

Watson-Marlow on the Future of Stainless Steel in Bioprocessing



Contributor:



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IS STAINLESS STEEL TECHNOLOGY OF THE PAST?

In the past 15 years, the biopharmaceutical industry has seen a steady uptake in the use of single-use technology in bioprocessing. Single-use technology is being developed for nearly every application from upstream mixing and bioreaction to downstream perfusion and chromatography. In the pursuit of personalised medicine and continuous processing, single-use is being hailed as the only way to achieve these goals.

Does this mean an end for traditional bioprocesses that employ stainless steel technology? Is stainless steel already being considered a legacy product as we journey towards fast, closed and process-intensified manufacturing systems?

Marc Pelletier, Director of CRB, and Mark Embury from ASEPCO, part of Watson-Marlow Fluid Technology Group (WMFTG), discuss whether stainless steel is a technology of the past.

In the late 1990s, single-use technology began to emerge as a viable alternative to stainless steel in bioprocessing. For many, it has been viewed as the holy grail of manufacturing, promising fast process set-up, low upfront capital investment, reduced maintenance costs, more flexible manufacturing layouts and a reduction in validation times.

For contract manufacturing organisations (CMOs), single-use systems are particularly appealing as clients often demand fast set up and an even faster production rate. By throwing out the previous system and replacing with new for each client, CMOs can give assurance that there will be no cross-contamination, even when timescales are tight.

But could single-use systems be a false economy?








PLASTIC FANTASTIC?

A recent BioPlan Associates report on biopharmaceutical manufacturing discovered the most critical reasons for using single-use technology: to eliminate **cleaning requirements, reduce capital investment in facility and equipment, avoid costs** associated with system redesign and modifications and **decrease the risk of product cross-contamination**.

Clearly, single-use technology is the ideal choice for particular applications, some of which are setting the theme for the future of biopharmaceutical production. In recent years, we have seen a huge growth in small-scale manufacturing processes, such as advanced therapy medicinal products (ATMP). The success of therapies such as CAR-T will surely attract greater attention and investment in these types of manufacturing processes, and where manufacturers are designing systems to be taken out in the field, in war zones or in disaster areas, a closed, wholly disposable system is essential.

Pros and cons of single-use

Pros	Cons
 Eliminate cleaning requirements	 Lower initial capital cost. Higher operational cost.
 Portable (war zones or use in disaster areas)	 Limited scalability
 Decrease the risk of product cross-contamination	

But we are at risk of assuming that single-use is the technology for everything, that it is the panacea for all procedures and situations. We can be at risk of throwing out state-of-the-art stainless steel systems that have evolved over decades for the latest new thing, only to find that it doesn't quite deliver what we need.

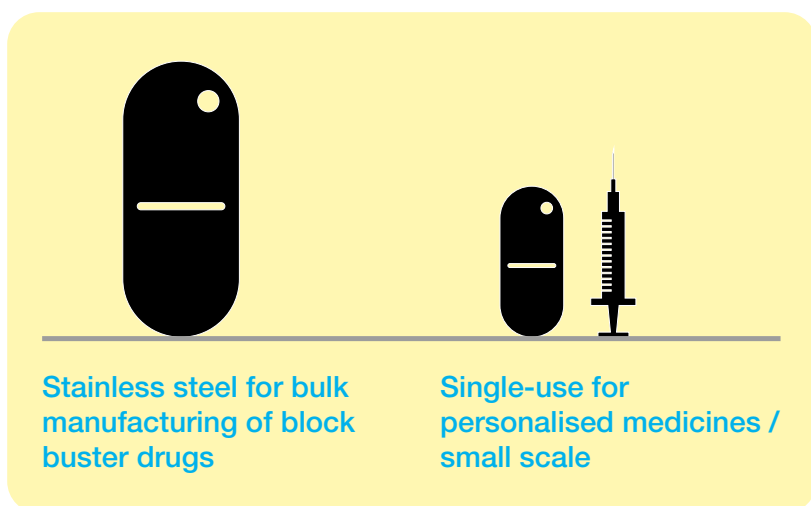
SHOULD WE PUT OUR TRUST IN STAINLESS STEEL?

