



sartorius stedim
biotech

Flexsafe[®]

New PE Film. New Benchmark.

New **Flexsafe**[®] Bag Family.

Sartorius Stedim Biotech introduced the first single-use bag for biopharmaceutical applications. Since then, demand for these bioprocessing bags has been rapidly increasing for use in critical applications. Their robustness, performance and compliance are crucial for ensuring process safety and economy.

Watch Video:

www.sartorius-stedim.com/flexsafe ◀



New Bag Family



We have developed a new polyethylene film and new bioprocessing bags to pave the way towards the single-use manufacturing facility of the future. Flexsafe® meets the most stringent customer needs for safe bioprocessing.

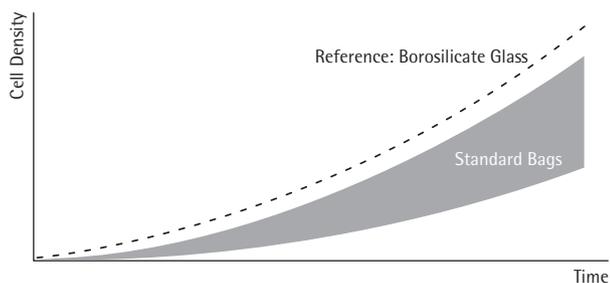


Flexsafe®



Cell Growth

The Challenge: Inconsistent and Poor Cell Growth



Several users have reported on poor or inconsistent cell growth in single-use bags.¹ Recent studies suggest that trace amounts of a degradation product derived from a commonly used antioxidant might impair cell growth. At the same time, such antioxidants are necessary to obtain robust and stable single-use bags.²

¹ Gammell P., et al. The impact of lot-to-lot variability of disposable cell culture bags on cell growth during the scale-up of a mammalian production cell line. Cell Culture Engineering XIII, April 2012.

Eibl R., et al. Recommendation for leachable studies - Standardized cell culture test for the early identification of critical films for CHO cell lines in chemically defined culture media. DECHEMA Jan 2014.

