

# Tecnologia Single-use e biossegurança na indústria biofarmacêutica



I SIMPOSIO DE SEGURANÇA QUÍMICA E BIOLÓGICA –  
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Sartorius do Brasil

## Contents

1



Technology and industry trends in fermentation

2

Single-Use Solutions

3

BIOSTAT® RM -Rocking Motion Bioreactor

4

BIOSTAT® STR - True Scalability in Single-Use





Technology and industry trends in fermentation

## Contamination Cases in the Biopharma industry

- Viral Infection – Vesivirus 2117
- Probably cause: media nutrient (never confirmed)
- Impact on CHO growth
  
- Over 150.000 people hours to decontaminate
- Market value decreased
- Cost of nearly \$ 300 million



2009 Genzyme plant in Allston Landing, Massachusetts – USA

### Sources:

<http://www.biopharma-reporter.com/Bio-Developments/Genzyme-offers-inside-look-at-Massachusetts-plant-under-consent-decree>

<http://www.nature.com/nbt/journal/v27/n8/full/nbt0809-681a.html>

<http://www.biopharminternational.com/genzyme-detects-virus-contamination-bioreactor-halts-production>

<http://cellculturedish.com/2013/09/bioprocess-international-conference-tuesdays-talks/>

[https://www.pharmamedtechbi.com/publications/the-gold-sheet/44/001/biotechs-urged-to-prevent-viral-risks-that-cost-genzyme-nearly-\\$300-million](https://www.pharmamedtechbi.com/publications/the-gold-sheet/44/001/biotechs-urged-to-prevent-viral-risks-that-cost-genzyme-nearly-$300-million)



## Contamination Cases in the Biopharma industry

- Viral contamination in the 90's – Minute Virus of Mice
- No definitive cause – probably cell media
- Implemented PCR and cell culture based methodology
- High temp short time heat sterilization treatment
- Use of disposable technology



Genentech, Inc., South San Francisco, CA, USA.

### Sources:

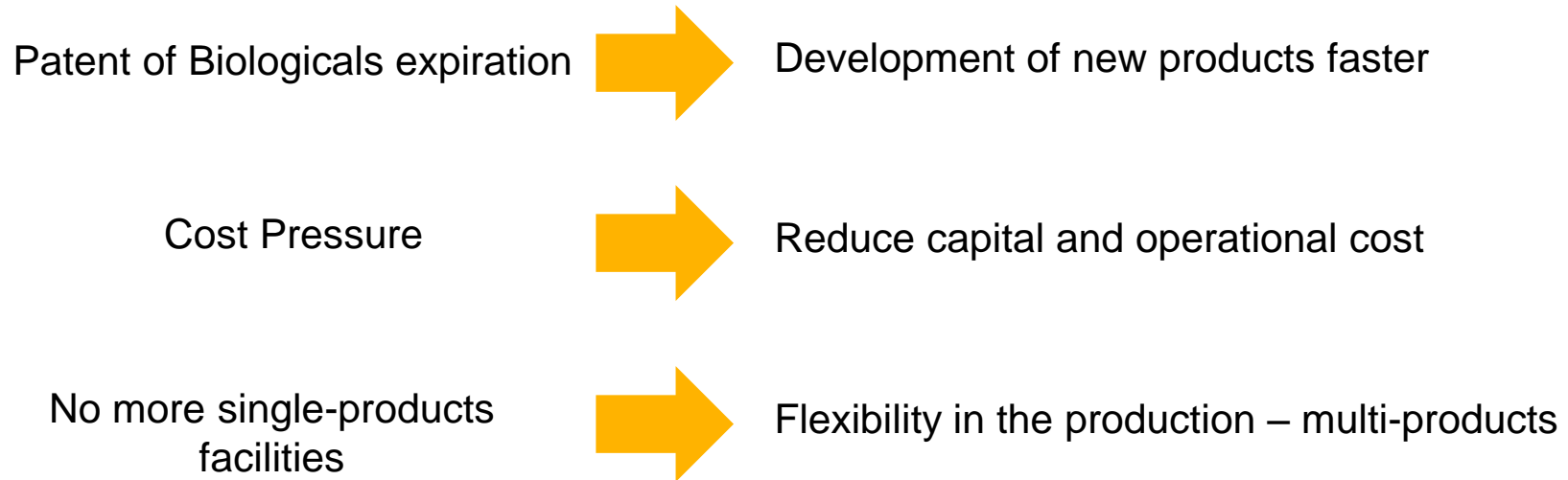
[https://www.pharmamedtechbi.com/publications/the-gold-sheet/44/001/biotechs-urged-to-prevent-viral-risks-that-cost-genzyme-nearly-\\$300-million](https://www.pharmamedtechbi.com/publications/the-gold-sheet/44/001/biotechs-urged-to-prevent-viral-risks-that-cost-genzyme-nearly-$300-million)

