



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.

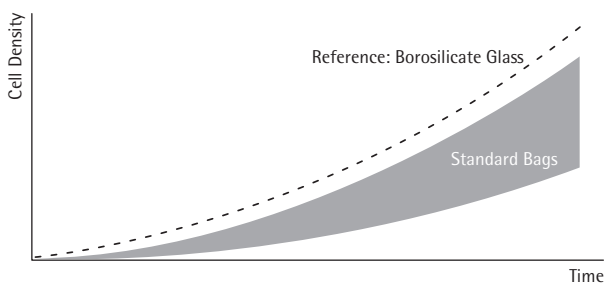


Flexsafe®



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.

² 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.

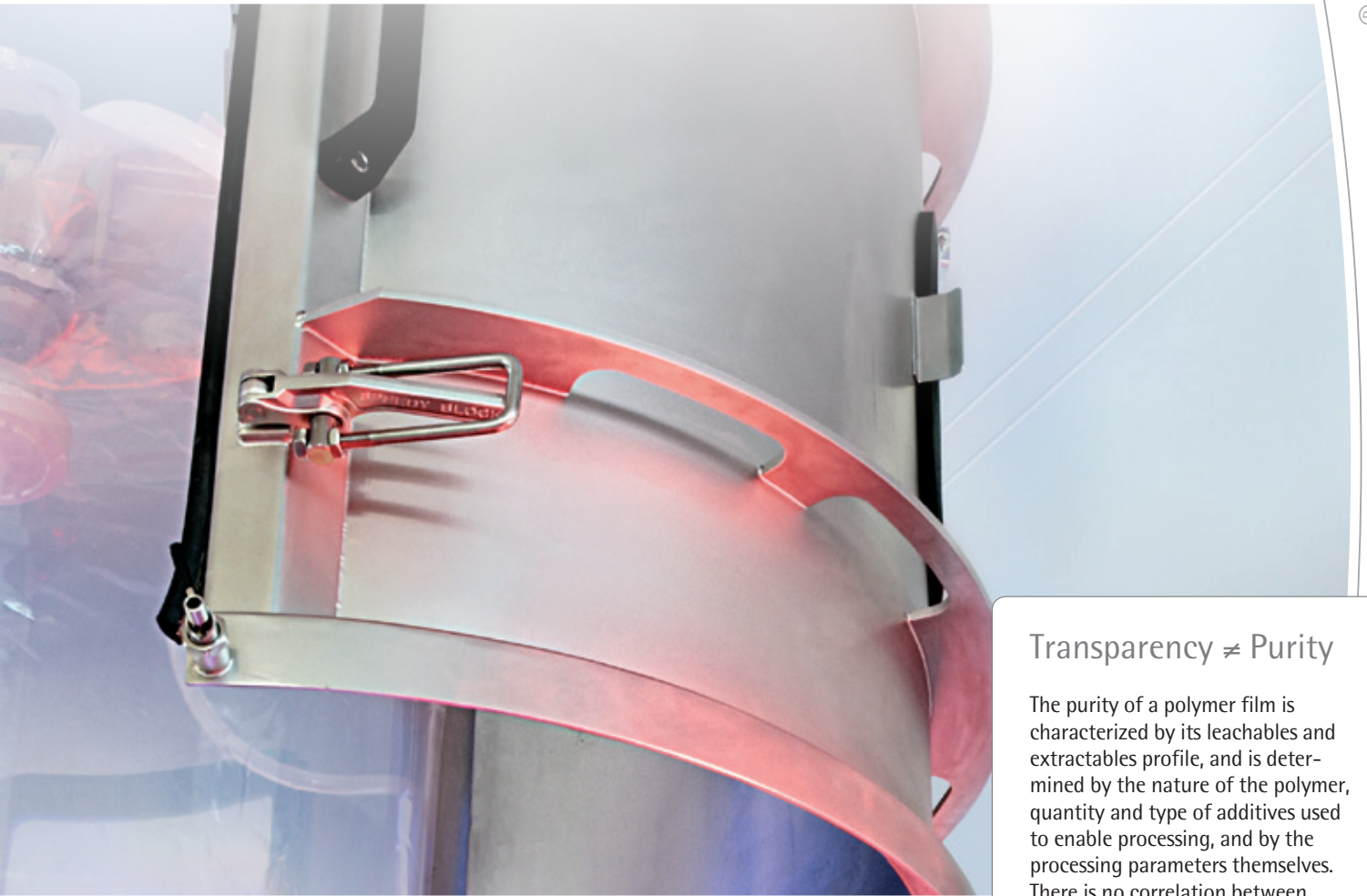
² Hammond M., et al. Identification of a Leachable Compound Detrimental to Cell Growth in Single-Use Bioprocess Containers. PDA J. Pharm. Sci. and Tech. 67 (2) 2013: 123-134.