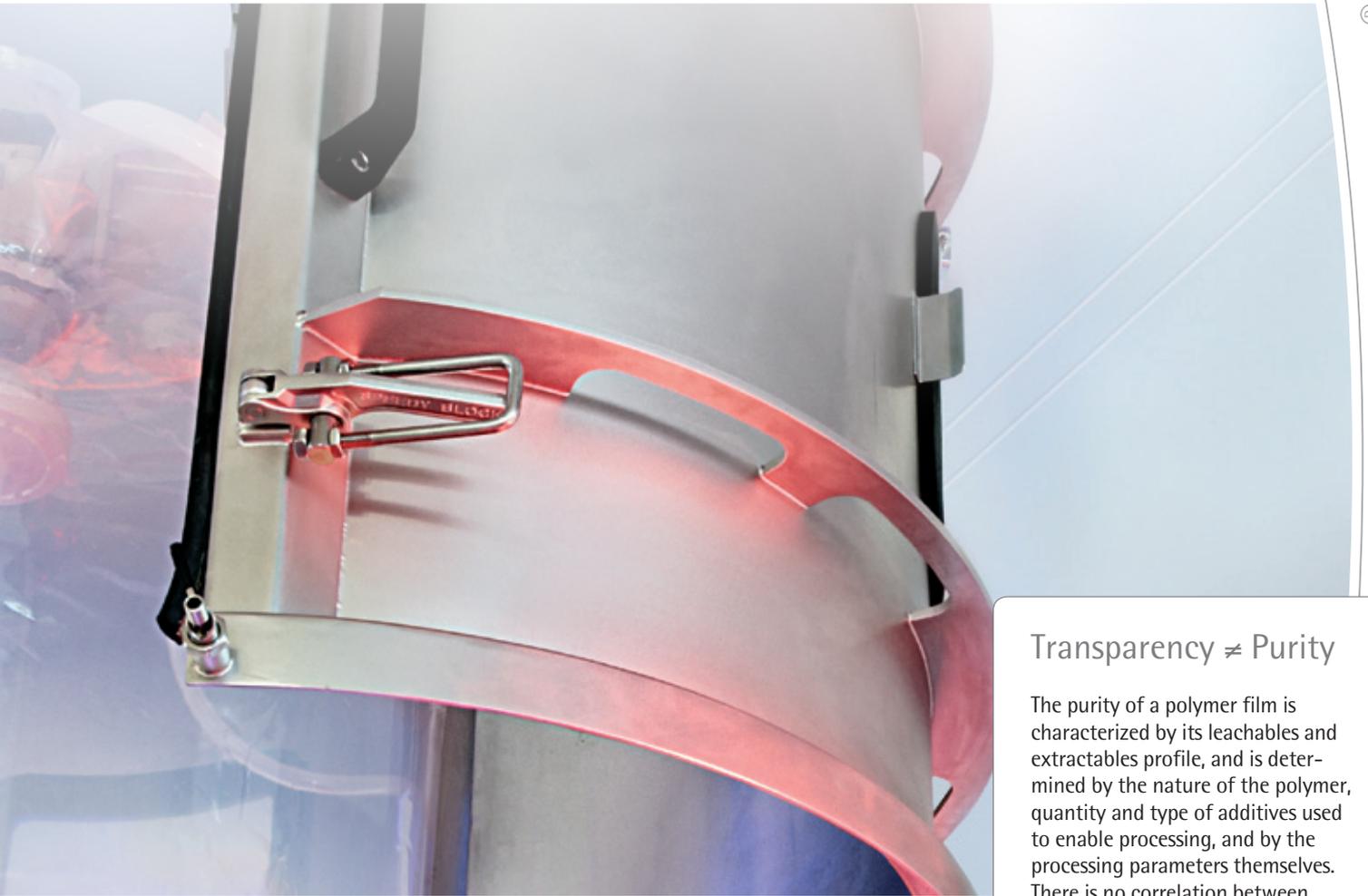
² Hammond M., et al. Identification of a Leachable Compound Detrimental to Cell Growth in Single-Use Bioprocess Containers. PDA J. Pharm. Sci. and Tech. 67 (2) 2013: 123-134.

Our Solution: Optimized Resin and Additive Formulation

Flexsafe® bags are designed to excel due to:

- | | | |
|--|---|---|
| Optimized antioxidant package | ▶ | Excellent cell growth of the most sensitive cells |
| Use of pharmacopeia-listed antioxidants only | ▶ | Simplified toxicology assessment |
| Zero slipping agents | ▶ | No risk of interference due to these agents |
| Mechanical anti-blocking | ▶ | Reduces stickiness, facilitates extrusion and bag handling |
| Meaningful specifications and process control from polymer resin to finished bag | ▶ | Reliable and reproducible growth performance, well-characterized extractables profile |

Independent labs have confirmed that Flexsafe® bags are free of cytotoxic leachables. No bDtBPP is identified in WFI extracts of Flexsafe® bags.



Transparency ≠ Purity

The purity of a polymer film is characterized by its leachables and extractables profile, and is determined by the nature of the polymer, quantity and type of additives used to enable processing, and by the processing parameters themselves. There is no correlation between transparency of a film and its leachables and extractables profile.

plus Full Control of Manufacturing Processes

In close collaboration with resin and film suppliers, our polymer scientists and biologists have developed a completely new polyethylene film, called S80. A standardized cell growth assay has been used to optimize film formulation, define the operating ranges for extrusion, welding and gamma-irradiation processes and to establish specifications and process controls.