<http://www.ncbi.nlm.nih.gov/pubmed/9119162>

EMA report from 03 August 2012 – EMA/488088/2013

<http://www.ipqpubs.com/news/genentech%E2%80%99s-experience-with-rituxin-process-bacterial-contamination-reveals-biotech-industry-vulnerabilities-and-defense-strategies/>

## Challenges in the Biopharma industry



**SINGLE-USE TECHNOLOGY**

- **Reduced CAPEX**
  - Reduction of equipment investment
    - bioreactor
    - CIP & SIP not needed
  - Simplification of facility design
  - Foot print reduction
  
- **Reduced Operational cost**
  - Elimination of CIP & SIP operations
  - Energy, WFI, cleaning agents
  - Reduction of qualification efforts

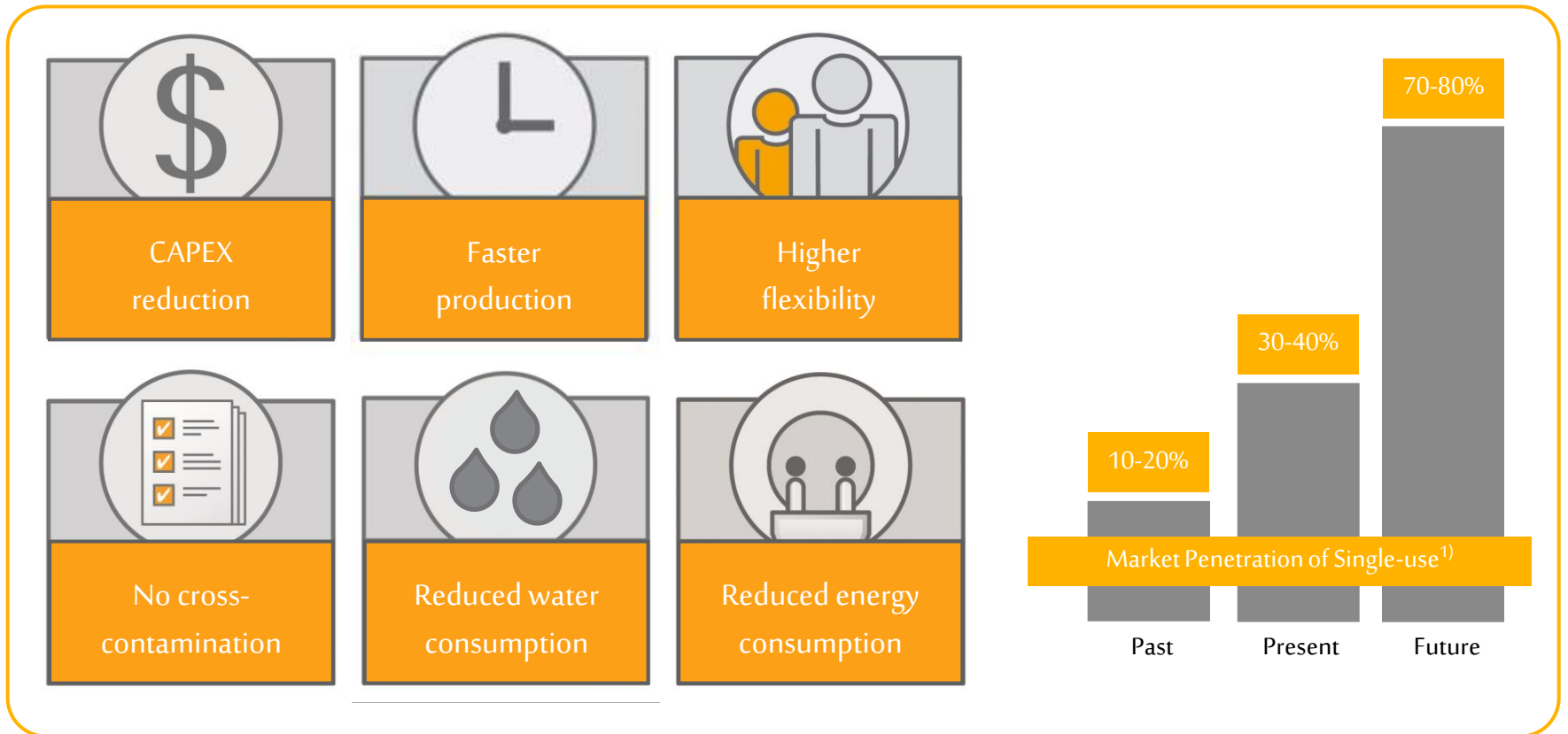




Multiuse Bioreactors (MUBs)	Single-Use Bioreactors (SUBs)
Customized designs	Standard or customized designs
<i>Long delivery times</i>	Short delivery times
Proven technology	<i>Relatively young technology</i>
<i>High capital investment</i>	Lower capital investment
<i>More qualification and validation time (cleaning and sterilization in place, CIP/SIP)</i>	Less qualification and validation time
<i>Water for injection and pure steam needed</i>	No CIP or SIP processes needed
