years exclusively dedicating my efforts to taking care of staffing for the strongly growing Chinese market. My new set of tasks turned out to be more complex than I had originally expected: the cultural differences between the countries are considerable, so handling job candidates requires a lot of tact, good instincts and skill. Since then, I have been learning something new every day. What I also enjoy about my job is the freedom to define my work schedule and activities. As a result, I can fulfill my personal needs and continuously broaden my horizons. I can't think of a better way to be motivated than working like this."



#### Dr Noushin Delmdahl

Protein biochemist who, together with her team, develops lab filtration technologies in Göttingen

**United by shared goals** "Before I joined Sartorius in 2001, I had mostly worked on scientific projects and spent a lot of time in the lab. After switching to the company, I took on new team-based and customer-facing tasks. Today, I work closely with co-workers all over the world and appreciate the dynamics that are generated in a team when you work towards achieving shared goals. I have experienced over and over again that borders and time zones play a minimal role when you're working in an enriching and stimulating environment. In addition, because I've been able to further develop my skills and knowledge at Sartorius, the years have flown by. Yet, with our expansion into the field of bioanalytics, the scientist in me still has the most exciting time ahead of her."



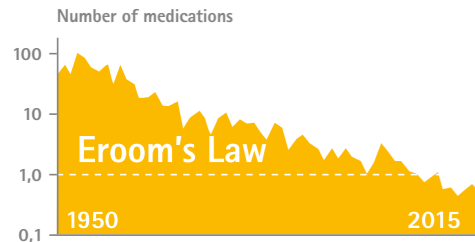
#### Amit Sharma

Director of project management in Singapore, in charge of implementing strategic sales and marketing projects in Asia

**Actively shaping the future** "Around 20 years ago, I joined Sartorius as a Regional Manager in India. Since then, I have experienced many times how Sartorius and its products have defined the future of technology. There are few sectors that have been evolving technologically and economically as fast as the biopharmaceutical market, especially in Asia. That I can actively shape these markets of the future is a major source of motivation for me. After all, a little bit of Sartorius goes into the making of almost every medication available."



# Did you know that ...?



... the number of approved drugs per US\$1 billion spent on R&D has halved every nine years since 1950?

As paradoxical as it may seem and despite many technological and medical advances, the development of new drugs is becoming increasingly inefficient. This is why we speak of "Eroom's Law," a reversal of the concept coined by Intel cofounder Gordon E. Moore in 1965, according to which the performance of processors doubles every two years. Sartorius helps to reverse this trend and shorten the time-to-results.

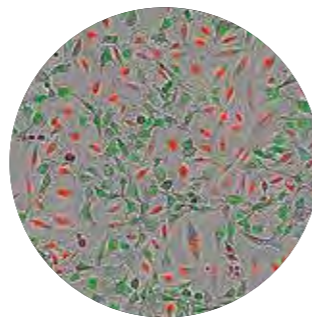
... medication can be tailored to a single person?

In CAR-T cell therapy for the treatment of certain forms of leukemia, the body's own defense cells are removed, genetically modified, multiplied and returned to the patient. This process is complex and expensive – and results in a drug that can only be administered to one person. Sartorius solutions accelerate the development of these treatments and ensure safe production.



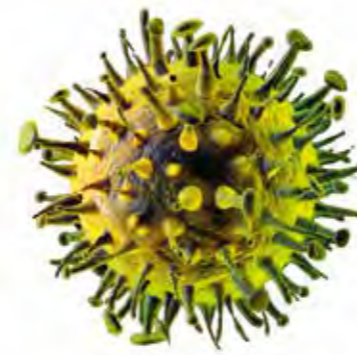
... company founder Florence Sartorius once brooded quite productively over the technologies that are now at the core of biopharmaceutical production?

Sartorius developed heat boxes that were used for bacteriological purposes and as incubators in poultry breeding. Thermostats regulated the ambient temperature so precisely that the cultivation and incubation process could be accurately controlled. The technology – a precursor of today's bioreactors – sold successfully throughout Europe.



... Sartorius also supplies surveillance technologies?

With the IncuCyte® S3, researchers can observe living cells in real-time directly in the incubator to analyze how active ingredients attack and destroy cancer cells. Until now, it was only possible to photograph cell cultures at certain times and document the changes afterwards. The IncuCyte® S3 reduces the effort compared with the manual method and provides better results without disturbing the sensitive cultures.



... biotechnology can reduce our dependence on drug sources?

Around 90% of flu vaccines are produced with the help of serum eggs. About half a billion of these are needed each flu season. The production method has long lead times and is subject to risk, such as not enough eggs being available in the event of a pandemic. The World Health Organization (WHO) therefore advocates a diversification of processes through, for example, cell-based production.

... even serious science sometimes transcends earthly things?

NASA used the Sartorius Air-Port MD8 on the International Space Station (ISS) to learn more about airborne microbial contamination and its possible effects on the crew. The device filters up to 125 L of air per minute and collects viruses, fungi and bacteria for subsequent cultivation and microbiological analysis.



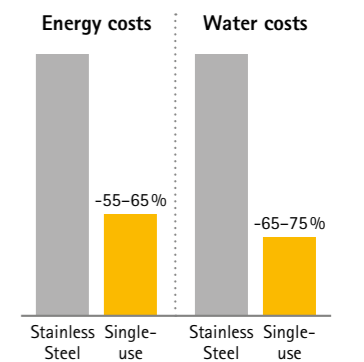
... it's possible to watch water dissolve into air?

The Sartorius mass comparator measures mass differences to the seventh decimal place. This makes it possible to observe in real-time how a Petri dish filled with water becomes lighter every second through evaporation. The mass comparator has an important function: after replacing the original kilogram, it makes it possible to create a mass scale traceable to the new SI standard by mass determination using 1 kg silicon spheres.



... single-use is more environmentally friendly than reusable?