Film Polymers



Additives



Extrusion Process



Assembly

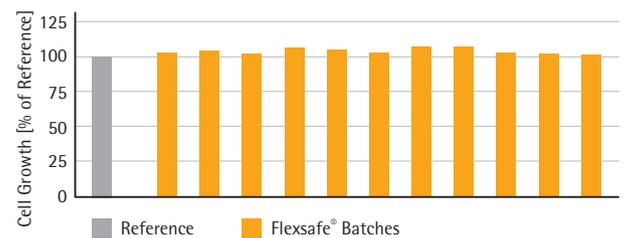


Gamma Irradiation



Your Results:

Excellent Growth and Lot-to-Lot Consistency



Flexsafe® bags ensure excellent and reproducible growth behavior of the most sensitive cell lines. This has been confirmed by biopharma companies worldwide using their specific cell lines.

Accelerated shelf life studies of dry bags confirm consistent cell growth from day one, as well as no aging effects after gamma irradiation. Further trials demonstrated that you can rely on Flexsafe® bags and store your serum-free or protein-free medium over extended periods.

Excellent process understanding and robust control of the entire manufacturing process guarantee the consistent quality of Flexsafe® bags.

Rely on a Sustainable Supply Chain and Robust Business Continuity Plans

Assurance of supply is a key success factor for long-term drug supply based on single-use technologies. This is why we set up a sustainable supply chain to give you real peace of mind.

Strong partnerships and long-term supply contracts with suppliers of polymers, additives and film suppliers enable us to achieve full traceability of raw materials, complete understanding of film formulation and robust control of the manufacturing process – from raw materials to sterile bags that are ready to use in your drug manufacturing process.

Together with our partners, we have established the design space for film extrusion of our new Flexsafe® bags. Based on defined operating ranges and controls, we provide consistent and reproducible bag quality. Flexsafe® supports your drug development and manufacture – ranging from initial clinical trials to long-term supply many years after the launch of your drug products.

To meet the highest business continuity requirements, we have a robust contingency plan in place for uninterrupted film supply. It is based on redundant resin crackers, film extrusion lines and multiple manufacturing sites. In addition, we maintain safety stocks of resins and extruded film rolls.

We control the entire manufacture of critical components, such as filters and tubing. Moreover, we assemble and sterilize single-use bioprocessing bag solutions at our multiple manufacturing sites located across the globe.

Assurance of S



Material
Science

▶ **Consistent Quality and Change Control**

- Established resin specifications
- Design space for film extrusion
- Full traceability of resins and additives

▶ **Long-Term Contracts with Suppliers**

- 10-year contract with film manufacturer
- 2-year customer change notification period
- Last-time buy option for a minimum of 2 years' resin demand

Global 
SUPPLY GUARANTEE

Complete control over our manufacturing process from resin and film extrusion to final bag assembly

▶ **Business Continuity**

- Backup resin crackers
- Safety stocks of resin and film for up to 2 years supply
- Multiple bag manufacturing and sterilization sites

▶ **Control of Critical Components**

- Own bags, filters and connectors
- Strategic partnerships for tubing and sensors

Supply

Multiple
Production
Sites

Process
Under-
standing

Strategic
Partner-
ship



Robustness

Safe and Convenient Single-use Processing

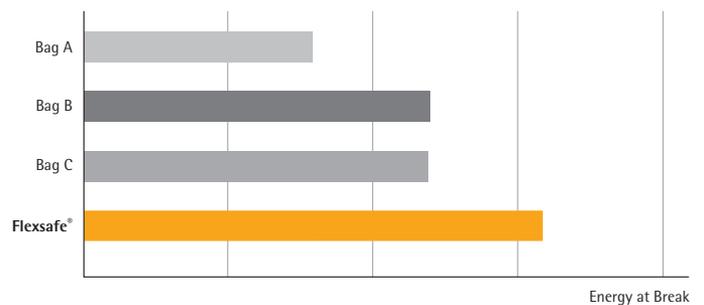
Flexsafe® meets your requirements for outstanding robustness and ease of use throughout all steps of single-use processing – from cell cultivation to shipping of drug substance.