<i>Large footprint</i>	Small footprint
<i>Higher energy costs</i>	Lower energy costs
<i>Time-consuming batch turn-over</i>	Quick-change, short nonoperation stops
<i>Higher maintenance costs</i>	Lower maintenance costs
Less dependence on supplier	<i>Total dependence on bag supplier</i>
No bags, no managing stocks	<i>Expensive bags; managing stocks and supply</i>
<b><i>Higher contamination risk</i></b>	Lower contamination risk
Lower leakage risk during culture	<i>Higher leakage risk during culture; consider BSL needs and managing this risk</i>
Good control of pO <sub>2</sub> and pH	<i>Optical sensors, sometimes not fully accurate</i>
Geometry of vessel and stirrer blades chosen by users	<i>Bag geometry and stirrer design may influence your process</i>
<i>Higher direct and indirect man-hours</i>	Lower man-hours
<i>Higher-level bioreactor operators</i>	Lower-level bioreactor operators
<i>Higher operator risk: e.g., hot pipes, pressure</i>	Lower operator risks
Suitable for any bioreactor volume	<i>Limited volumes, ≤2,000 L</i>



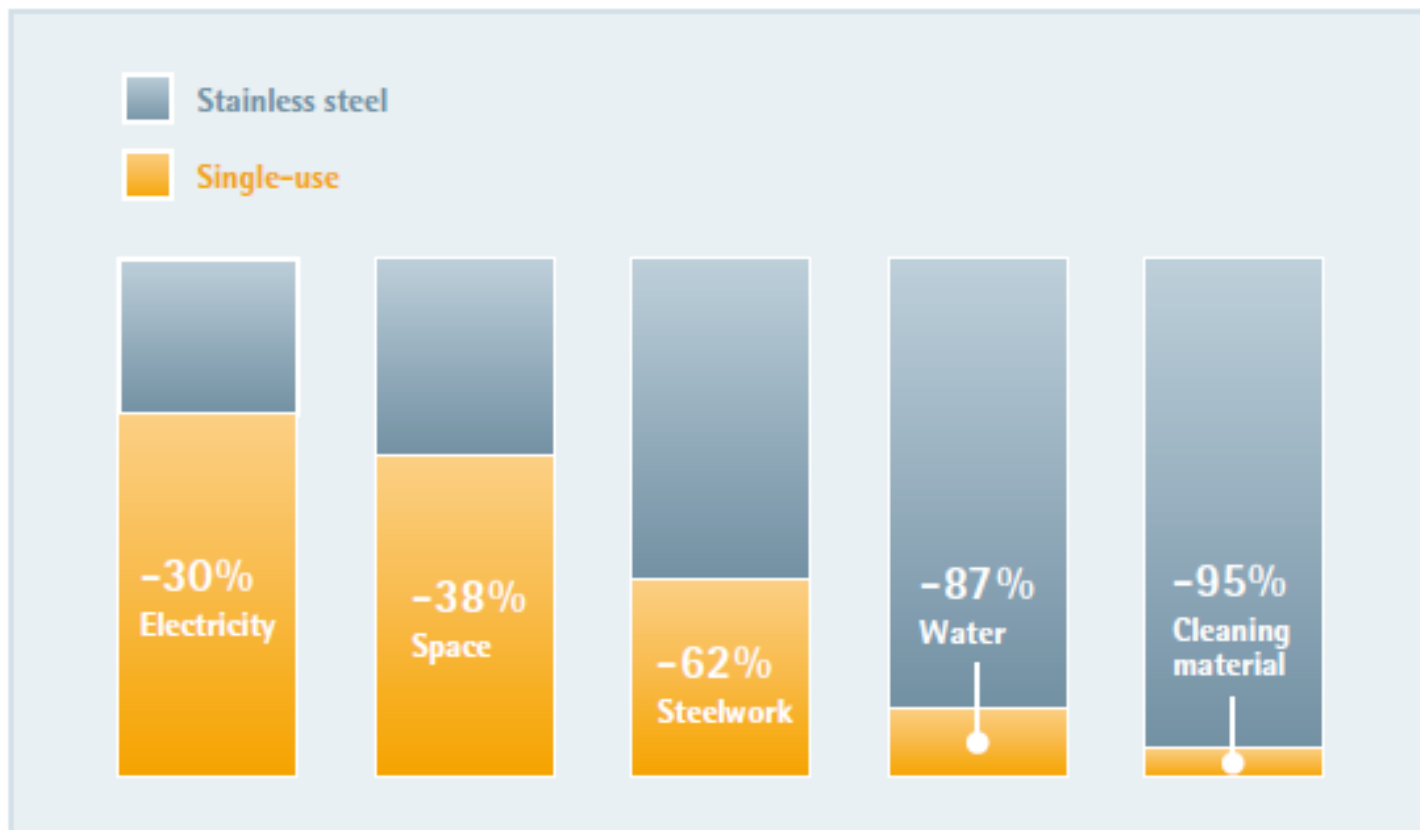
# Single-use Technologies Reduce Production Costs by up to 40%