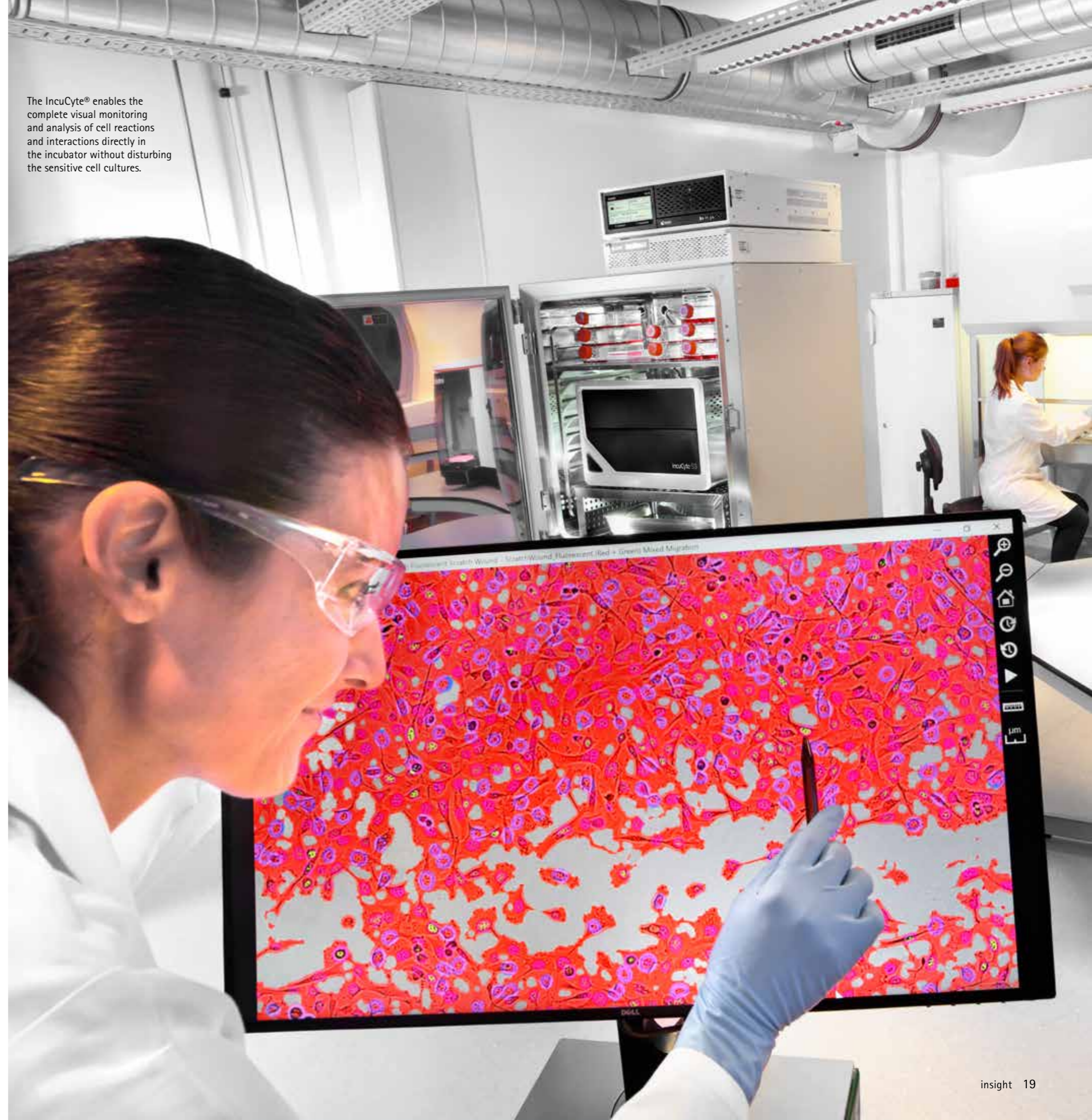
Single-use technologies such as bags, filters and centrifuges eliminate the need for costly cleaning procedures. A client of Sartorius was able to reduce water and energy usage by more than 60%, while increasing product safety at the same time. After use, the energy rich materials are used to generate heat or electricity. Sartorius is a pioneer in the field of single-use technologies and supports its customers to make production processes more efficient with the help of single-use products.



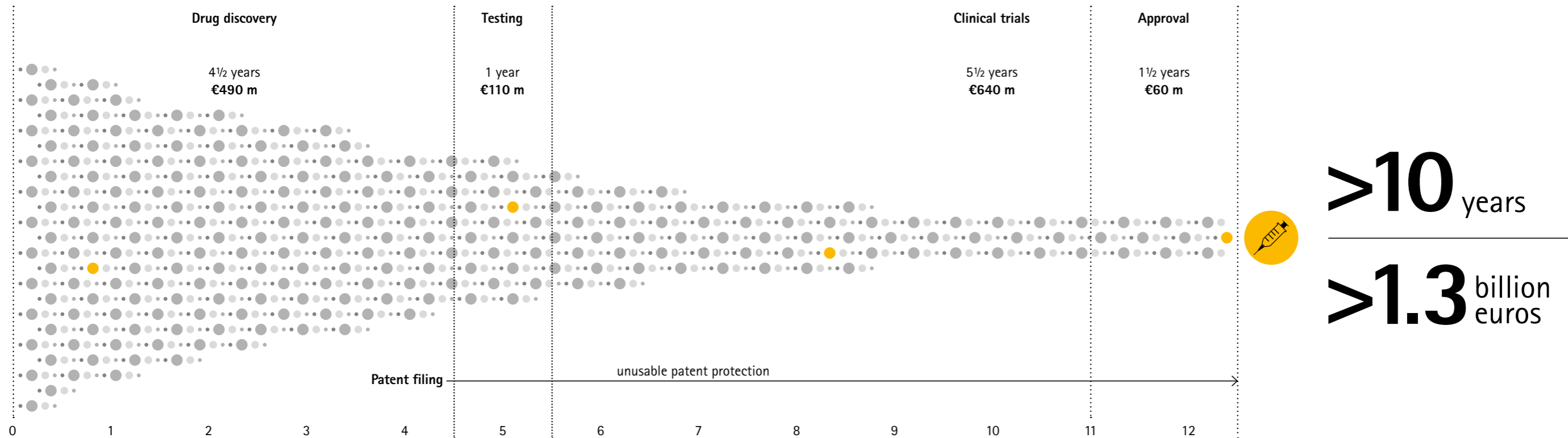
# Faster to Market

Biopharmaceutical research and development can be likened to looking for a needle in a haystack. With groundbreaking analytical technologies and premium laboratory instruments, Sartorius is providing researchers with the tools that help to identify new active drug compounds faster.

The IncuCyte® enables the complete visual monitoring and analysis of cell reactions and interactions directly in the incubator without disturbing the sensitive cell cultures.



Only one out of 10,000 drug candidates reaches the market\*



\* Schematic visualization with data from the Association of the British Pharmaceutical Industry

Pharmaceutical companies invest a lot of time and money to bring a new drug to market. Technologies from Sartorius accelerate the research process and reduce costs.

The rate of finding a successful candidate gives even the uninitiated among us an idea of how complex and laborious biopharmaceutical research and development is: only one in 10,000 potential drug candidates passes muster as a new marketable therapeutic. Until then, it's a long haul, involving thousands upon thousands of experiments, sample preparation procedures and analyses. Therefore, one of the biggest challenges in biopharmaceutical research and development is to significantly reduce the drug discovery timeline. This is all the more true because active ingredients have to be patented early in the R&D process. With a patent protection period of 20 years from

the filing date, only about twelve years of market exclusivity remain on average after final approval of the drug. Sartorius technologies help to achieve results faster.

**The Turbo in Biopharma Research: Automated Bioanalytics**

In the search for new therapies, researchers must first find a gateway to combat the disease, such as a specific type of cancer. Unlike chemotherapy or radiation treatment, biopharmaceuticals use a patient's own immune system. For instance, monoclonal antibodies (mAbs) are of great importance in this therapeutic approach. These proteins, produced by living organisms and developed in the lab, are designed so that they specifically bind to sites on cancer cells, marking them for destruction by the immune system.