Today, almost all unit operations in biologics development and production can be performed using single-use equipment. However, the requirements on mechanical and physical properties can vary considerably, depending on your application.

Rocking-motion cell cultivation or liquid shipping applications require a highly flexible bag resistant to material fatigue. A bag used for large-scale mixing or in a stirred tank bioreactor has to withstand the significant hydrostatic pressure generated by liquid volumes of 2,000 L to 3,000 L. Here, the strength of the film and its welds is critical. Apart from the robustness of a bag, it must be easy to install and use in routine manufacture of drugs.

Therefore, the development of our new Flexsafe® bags focused on combining strengths with flexibility to provide outstanding robustness and ease of use for your most demanding applications.

Superior Strength and Flexibility



The thickness, strength and flexibility of the new S80 film enhance the mechanical robustness of Flexsafe®, making it ideal for all bioprocessing applications.

The strength of Flexsafe® significantly reduces the risk of accidental damage to the bag due to inappropriate handling. Its flexibility enables convenient installation and self-deployment of the bag in its container.



Passed
ASTM Shipping Test ✓

Filled Flexsafe® shipping bags in Palletank® passed the most stringent shipping validation test according to ASTM D4169.

Watch Videos:
www.sartorius-stedim.com/flexsafe ◀



of Film and Welds

Excellent flexibility of each layer of our new polyethylene film and a total thickness of 400 µm provide extraordinary robustness.

Strength and flexibility of film material and welds qualified using multiple methods:

- | | | |
|--|---|--|
| Standard flex durability of film | ▶ | Highly resistant to fatigue and pinhole formation |
| Tensile strength | ▶ | Strength of film and welds |
| Elongation and energy at break | ▶ | Flexibility, ease of installation and use |
| In-house water burst test | ▶ | Strength of bag |
| Extensive worst-case testing in actual use | ▶ | Robustness of Flexsafe® in stirred tanks, in rocking motion bioreactors and under actual shipping conditions |



ASTM Shipping Test



Welding Robustness Test

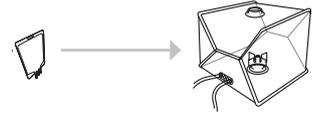
Get Peace of Mind with a Future-proof Concept

Our range of scalable Flexsafe® bags enables you to implement single-use bioprocessing throughout all steps of drug manufacture, from process development to production – all using just one film.

Featuring high-performance polyethylene film, our new Flexsafe® bags will give you peace of mind based on their consistent performance, even in the most stringent bioprocessing applications like cell cultivation, long-term storage and shipping of drug products.

Flexsafe® Range

Bag volumes from 20 mL to 3,000 L



Facilitate single-use process implementation from process development to commercial manufacturing

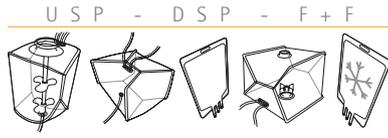
One for All



Biostat® RM | 1 L – 200 L

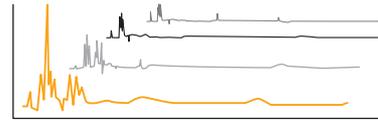
Biostat® STR | 50 L – 2,000 L

Bags for all bioprocessing steps



- Reduce time and expense for process validation, extractables and leachables studies, toxicology assessment and stability studies
- Benefit from robustness, consistent quality and assurance of supply
- Ensure worry-free operations, quality and supply chain

A well-characterized, consistent extractables profile due to raw material and process controls



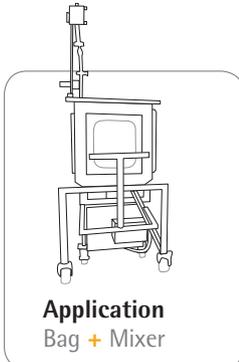
- Facilitate leachables validation and toxicology assessment
- Obtain sustainable, reproducible and reliable process validation data