<sup>1)</sup> Pharmaceutical Technology Europe Vol. 22 No. 10, Oct. 2010; own estimates



## Environmental impact of single-use technologies



\* Reference: Sinclair, A.; Leveen, et al.;  
The Environmental Impact of Disposable  
Technologies, The Biopharm International  
Guide, November 2008; Base of the analysis:  
Typical mAb process at 3 × 2000 L scale

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## Single-Use Solutions



## SSB is a Part of the Sartorius Group

Sartorius Group

€891mn sales revenue

74%

26%

### Sartorius Stedim Biotech



€684mn

sales revenue

Innovative single-use products and equipment  
for the manufacture of biologics

### Subgroup Lab Products & Services



Premium lab instruments, consumables  
and services for R&D, QA and QC

## Our Portfolio

Filtration

Fluid  
Management

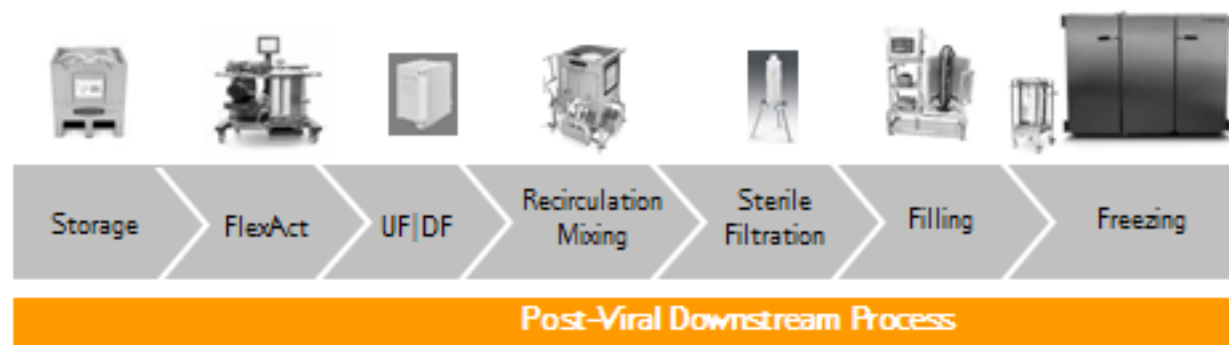
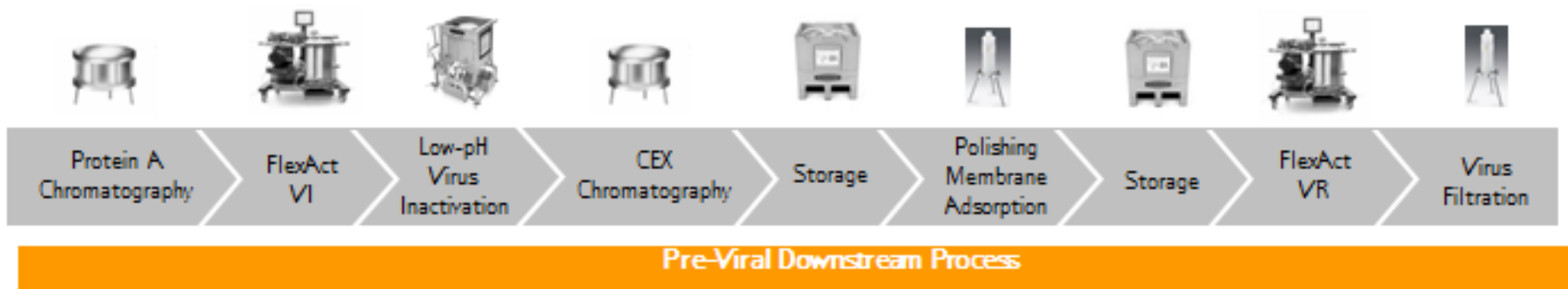
Fermentation