What sounds simple in theory is, in fact, a long and painstaking process. To facilitate and substantially accelerate the screening and selection of drug candidates, Sartorius offers innovative bioanalytic systems. For example, IncuCyte® and iQue® Screener deliver answers to essential questions, such as "Is the cell alive? Is it dividing? Is it producing the desired antibody? How does my active pharmaceutical ingredient interact with diseased or healthy cells?"

While IncuCyte® with its live-cell imaging enables the continuous visual monitoring and analysis of cell reactions and interactions directly inside an incubator,



1 The fluorescence-based Intellicyt iQue® Screener platform rapidly examines thousands of samples and delivers multivariate cell and protein analysis.

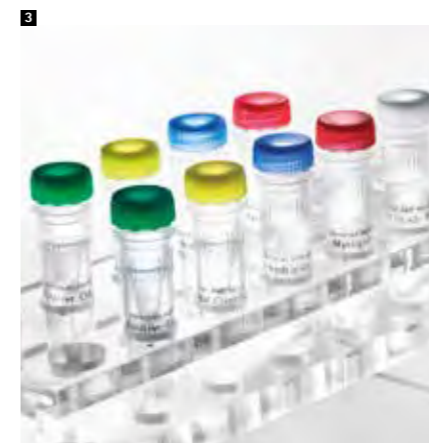
2 The precision pipetting of samples and reagents is the basis of reliable analytical results. The ergonomic design of Sartorius pipettes protects muscles and joints during daily routine tasks.

3 Microsart® kits enable the detection of mycoplasma within only a few hours and are used in many stages of biopharmaceutical research and manufacturing.

4 The extensive functionalities of Sartorius laboratory balances make complex applications easier and ensure conformity with the required standards.



2



3



4

the advantages of the fully automated Intellicyt iQue® Screener platform lie in the combination of data depth and high speed. A simultaneous feed of up to 1,536 samples, analysis, data evaluation and even cleaning of the instrument are all performed with walkaway convenience. The smallest samples of only one microliter are sufficient to provide informative, multi-parametric data on the most diverse cell parameters. As a result, iQue® Screener not only accelerates analysis ten-fold, but is also gentle on costly cell cultures, reducing the use of expensive reagents.

**Better Results, Less Effort**

Despite progress in digitalization and automation, manual processes still dominate daily lab work. In this area as well, Sartorius products ensure that better results can be obtained reproducibly, faster and safer. Premium laboratory instruments, such as high-precision balances with intelligent assistance systems, ergonomic pipettes to minimize muscle and joint strain and ultrapure

water systems both reduce manual effort and set the foundation for reliable sample preparation and analyses. For microbiological quality control, Sartorius offers a wide array of products, such as filtration systems, sterility testing units and solutions for airborne microbe sampling, virus quantification and for the detection of mycoplasmas. They are not only used for pharmaceutical research, but also in the quality control laboratories of the food and beverage industry, to test clinical products and for monitoring both water and wastewater.

Yet, regardless of where our products are used, they consistently help to prevent errors, simplify workflows and reduce physical workloads. On average, it takes more than ten years for a new biopharmaceutical drug to be ready for the market. Sartorius solutions can help to shorten this timeline and reduce costs. ●

3D bags for biopharmaceutical solutions of up to 3,000 L offer a safe, ecological and economical single-use alternative to conventional containers made of stainless steel or glass.

# Single-Use, Single Objective: Efficiency in Production

In biopharmaceutical production, a combination of the most diverse factors is decisive for the quality and cost-effectiveness of a finished drug product. It's no coincidence that experts claim that "the process is the product". With scalable single-use technologies for bioreactors, filters and bags, as well as tools for process development and monitoring, Sartorius helps its customers to obtain the best possible results from their manufacturing processes, both qualitatively and quantitatively.



1

BACKGROUND

Microsize for Maximum Impact



Sartorius' smallest single-use bioreactor holds 15 mL, approximately the same amount as a shot glass. The microreactor mimics the characteristics of lab scale bioreactors to enable optimal cell growth, productivity and product quality, thus helping scientists to select the best cell line and optimize the media and feed strategy.

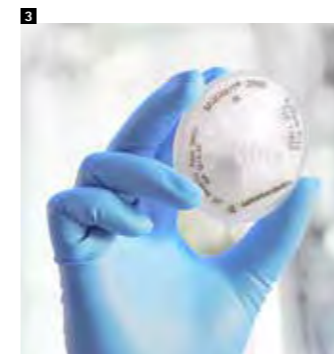
The cell line used, composition of a liquid culture medium, dissolved oxygen and pH, temperature, stirring speed ... – the list of factors governing the success or failure of a biopharmaceutical production process is long. Why? Cells are demanding and require optimal conditions to grow and produce the target drug in as large quantities as possible. Sartorius, with its broad-based portfolio of single-use solutions, covers almost every stage of biopharmaceutical manufacturing – from cell cultivation and propagation to harvesting, purification and filling of the final product.

High Tech Solutions that Fit in a Shot Glass

To ensure successful commercial-scale manufacture, a production process is initially tested at a much smaller scale. Similar to the drug discovery phase, Sartorius digitalization and automation solutions also help in process development to obtain better quality results within the shortest timeframe. The ambr® automated bioreactor platform, for example, can accommodate vials of 15 mL or 250 mL, enabling up to 48 experiments to be run in parallel with a small footprint. For each of these miniature bioreactors, the individual parameters, such as media and feeds or pH, can be set independently. The system regularly takes samples to monitor and document cell development, autonomously maintaining stable cell cultivation conditions.



2



3

1 With the automated microreactor system ambr® 15, researchers can conduct up to 48 independent cell culture experiments in a very small space.

2 The fully preassembled UniVessel® single-use bioreactor for volumes of up to 2 L reduces the time and effort required to develop, optimize and validate cell culture processes.

3 The hydrophobic Midisart® sterile filters allow the safe venting of small culture vessels and prevent moisture from penetrating.

Cells are demanding and require optimal conditions to grow and produce the target drug in as large quantities as possible.

THREE QUESTIONS FOR ...

Prof. Oscar-Werner Reif, PhD

Chief Technology Officer, Corporate Research



What will biopharma production look like ten years from now?

Production lines with a modular and flexible equipment set-up that are mostly or completely based on single-use technologies will be the norm. These lines will no longer be installed in expensive and maintenance-intensive cleanrooms, but rather in a more efficient production environment under controlled conditions. This will enable manufacturers to adapt their production capacities faster to respond to new requirements and simplify technology transfer. As a result, production will not only become much more flexible, but also less expensive. New medications will be available to patients faster, effectively helping people suffering from rare diseases.

Lowering the costs of biopharmaceuticals is not just about optimizing development and production processes for new active drug compounds, is it?