An indication emerged in the BioPlan Associates report that might signal a shifting view towards single-use. Between 2016 and 2018 we see a **drop of 13%** on the 'reducing capital investment in facility and equipment' reason for using single-use response.

This hints at a potential problem with single-use equipment. Although this technology may have a lower initial capital cost, it can often have a much higher operational cost. You might remove a large portion of your cleaning and validation budget, but you'll be signing up to an ongoing consumables plan that will tie you to an individual supplier. Surety of supply is a critical consideration here. Can you guarantee a secure and steady feed of consumables when you need it? If your single-source supplier was to cease trading, could you transfer to an alternative system without risking your product or critical deadlines?

Single-use technology is still a new industry. Chromatography and perfusion stages are still widely dominated by stainless-steel equipment and although there are innovative new products being released regularly, some stages of bioprocessing simply cannot be carried out as effectively as they can with a stainless-steel system. In fact, in conversations with our clients, we find that downstream processing is much less likely to be provided by single-use technology for that very reason.

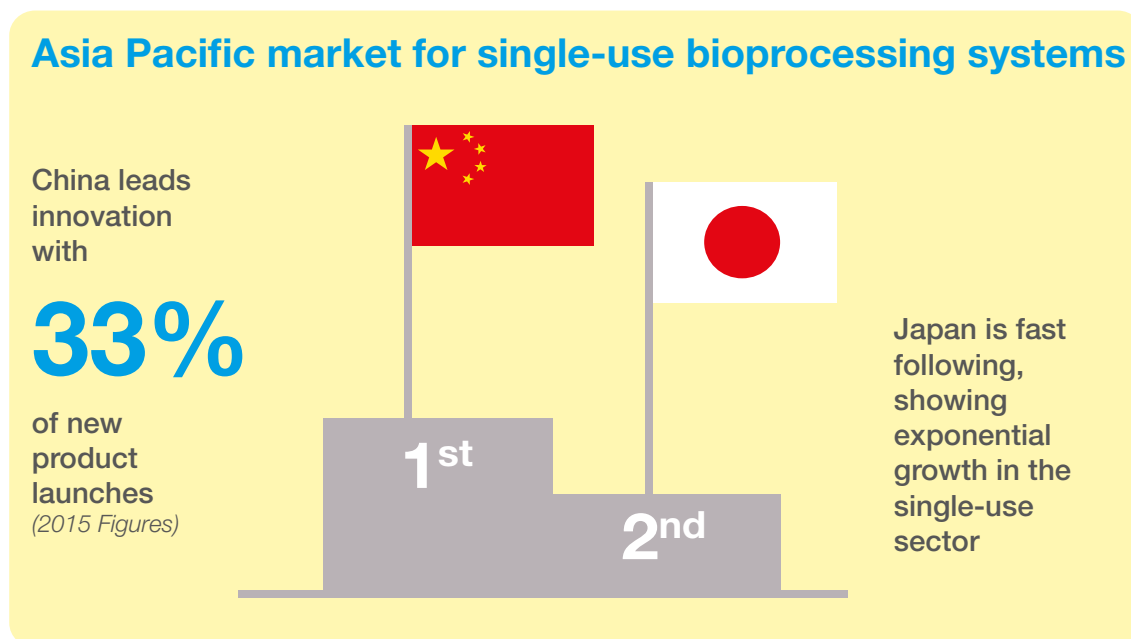
But we also see this in upstream processing too. **Single-use bioreactor bags are only available up to 4,000 litres.** Anything more than that, and stainless steel is the only way to go. Although reaction processes and increased titers are setting a trend towards smaller vessels, we still have a way to go, especially for blockbuster and larger batch processes.