Purification

Integrated  
Solutions

Service





# Long history in single use bioreactors

Sartorius acquires Wave Biotech AG



BIOSTAT® STR 2000



First Wave Bioreactor



BIOSTAT® RM 20/50 & 200



BIOSTAT® STR 200



BIOSTAT® STR 50



BIOSTAT® STR 500 & 1000



BIOSTAT® B with Rocker



BIOSTAT® RM 600



BIOSTAT® RM perfusion systems

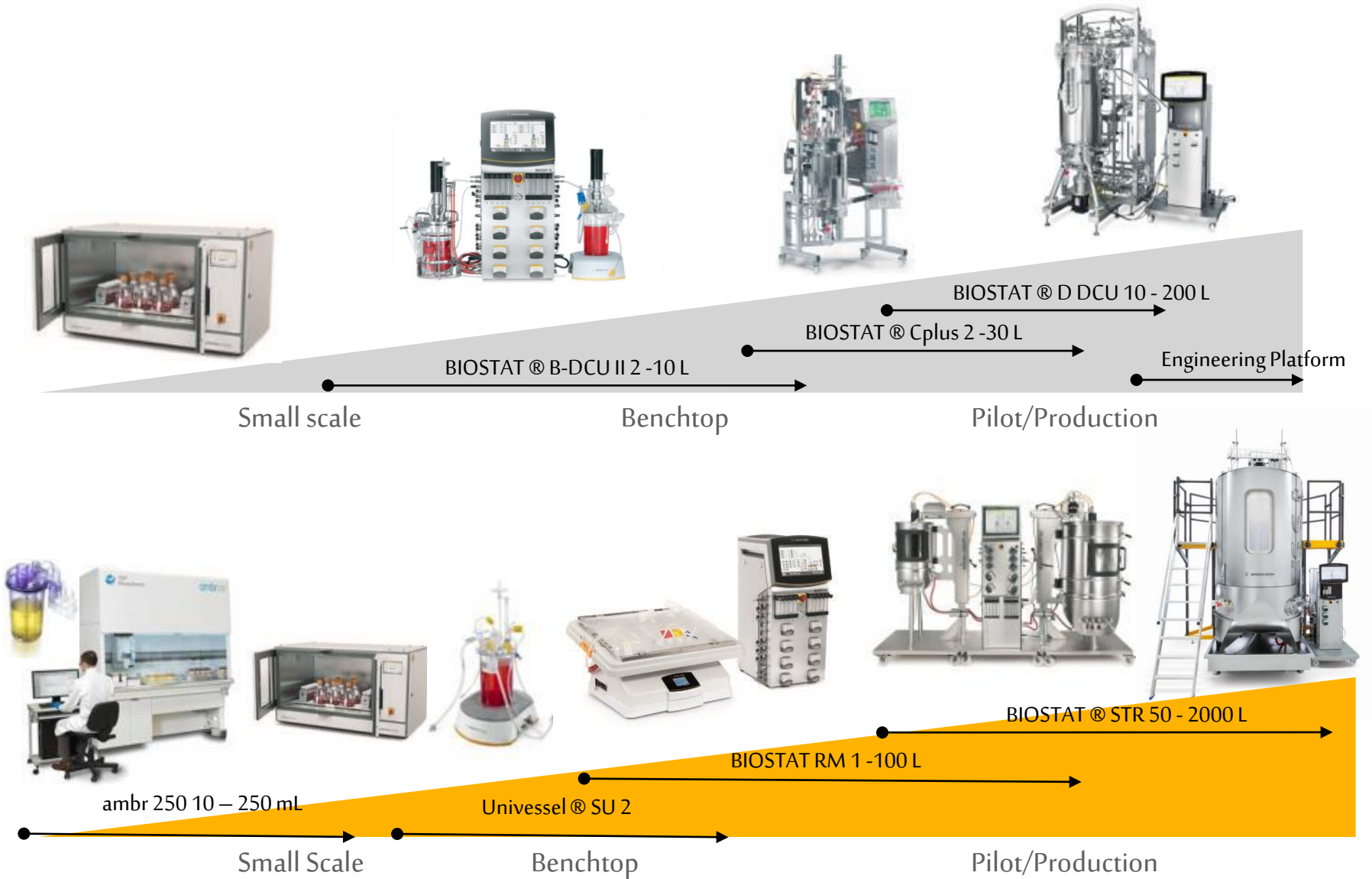


BIOSTAT® RM 20/50

1998 2006 2008 2008 2008 2008 2009 2011 2012 2014



# Sartorius bioreactor product overview – market leader in fermentation



## Contents

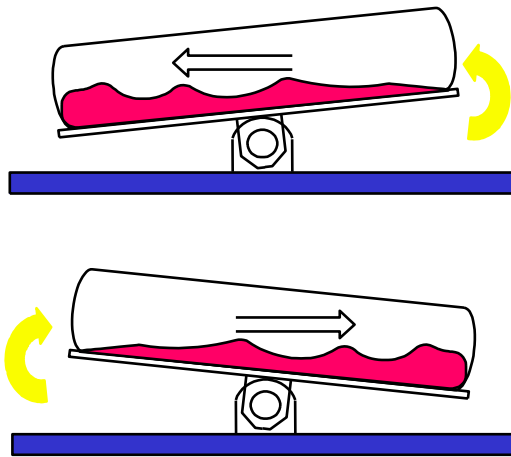
- 1 Technology and industry trends in fermentation
- 2 Single-Use Upstream Solutions
- 3 **>>** **BIOSTAT® RM -Rocking Motion Bioreactor**
- 4 **BIOSTAT® STR - True Scalability in Single-Use**