That's correct. In the coming years, many original biopharmaceuticals will go off-patent. Currently, more than 200 companies around the world are working on more than 1,000 products called biosimilars or me-too drugs. As the development of biosimilars is much more complex and expensive than for conventional generics, we can assume that the potential savings will be much lower. Owing to the relatively high prices of original medical drugs, though, the use of biosimilars as substitutes for such generics will undoubtedly provide financial benefits for healthcare systems.

How do joint ventures impact Sartorius' innovative strength?

No one can be an expert in every field. We primarily focus our development work on our core technologies; therefore, we have also maintained partnerships with other companies and research centers for a long time. This is what enables us to integrate new technologies and products rapidly into our portfolio. The successes of recent years, as well as the breadth and quality of our portfolio, suggests that we are on the right track. I would even venture to say that we have developed true core competencies in co-operation management and the integration of new technologies.



**A Singular Approach: Single-Use**  
Once the ideal interaction between parameters has been established, it is important to be able to reproduce the same conditions independently of the size of a bioreactor. Sartorius single-use technologies enable processes to be scaled from 250 mL to 2,000 L. But this isn't their only advantage. To overcome many industry hurdles, such as time and cost pressure, hygiene standards and regulatory requirements, as well as the trend toward ever-smaller production batches, single-use offers a safe and cost-effective solution. Compared with stainless steel systems, the initial investment in single-use equipment is much lower, the time needed for planning and commissioning is less, single-use systems are easier to changeover to manufacture other products and the risk of contamination by bacteria, fungi or viruses is minimized. This is achieved because any part that comes into contact with the

liquid cell broth is disposed of after each production run and completely exchanged for new, sterile-packaged components. The procedures required to clean stainless steel systems using chemicals and steam sterilization are eliminated entirely. This is not only more environmentally friendly, but also reduces the time needed to ready the system for the next production process to just a few hours. Therefore, it's no surprise that single-use technologies are being increasingly used in biopharmaceutical research and production, especially for relatively small drug batches. Sartorius, with its broad and innovative array, is actively contributing to this trend and is the leading global provider of single-use bioreactors and bags.

**Precise Control of Sensitive Processes**  
What works in cell cultivation and scale-up may not always do so during production in a 2,000 L bioreactor. As cell cultures are highly sensitive and react to the slightest changes, strict monitoring of the production process is vital. In this phase, Sartorius uses process measurement technology and software for multivariate data analysis to ensure that relevant parameter measurements can be collected, documented and evaluated in real-time. The system reveals correlation patterns between the individual parameters so that the right conclusions can be drawn and countermeasures taken in good time in the event of process deviations. This ensures that each batch meets the highest quality requirements and reduces the risk of losing a production batch.



4 Multivariate software for modeling and monitoring cell culture processes helps to improve product quality and increase drug yield.

5 Sartoclear® depth filters are developed for demanding clarification applications in the biotechnological and pharmaceutical industries. The modular devices provide linear scalability from small to large scale processes.



6 The preassembled Maxi-Caps® MR single-use filter configuration for the filtration of large volumes requires 90% fewer hoses and connections than comparable stainless steel systems.

**Purification Expertise from the Source**  
Downstream processing begins once the cells have produced the desired amount of antibodies. During this stage, the active drug compound is harvested and purified in steps to remove undesirable components in the cell broth. This is when mechanical separation applications using different membranes play a key role. Sartorius' extensive filtration portfolio is based on more than nine decades of experience as a manufacturer of membranes. It's been a core competence of the Sartorius Group since 1927 when Wilhelm Sartorius, together with Richard

Single-use technologies are a safe and cost-effective alternative to conventional stainless steel systems.

7 Celsius®-Pak enables the uniform, reproducible freezing and thawing of biopharmaceutical liquids and is suitable for long-term deep-freeze storage.

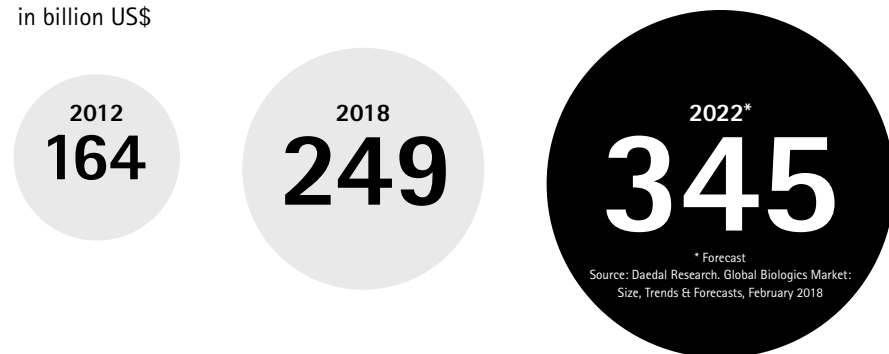


Zsigmondy, the Nobel Prize winner for chemistry and inventor of the membrane filter, founded a membrane filter company called "Membranfiltergesellschaft mbH," a "joint venture" that laid the cornerstone for today's comprehensive filtration portfolio. Ever since, the company has continued to refine, differentiate and diversify its membrane technology. Now, the Sartorius Group is among the three global market leaders for filtration technology. However, Sartorius is not, and never will

be, content to rest on the laurels of its past successes. Together with its clients, the company is continuously working to further enhance, optimize and expand its product solutions throughout the biopharmaceutical value chain, with customer benefits in mind. The corporate objective is clearly defined: Sartorius, with its innovative tools and technologies, aims to accelerate research, simplify production and contribute toward giving more people access to better medicines. ●

Together with its clients, Sartorius is continuously working to further enhance, optimize and expand its product solutions

Worldwide expenditure on biopharmaceuticals  
in billion US\$



Every production process is different. Together with its customers, Sartorius supplies and implements individual solutions from the development phase through to industrial production.



# Everything From a Single Source

Today, monoclonal antibodies represent one of the most successful strategies in the fight against various cancers. They are developed and produced using living, genetically modified mammalian cells in sophisticated processes. Sartorius' innovative solutions are used for key steps of biopharmaceutical

research and industrial manufacturing – from molecule and cell line development to cell growth, production and harvesting of the active ingredient, as well as the purification and filling of the final product.

## Molecule Development

### Identification of target molecules

Drug development begins with the search for a "target" in the cancer cell, such as a specific protein on the cell surface. The focus often centers on ascertaining which signaling pathways are the basis of the disease and what role the target plays in this process. The cell analysis platform IncuCyte® facilitates the monitoring of living cell cultures directly in the incubator and provides detailed insights into biological mechanisms.

### Library screening

In the next step, researchers will investigate which antibodies bind to the most promising targets and might potentially produce the desired effect. Candidates are identified using antibody libraries containing millions of different antibodies. On average, about 1,000 of them are shortlisted. The high-throughput screener iQue®, which combines speed with in-depth data, helps to assess the binding capability.

### Lead optimization

The antibodies that remain post-screening will be further analyzed in terms of their stability, for example, and their potential to trigger desired or undesired reactions in the patient. Targeted modifications are also used to optimize the properties of the antibodies. Through its subsidiary, BioOutsource | Cellca, Sartorius offers services for the physicochemical, structural and biological analysis of mAbs.