In fact, in the 2018 BioPlan report, the limited scalability of single-use systems tied as the top reason for not using disposables in the US, along with the high cost of consumables and the investment that has already been made in current equipment. But the **US market** is optimistic about a single-use future, **with 67.4% of respondents expecting to see a 100% single-use facility in operation within five years.**

This optimism continues into the Latin American and Asia-Pacific markets. A recent Market Data Forecast² report indicated that the current single-use bioprocessing market in Latin America is worth almost **\$0.27 billion (USD)** and is forecast to be worth **\$0.57 billion by 2024.**

Similarly, a Transparency Market Research report³ indicated that current single-use bioprocessing market in the **Asia-Pacific region will be worth \$1.4 billion by 2024.** China currently leads innovation with 33% of new product launches in single-use technology in 2015, but Japan is fast following, showing exponential growth in the sector.

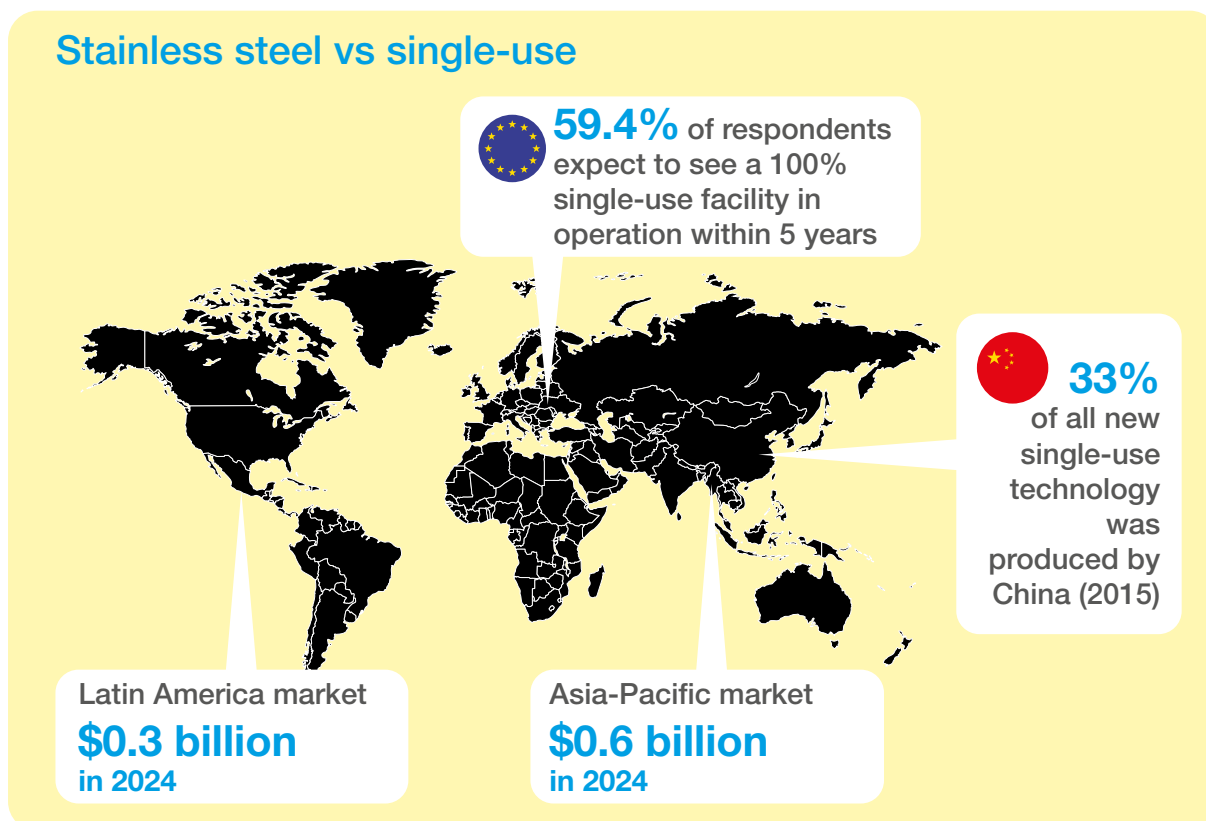


However, because single-use is still a fledgling industry in many respects, companies that we work with ask serious questions about product safety and failure modes and effects analysis (FMEA), particularly around leachables and extractables. This is an issue throughout the product lifecycle, not just during manufacturing, but as we move from tried and tested stainless steel to other plastics and polymers, pharmaceutical and regulatory bodies alike are demanding data to prove the safety and efficacy of these new materials.