BIOSTAT® RM - Rocking Motion Bioreactors  
Single-Use solutions for screening, seed & small scale production

## Principle: Wave Induced Motion



### Wave Induced Motion:

- Single-use device for cell culture applications.
- It does not use gas permeable membranes for oxygen transfer.
- Instead, oxygen transfer and mixing are accomplished by the principle of wave-induced motion (WIM).
- Bubble free overlay aeration
- Low shear stress



**200 Liter (100 L)**

**100 Liter (50 L)**

**50 Liter (25 L)**

**20 Liter (10 L)**

**10 Liter (5 L)**

**2 Liter (1 L)**

**1 Liter (0.5 L)**

*total volume / max. working volume*



BIOSTAT® RM 200




BIOSTAT® RM 20/50 with BIOSTAT® B



BIOSTAT® RM 20/50 basic

## Contents

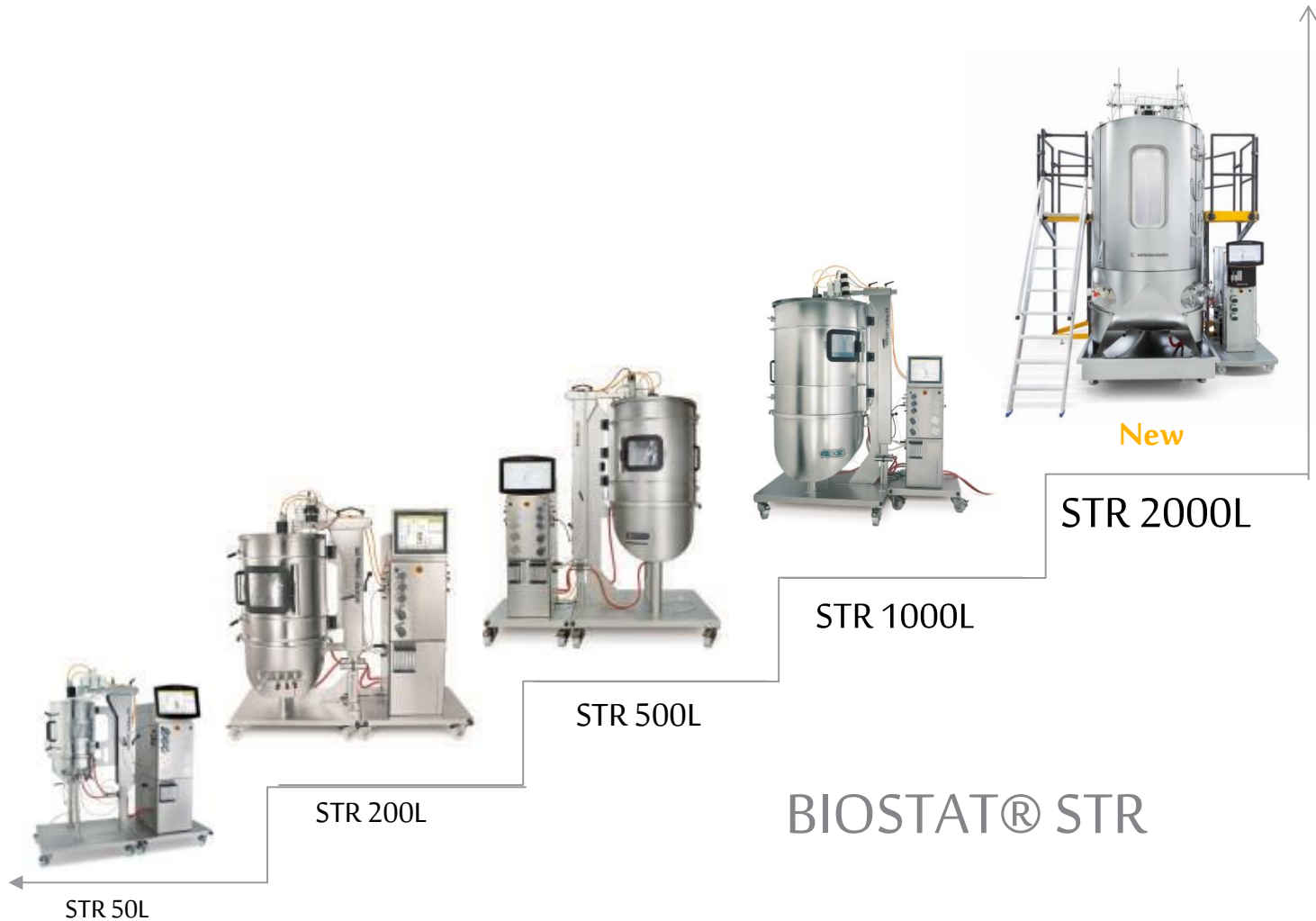
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BIOSTAT® STR – True Scalability in Single-Use