### Candidate characterization

The optimization is followed by analyses to fully define and characterize the antibodies, including properties such as efficacy, chemical structure and toxicology. It's also important to establish whether changes to the molecule would endanger the safety of the patient. Finally, it must be ensured that the active ingredient can be produced and that it survives the complex cleaning process undamaged.

## Cell Line & Process Development

### Gene cloning and transfection

A stable cell line that reliably produces the antibody in large quantities is required for the production of the active substance. A DNA sequence that has been cloned millions of times with the help of bacteria, and serves as a construction manual for the protein, is inserted into the DNA of the host cells for this purpose. However, this so-called transfection is only successful in some of the cells. The corresponding cell populations are selected and cultivated using a special procedure.

### Cell line selection

Individual cells ("clones") from the best cultures are isolated for further propagation. This creates the monoclonal populations required for industrial production. The selection is based on parameters such as cell growth, productivity, viability and quality of the mAbs produced. The search for the optimal clones is expedited by the fully automated ambr® 15 microbioreactor system, which can perform up to 48 experiments simultaneously.

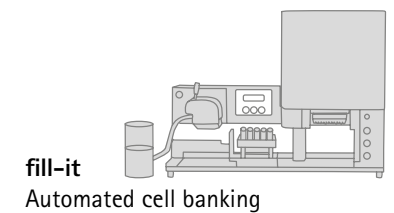
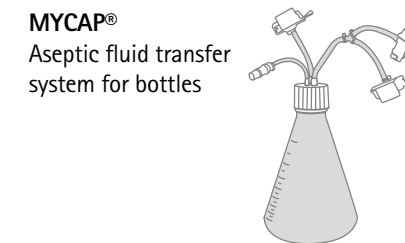
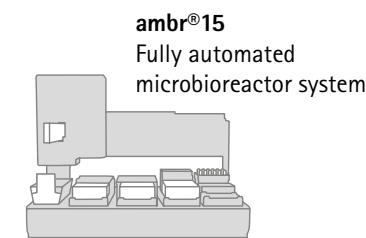
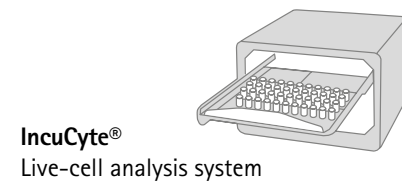
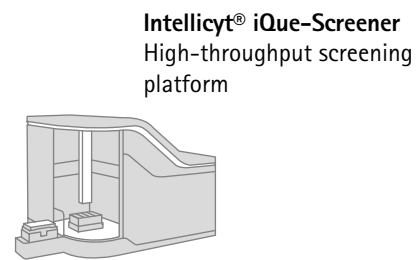
### Cell line characterization

A prerequisite for the further use of the cell lines is their complete characterization. The sterility of the cell culture must also be guaranteed to prevent contamination by bacteria, mycoplasma or viruses. BioOutsource | Cellca supports the entire process from cloning the DNA sequence to creating the cell bank.

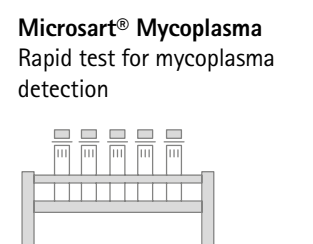
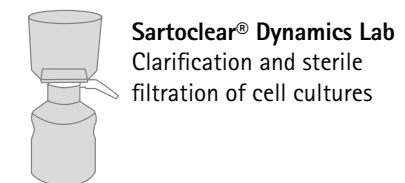
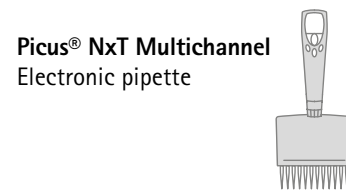
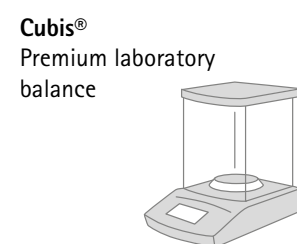
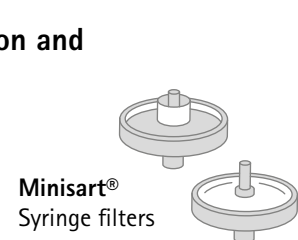
### Cell banking

Cell aging or repeated subcultivation can lead to changes in the genome that have a negative effect on the desired antibody. In a master cell bank, clones of a single cell culture are frozen for later use. Thus, every production process can be started with "fresh" cells. The Sartorius fill-it system enables the rapid dispensing of cell cultures into cryotubes.

## Analysis and development

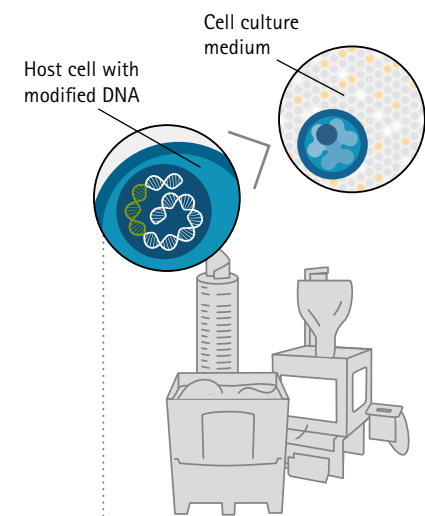


## Sample preparation and quality control



Upstream

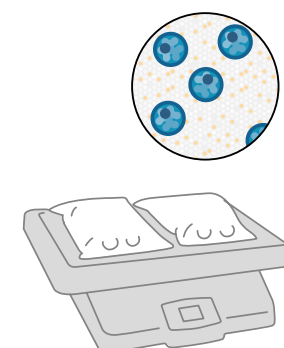
Downstream



**Culture media preparation**

Cell culture media  
Sterile filter cartridges  
Single-use bags for storage and mixing  
Virus removal filter cartridges

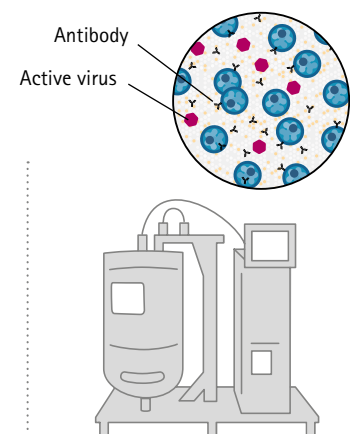
For optimal division of the thawed cells, they need perfect conditions. The culture medium – adapted to the respective cell culture – plays a critical role. It contains nutrients such as proteins, sugars and salts and provides the cells with everything they need to grow and thrive.



**Seed cultivation and preculture**

A range of different size bioreactors

The cells grow and are gradually transferred to ever-larger bioreactors in which they continue to propagate. Here, ideal conditions must prevail, including oxygen content, pH value and temperature. This process can take several weeks.