We see this particularly in Western Europe, as indicated in the 2018 BioPlan report where leachables and extractables tied as the top reason for not using consumables, along with cost in this region. **The Western European market** also seems more reserved when it comes to a single-use future, with **59.4% of respondents expecting to see a 100% single-use facility in operation within five years, versus the 67.4% result seen in the US.**

Single-use technology is surely treading a path into a brave new world, for continuous processes and personalised medicine, but already we see single-use equipment being used in processes that it was never designed for.

We see single-use valves and piping being used for upwards of 180 days in continuous processes and bioreactor bags being washed and sterilised for multiple use to save money. Of course, this can all be a false economy if the process fails and a whole batch needs to be discarded. This all highlights the importance of using trusted suppliers that can provide quality-assured single-use equipment with the appropriate and relevant validation documents.





THE REAL PURPOSE OF SINGLE-USE TECHNOLOGY

When you get to the heart of any pharmaceutical business, the very reason for being is patient care and to produce high-quality treatments as consistently and inexpensively as possible. With this focus in mind, the design of a bioprocessing plant should look at all available technology in order to achieve this goal.

That's the place of single-use technology: one choice in each element of the process.

Stainless steel isn't a dead or dying industry. The equipment still works and provides the most effective solution in many situations, including large pharmaceutical applications for over-the-counter active pharmaceutical ingredients (API) and human vaccine production. These big brothers of single-use systems scale from 10 – 30 kilolitres and have the capacity to keep pace with market demand. You will have to clean, sterilise and validate the equipment, but this may well prove to be less expensive than ripping out and disposing of all equipment every time you run a new product - even for CMOs.

We know that there will be situations when a client will demand a single-use, closed system, even if it is going to be placed in a clean room, when a single-use system will be specified to eliminate cross-contamination and when a client may just demand the latest technology. But, as experts in designing and manufacturing systems, engineers should have the right to speak up, to be the voice of reason when the motivation isn't in the right place and to bring the focus back to the end goal: high-quality therapeutics produced as efficiently and inexpensively as possible.

When you look at system design this way and when unnecessary equipment or processes are specified, it is right to push back.

We are encouraged and enthused by the recent innovative developments in the stainless-steel industry, some of which have taken inspiration from the fast-moving single-use space. We are already seeing the use of new materials that extend the life of diaphragms and gaskets and increased focus on new products that eliminate the risk of contamination and reduce maintenance time, such as [ASEPCO's Weirless Radial Diaphragm™ valves](#).

In fact, ASEPCO is investing heavily in its stainless-steel bioprocessing technology, demonstrated by the opening of a new location in Milpitas, California. The plant has a dedicated research and development department as well as a sanitary products training centre. The focus is clearly on development for a thriving market but with a requirement to better educate and inform pharmaceutical leaders of the benefit of evaluating all available technology.