## Scalability in Single Use from Cell Line and Process Development to Production Scale



## BIOSTAT® STR – Description of the system



BIOSTAT® STR 2000

### **The system consists of**

- Stainless steel bag holder
- Single-use Flexsafe STR bag
- Control system

### **Optimized technology for:**

- High cell density suspension cell culture
- Adherent cell culture on micro-carriers
- Mammalian, insect and stem cells
- Low to medium cell density microbial culture



## BIOSTAT® STR – Description of the system



BIOSTAT® STR 50 & BIOSTAT® STR 200  
extra small place requirement in Twin  
configuration

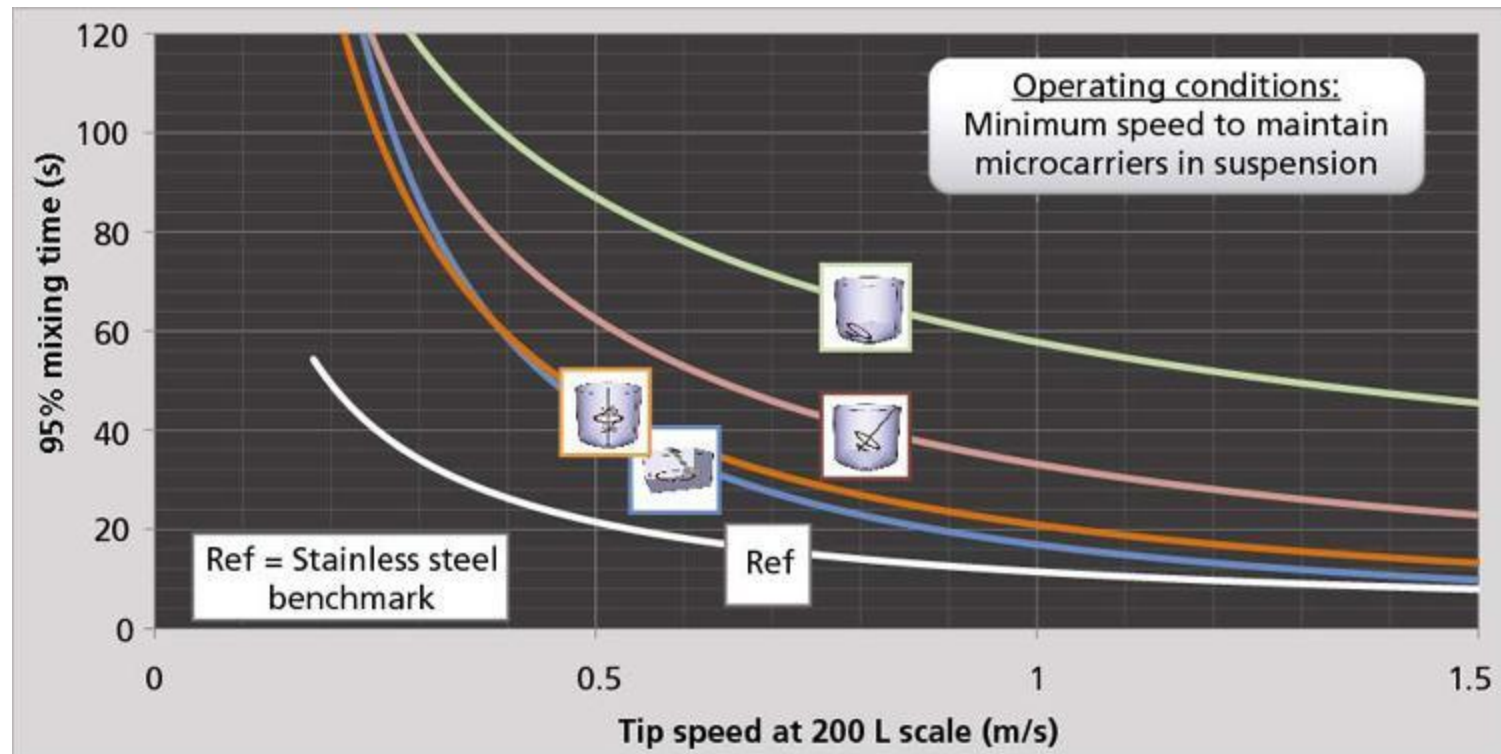
### The system consists of

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### Optimized technology for:

- High cell density suspension cell culture
- Adherent cell culture on micro-carriers
- Mammalian, insect and stem cells
- Low to medium cell density microbial culture