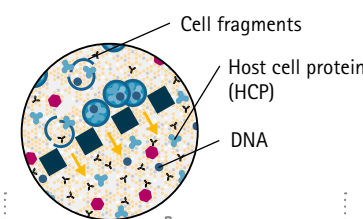


**Production**

Production bioreactors up to 2,000 L (single-use)

Sensors for Process Analytics (PAT)

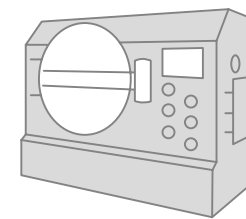
During this phase, the cells begin to produce the desired antibody and release it into the liquid culture medium. No impurities, such as bacteria or viruses, may enter the bioreactors during the entire process. Therefore, production takes place in a sterile environment.



**Clarification**

Depth filter

The antibodies are harvested at the end of each production run. The cells and their fragments are separated from the solution containing the antibodies by depth filtration or centrifugation. What remains are finer contaminants and by-products such as certain host cell proteins (HCPs) or DNA, originating from and released by the cells into the culture medium.



**Centrifugation**

Single-use centrifuge

For cell therapy, vaccine production or blood processing applications, single-use centrifuges are increasingly being used for the continuous recovery of cells or particles.

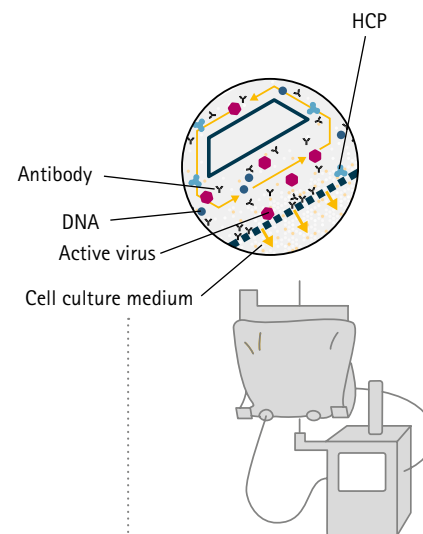
They can process very high cell densities, deliver excellent yields and maintain product quality at the same time.



**Sterile filtration**

Sterile filter cartridges

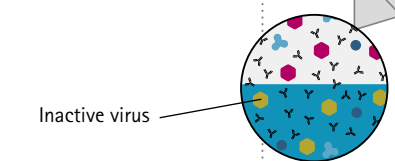
After the harvest, the so-called purification of the active ingredient begins. Prior to this, the solution is preventively subjected to sterile filtration. The entire purification process must be very thorough to ensure that patients receive a safe drug. In addition, it must also be performed carefully to ensure that the stability and efficacy of the sensitive antibody are not compromised.



**Ultra- and Diafiltration**

Crossflow filter systems

In a first step, the mixture of antibodies and culture media is concentrated by cross-flow filtration. The liquid is pumped across a membrane and the purified solution is drawn off transversely to the direction of flow. This technique removes water, salts and small proteins. At the same time, the pH value is also changed for the next step.

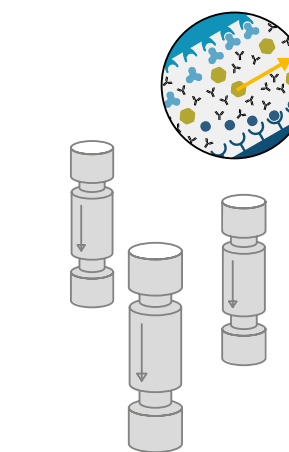
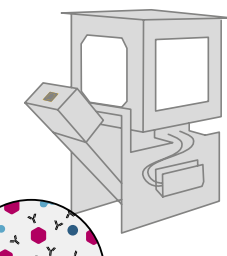


**Viral clearance**

Mixing tanks

Virus filter cartridges  
UV-C irradiation inactivation system

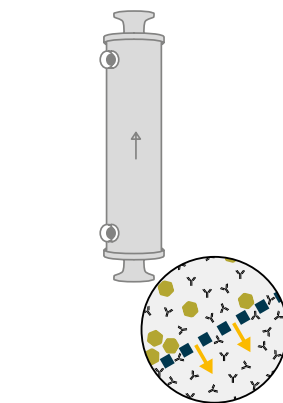
Now, the antibodies are further isolated from the other components of the solution by binding them to a "partner" in columns. In the case of antibodies, for example, this could be an antigen. This binding is reversible: if the pH value changes again, the antibodies are released from their binding partners.



**Polishing**

Membrane chromatography

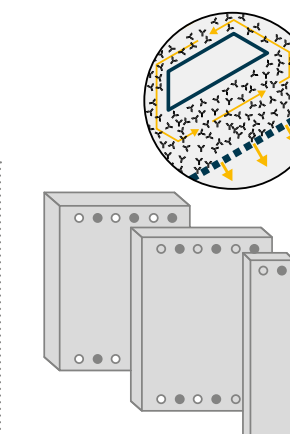
Membranes are also used at this stage. Their surfaces have been modified so that any remaining impurities – such as DNA or HCPs – adhere to them.



**Virus filtration**

Virus filter cartridges

At the end of the purification process, any potentially present viruses must be eliminated from the solution for the patient's safety. They are retained by special virus filter cartridges. What remains is the solution containing the antibody – the pure active ingredient. Sartorius offers the most comprehensive portfolio of virus removal filters and is therefore one of the leading suppliers in this field.



**Concentration**

Crossflow filter systems

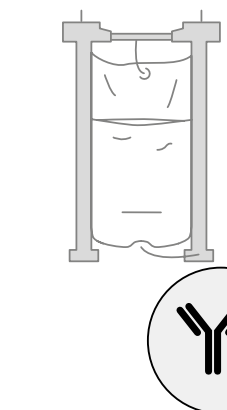
The final steps in biopharmaceutical production are also demanding: the active substance must now be converted into a drug that can be administered in the correct concentration and that can be absorbed by the patient's body. For this purpose, the antibody solution is adjusted to the final concentration, its pH value is optimized and it is combined with suitable excipients.



**Sterile filtration**

Sterile filter cartridges

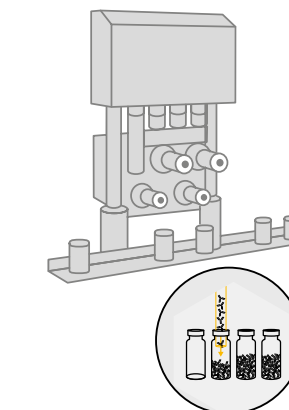
Before storage or filling, the medical drug is once again filtered for safety reasons. To avoid contamination, biopharmaceutical production facilities are strictly controlled, self-contained systems and many of the individual steps are now fully automated.



**Cryopreservation**

Freeze and thaw systems

Sartorius has developed innovative freeze and thaw systems so that manufacturers do not have to fill the drug immediately after production. They can be used to quickly and evenly freeze intermediate products or the finished drug in single-use bags, store them or transport them to other locations where they can be thawed again. This enables manufacturers to produce and stockpile large quantities of an active ingredient to respond to changes in demand.