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

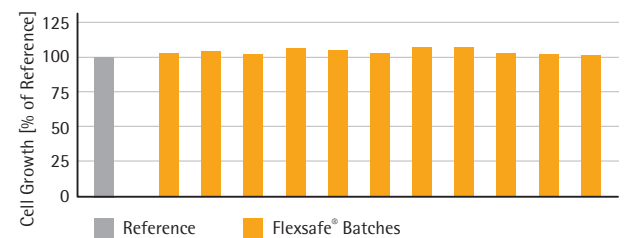


Gamma Irradiation



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

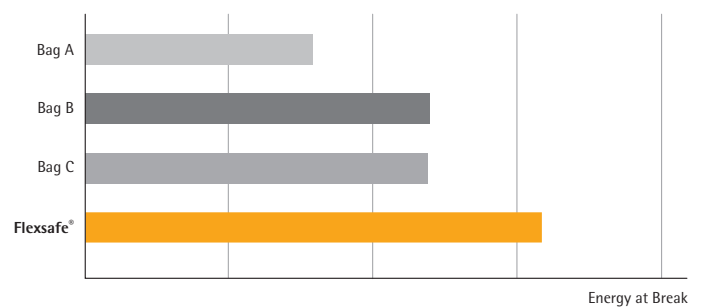
Flexsafe® meets your requirements for outstanding robustness and ease of use throughout all steps of single-use processing – from cell cultivation to shipping of drug substance.

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

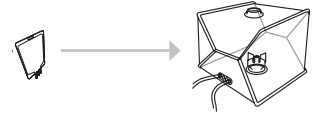
Get Peace of Mind with a Future-proof Concept

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

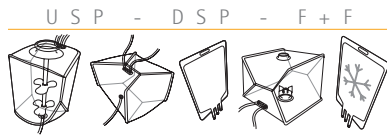
One for All



Biostat® RM | 1 L – 200 L

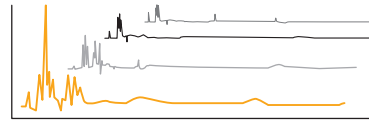
Biostat® STR | 50 L – 2,000 L

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

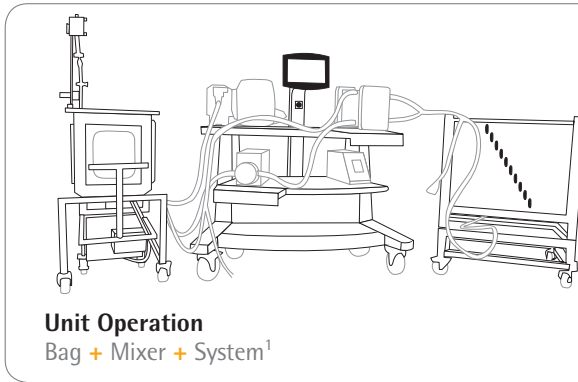
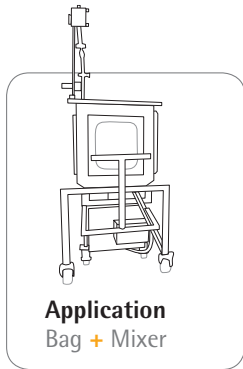
A well-characterized, consistent extractables profile due to raw material and process controls



- 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.



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



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



Single-use Factory

FlexAct® | 50 L – 3,000 L

OctoPlus FF®

Flexsafe®

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