## Importance of conventional stirrer design for critical processes



Chaubard et al., BioPharm International, Nov. 2, 2010



BIOSTAT® STR

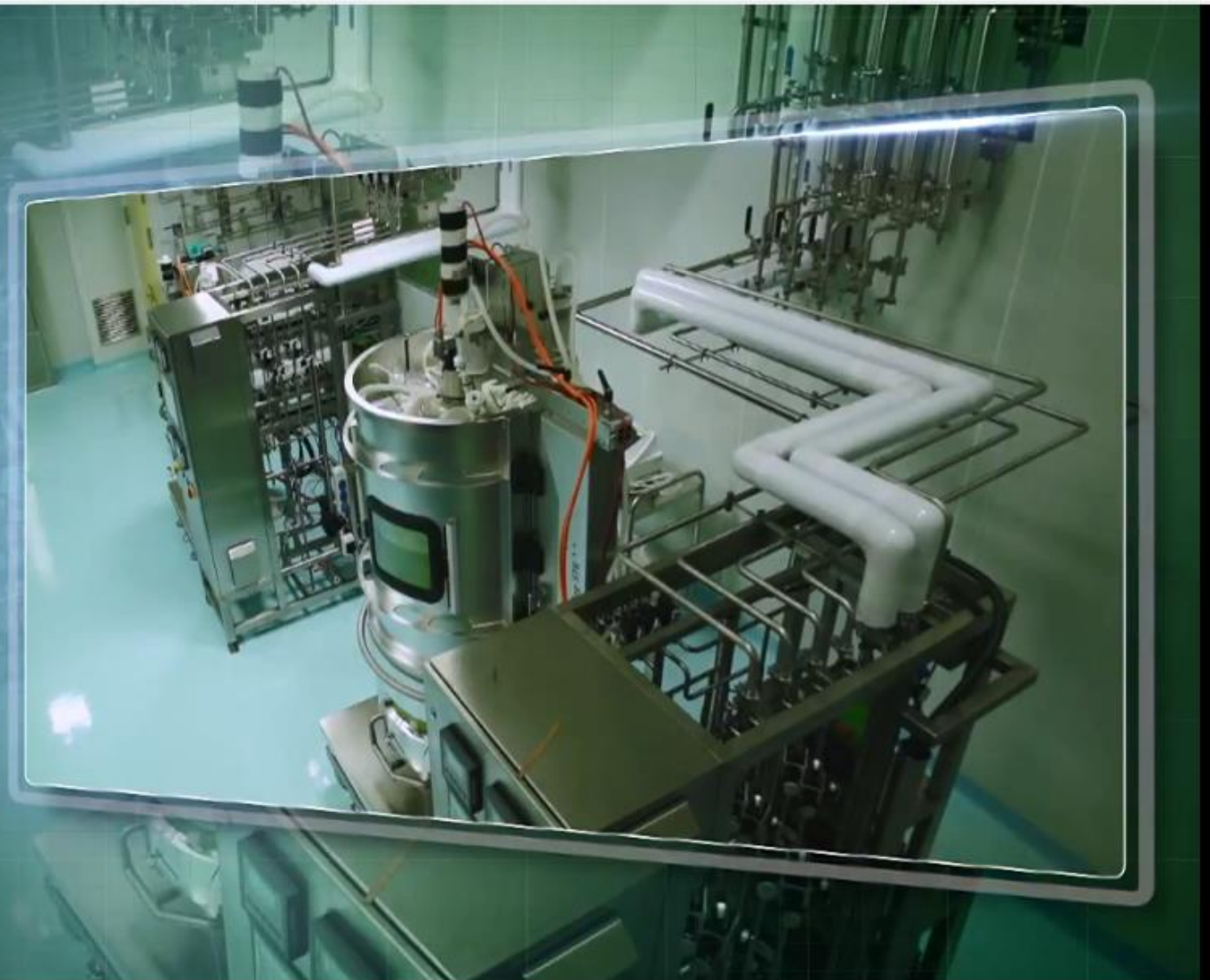
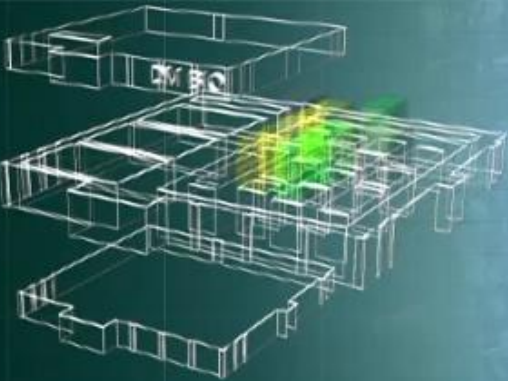
Bag testing – Sartochek® 4 plus Bag tester







DM BIO  
DONG-A (株)







Thank you very much for your attention