**Final filling**

Filling systems

In the final production step, the medication is aseptically filled into syringes or ampoules. Like all biopharmaceuticals, antibodies against cancer are too fragile to pass through the gastrointestinal tract unharmed. Therefore, the drug is administered to the patient by syringe or infusion.

To model and optimize biopharmaceutical manufacturing processes, innovative data analysis software is used at many points during the process chain. These data-based digital tools make the processes even more efficient.



Its comprehensive bioreactor portfolio makes Sartorius the worldwide leader in upstream processing. In the downstream sector, Sartorius is advancing these procedures by developing innovative and enhanced single-use technologies, such as membrane chromatography, body feed filtration for antibody harvesting, and freeze and thaw systems.

# Strong Company Values

Sustainability, openness and enjoyment are the values that shape our work with colleagues, customers and business partners alike. By incorporating them into our thoughts and actions on a daily basis, we create a positive corporate culture, which is an important source of long-term economic success, lasting motivation and above-average performance.

## Sustainability



**Growing profitably and acting responsibly towards all stakeholders**

**B**ased on a foundation of customer orientation, excellence and innovation, sustainability for Sartorius means working towards positive and mutually successful relationships with various stakeholder groups in all our business activities. With our customers and business partners, we rely on trusting and lasting relationships that benefit everyone involved. We offer our employees a working environment in which they can continuously develop, both professionally and personally. Investors can expect a corporate policy that is geared to continuous and sustainable value enhancement. Wherever we are in the world, we want to be a responsible member of society and a good neighbor. ●

## Openness



**A source of change and progress**

**I**t's well known that "the better is the enemy of the good". We regard openness – both internally and externally – as a basic prerequisite to exploit our Group-wide potential, question tried and tested methods, learn from others and recognize the better in the new. Combined with our technological know-how, openness is key to developing innovations that really make a difference and create value for our customers. ●

## Enjoyment



**A working environment with freedom and appreciation**

**A**t Sartorius, hard work and pleasure go hand in hand because our employees not only work with their minds, but also with their hearts. In return, Sartorius offers them plenty of freedom and tasks that allow them to grow and realize their personal potential. The company appeals to people who like working in international teams, who enjoy taking on responsibility and who appreciate breaking new ground and celebrating their success together. This team-oriented and open manner is also how we work together with our customers. ●

# From a Good Idea to an Innovative Solution

The pressure to innovate in (bio)pharmaceutical research and production is intense. For Sartorius, strategic innovation management is therefore fundamental to the sustained growth of the Group. This means improving existing solutions in a user-oriented way, quickly recognizing the potential of new technologies, forging partnerships and transforming technologies into groundbreaking innovations through intelligent integration. The single-use BIOSTAT® STR bioreactor family, for example, is the result of successfully integrating proprietary core technologies, acquisitions and the products of strategic partners. ●

**Aseptic single-use bags** | With the acquisition of Stedim Biosystems, the “inventor” of single-use bags for biopharmaceutical applications, Sartorius paved the way in 2007 for the development of fully scalable single-use bioreactors with properties that matched those of classic stainless steel stirred vessels. The sterile, three-dimensional bags form the core of the reactor and are disposed of after production, including all tubes.

**Bioreactor Technology** | In 2000, Sartorius acquired B. Braun Biotech, the world’s leading provider of fermentation technology, to expand its portfolio to include the central process step in biopharmaceutical production. Although customers with large-volume applications continue to rely on stainless steel equipment from Sartorius, the trend for smaller product batches is driving the use of flexible and cost-effective single-use solutions. The reusable bag holder, which does not come into contact with the cell culture, carries the temperature control system, the drive motor for the stirrer and the filter holder.



**Filter technology** | Filtration has been one of the core technologies of the Sartorius Group for more than 90 years. In addition to product quality, simple handling is also important for reliable filtration processes. With presterilized filters in capsules or preassembled units with hoses and connectors, Sartorius reduces the risk of user error and contamination.

**Control and analysis software** | The continuous monitoring and control of critical parameters are crucial for bioprocess efficiency and the quality of the end product. In co-operation with Siemens, Sartorius is currently working on the cross-product introduction of a globally standardized automation platform that will make it easier for customers to integrate their systems into higher-level automation solutions such as SCADA, MES or ERP.

The multivariate data analysis software of Umetrics, acquired in 2017, enables customers to model and optimize biopharmaceutical development and production processes. The real-time analysis of production data provides deep insight into the ongoing process and ensures consistently high product quality.

**Single-use sensors** | The single-use sensors of our collaboration partners provide precise information about critical process parameters – such as pH value, oxygen content, temperature, glucose, lactate value, living biomass – in real-time without having to interfere with the sensitive cell culture process.

# On Site Worldwide

Customer proximity begins with short distances. As a global player, Sartorius is present in more than 110 countries with its own production facilities, sales offices and local commercial agencies.

Customers benefit from this geographical presence through short delivery times, fast order processing and personal service. Conversely, Sartorius uses its many years of close contact with its customers to gain a precise understanding of their processes and requirements.

Sartorius concentrates its business activities on the three core markets of Europe, North America and Asia, whereby the network of locations in Europe is historically the most dense. Since its foundation in 1870, the university town of Göttingen in Lower Saxony has been the headquarters and the largest production and development location. This is where Sartorius develops and manufactures two of its core technologies: membrane filters and laboratory instruments. Single-use bags and tubes are produced in Aubagne, France.

From its sales headquarters in Bohemia, New York, Sartorius serves North America as the world's largest pharmaceutical

and laboratory market, the headquarters of many major customers and the source of numerous innovations. The most important production facility is the plant in Yauco, Puerto Rico, where Sartorius recently invested in expanding its production capacities. From here, the Group supplies its American biopharmaceutical customers with membrane filters and sterile single-use bags.

Sartorius is active in the dynamically growing Asian market from its sales headquarters in Shanghai, China. Important production centers are Beijing and Bangalore, where Sartorius manufactures stainless steel bioreactors, single-use bags and laboratory balances.