Flexsafe®: All the Options Are Yours

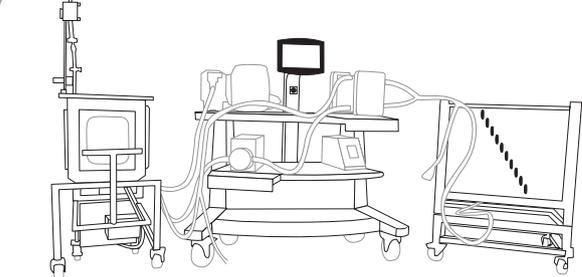
Sartorius Flexsafe® bags are an integral part of our total solution offering for single-use manufacturing. Flexsafe® gives you all the options you need. For example, you can choose to use bioprocessing bags in a "stand-alone" configuration or set up a complete single-use factory.



Single Bag

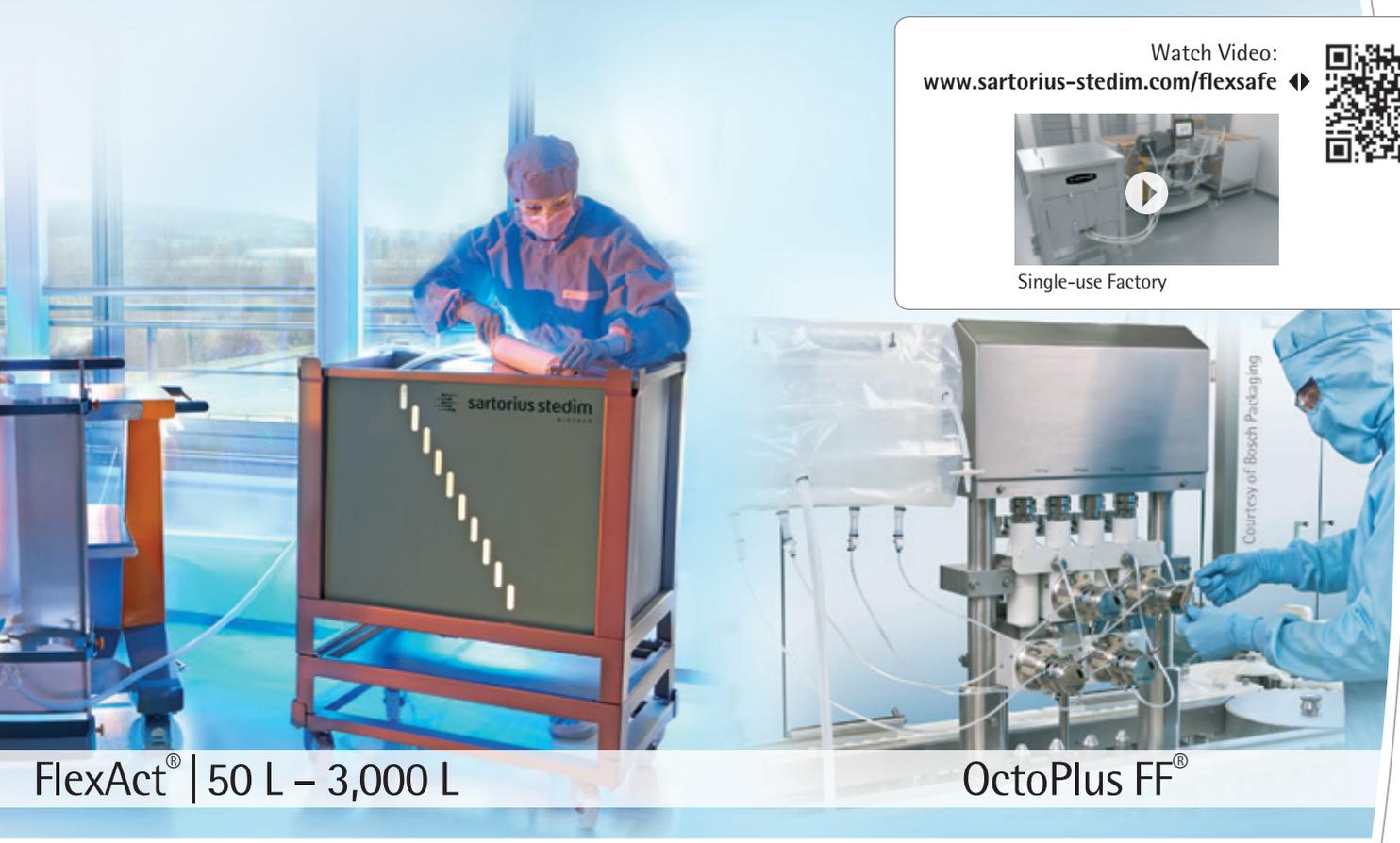


Application
Bag + Mixer



Unit Operation
Bag + Mixer + System¹

¹ Example of FlexAct® UD for ultra- and diafiltration: Mixing bag and mixer, vent filters, trolley with controller, pressure transmitters and pumps, crossflow cassettes, holder and recirculation bag, storage container and bag, complete tubing



FlexAct® | 50 L – 3,000 L

OctoPlus FF®

Watch Video: www.sartorius-stedim.com/flexsafe



Single-use Factory

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 FMT S.A.S.
ZI des Paluds
Avenue de Jouques – CS 91051
13781 Aubagne Cedex

Phone +33.442.845600
Fax +33.442.845619

Sartorius Stedim France SAS
ZI des Paluds
Avenue de Jouques – CS 71058
13781 Aubagne Cedex

Phone +33.442.845600
Fax +33.442.846545

Austria

Sartorius Stedim Austria GmbH
Modecenterstrasse 22
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.

Phone +31.30.60.25.080
Fax +31.30.60.25.099

filtratie.nederland@sartorius-stedim.com

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" and LLC "Biohit"
Uralskaya str. 4, Lit. B
199155, Saint-Petersburg

Phone +7.812.327.5.327
Fax +7.812.327.5.323