Yauco, Puerto Rico

## Americas

- Argentina – Buenos Aires
- Brazil – São Paulo
- Canada – Oakville (ON)
- Mexico – Mexico City
- Puerto Rico – Yauco
- USA – Albuquerque (NM), Ann Arbor (MI), Arvada (CO), Bohemia (NY), Boston (MA), New Oxford (PA)

Bohemia, USA



Göttingen, Germany

Kajaani, Finland



Beijing, China



Aubagne, France



Bangalore, India

## EMEA

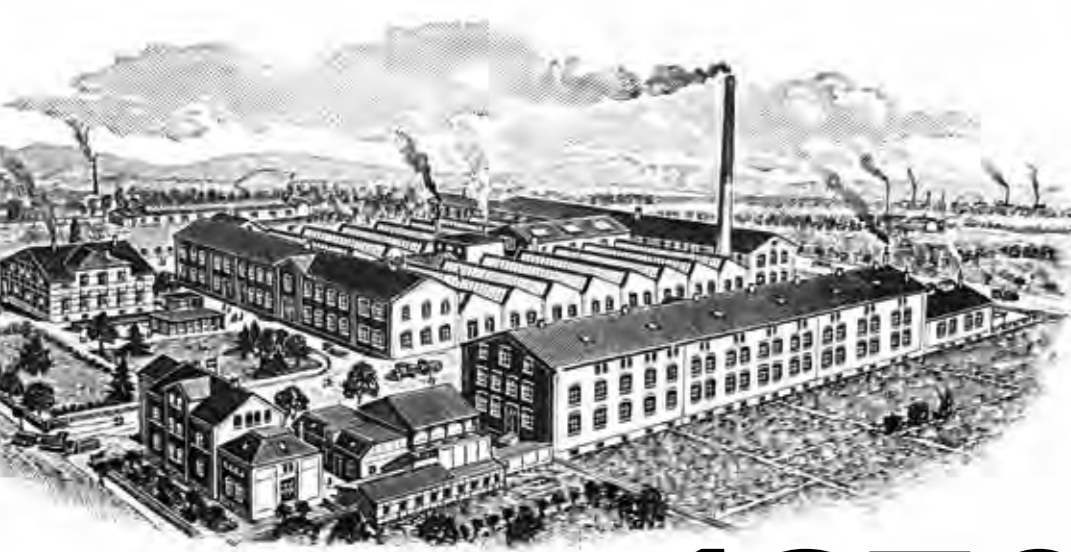
- Austria – Vienna
- Belgium – Brussels
- Finland – Helsinki, Kajaani
- France – Aubagne, Dourdan, Lourdes
- Germany – Berlin, Göttingen, Guxhagen, Ulm
- Hungary – Budapest
- Ireland – Dublin
- Israel – Beit Haemek
- Italy – Florence, Mailand
- Netherlands – Amersfoort
- Poland – Poznan
- Russia – Moscow, St Petersburg
- Sweden – Malmö, Umeå
- Switzerland – Tagelswangen
- Spain – Barcelona, Madrid
- South Africa – Midrand
- Tunisia – Mohamdia
- United Kingdom – Epsom, Glasgow, Royston, Stonehouse, Welwyn Garden City

## Asia | Pacific

- Australia – Melbourne
- China – Hong Kong, Beijing, Shanghai, Suzhou, Taipeh (Taiwan)
- India – Bangalore
- Japan – Tokyo
- Malaysia – Kuala Lumpur
- Singapur – Singapore
- South Korea – Seoul
- Thailand – Bangkok
- Vietnam – Ho Chi Minh City

# A Pioneering Spirit for 150 Years

The products may have changed, but the very core and driving force of Sartorius has remained unaltered since 1870: applying the latest scientific findings to simplify, accelerate and improve methods, processes and results. For more than one and a half centuries, we've been helping to ensure that more people have access to better medicines.



## 1870

**Company foundation**  
Florenz Sartorius, "Mechanician" of the Georg-August-University, builds instruments for the research laboratories of the Göttingen professorship. In 1870, he founds his own company with a technology he developed: his short-arm analytical balance reduces the time required for precise measurements in pharmacies and laboratories. With this invention, he secures numerous prizes at international trade fairs.



## 1890

**Generation change**  
In the 1890s, his craftsmanship and scientific curiosity lead Florenz Sartorius to develop incubators for poultry breeding. They are followed by warming cabinets for bacteriological purposes. Sartorius uses the profits from the manufacture of weighing instruments to buy companies whose technologies complement each other. As of 1906, Florenz Sartorius involves his sons in the business.

## 1880

## 1910

## 1920

**Developments for the future**  
In 1927, Sartorius cofounds a company to manufacture membrane filters. As an alternative to thermal sterilization, they enable the processing of heat-sensitive solutions. The company goes on to develop a process for large-scale production. With the advent of biotechnology at the end of the 20th century, membrane filter technology becomes the foundation of today's bioprocess solutions business.



## 1930



## 1940

**During the Second World War**  
In 1938, Sartorius delivers his 50,000th analytical balance. After the outbreak of the Second World War in 1939, precision mechanical production was increasingly converted to military equipment such as bomb control units and time fuses. For this purpose, forced laborers and prisoners of war were also used in the company. Sartorius had its role in the National Socialist era reviewed by independent scientists and published the results in November 2019.



## 1950

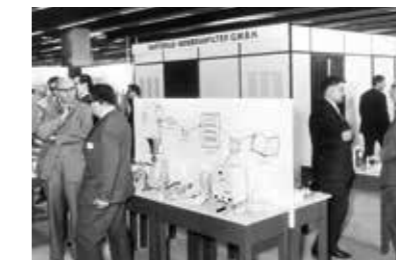
**The economic miracle period**  
With its traditionally well-trained workforce of skilled employees, Sartorius contributes to the German "Wirtschaftswunder" (economic miracle): production is resumed shortly after the end of the war. Beginning with commodities such as hand carts and waffle irons, the first analytical balances soon follow. Against the backdrop of post-war reconstruction, the demand for high-performance equipment increases.



## 1960

**Pacesetters**  
After the successful Apollo 11 mission at the end of the 1960s, Sartorius employees analyze 20.2 milligrams of precious lunar rock to determine its absolute surface. In the 1970s, electronics finally finds its way into scales. This simplifies the weighing process and shortens the measuring time. In membrane filtration, the portfolio of single-use products is growing.

## 1970



## 1980

**Worldwide network**  
Since its foundation, Sartorius has been operating internationally, advertising at trade fairs abroad and concluding business deals in the USA and Great Britain right from the start. Initially through sales offices, from the 1980s also through own production sites, the company expands its global presence in order to be close to its customers.



## 1990

**IPO**  
At the end of the 1980s, new opportunities arise for Sartorius. However, the expansion of the portfolio requires significant investment. To facilitate sustainable growth and broaden the funding base, the company, which had previously been family-run, is being restructured: Sartorius goes public in July 1990.



## 2010

**Single-use technologies**  
Single-use technologies not only make pharmaceutical production more environmentally friendly; lower initial investments and more flexible processes also make the production of biologics cheaper. Through strategic acquisitions and a steadily growing product range, Sartorius develops into a full-service provider to the biopharmaceutical industry: from molecule development to production.

## 2000

**Focus on biopharmaceuticals**  
Since the mid-1990s, Sartorius has focussed on biotechnology, which was still young at the time. As the first biopharmaceuticals such as human insulin reach market maturity, industrial-scale production facilities are needed for the first time. Whereas Sartorius previously mainly supplied filters, the company now expands its product range.

# 2020+

## **Making medical progress possible**

Automation, digitization and networking will increasingly shape processes in the biopharmaceutical research and industry. Sartorius supports this development with automation and data analysis software, assistance systems and intuitive user guidance – always with the goal of achieving technological breakthroughs that lead to better health for more people.



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