Spain

Sartorius Stedim Spain, S.A.U.
Avda. de la Industria, 32
Edificio PAYMA
28108 Alcobendas (Madrid)

Phone +34.902.110.935
Fax +34.91.358.96.23

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

Ukraine

LLC "Biohit"
Post Box 440 "B"
01001 Kiev, Ukraine

Phone +380.44.411.4918
Fax +380.50.623.3162

Americas

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. Avalos 4251
B1605ECS Munro
Buenos Aires

Phone +54.11.4721.0505
Fax +54.11.4762.2333

Brazil

Sartorius do Brasil Ltda
Avenida Senador Vergueiro 2962
São Bernardo do Campo
CEP 09600-000 - SP- Brasil

Phone +55.11.4362.8900
Fax +55.11.4362.8901

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.
No. 33 Yu'an Road
Airport Industrial Park Zone B
Shunyi District, Beijing 101300

Phone +86.10.80426516
Fax +86.10.80426580

Sartorius Stedim (Shanghai)
Trading Co. Ltd
3rd Floor, North Wing, Tower 1
No. 4560 Jinke Road
Zhangjiang Hi-Tech Park
Pudong District
Shanghai 201210, China

Phone +86.21.68782300
Fax +86.21.68782332 | 68782882

Sartorius Stedim Biotech (Beijing) Co. Ltd.
Guangzhou Representative Office
Unit K, Building 23
Huihua Commerce & Trade Building
No. 80 Xianlie Middle Road
Guangzhou 510070

Phone +86.20.37618687 | 37618651
Fax +86.20.37619051

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.
4th Fl., Daiwa Shinagawa North Bldg.
8-11, Kita-Shinagawa 1-chome
Shinagawa-ku, Tokyo, 140-0001 Japan

Phone +81.3.4331.4300
Fax +81.3.4331.4301

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