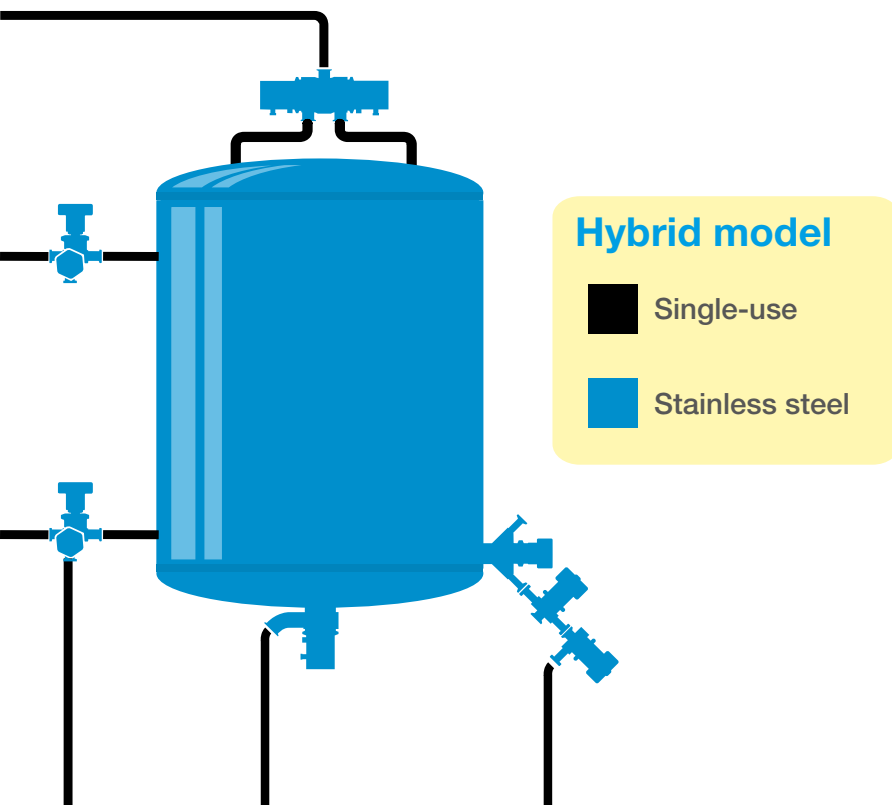
And, of course, there are learnings to be transferred from the single-use industry to reusable technology when it comes to manufacturing lead times and deliveries. The single-use industry can only survive when products are available as and when customers demand it, and that is a transferable mindset that stainless-steel manufacturers are fast adopting.

WHAT WILL THE FUTURE HOLD FOR BIOPROCESSING SYSTEM DESIGN?

We firmly believe that we will see a hybrid bioprocessing future, where tried and trusted stainless-steel systems are seamlessly integrated with single-use technology. This flexible approach will enable CMOs and biopharmaceuticals alike to find the ideal solution for their therapeutics in the best of both worlds.

We see this already in sampling systems, where a customer may use single-use sampling bags with a stainless-steel valve. The customer reduces the cost of the single-use sampling system, which might only service five sampling bags, by using a semi-permanent one.

Stainless steel is not dead nor dying, but the emergence of new technology continues to shake up the industry, calling on engineers to be more creative, to pave the way for smarter, more personalised manufacturing techniques and, above all, to develop more effective and inexpensive therapies.





COMPANY BIOGRAPHIES



ASEPCO is part of the Watson-Marlow Fluid Technology Group, which is part of Spirax-Sarco Engineering plc, a FTSE 100 company. The company is an award-winning, global leader in fluid management technology and for over 60 years has engineered components and systems for customers in a wide range of pharmaceutical and industrial markets.



CRB is a global consulting, design and construction organisation working in advanced technology industries. CRB delivers high-quality bioprocess facilities, utilising state-of-the-art methodologies and practices and working across the entire project lifecycle, from conceptual design through preliminary and detailed design, construction, commissioning, and validation.

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² *Latin America Single-use Bioprocessing Market Research Report - Segmented By Product Type, By Application , By Country (Mexico, Brazil, Argentina, Chile and Rest of Latin America) – Size, Growth, Trends & Forecasts (2019-2024)*, Market Data Forecast, August 2019: <https://www.marketdataforecast.com/market-reports/latin-america-single-use-bioprocessing-market>

³ *Asia Pacific Single-use Bioprocessing Systems Market*, Transparency Market Research, 18 April 2017: <https://www.transparencymarketresearch.com/asia-pacific-single-use-bioprocessing-systems-market.html>

⁴ <https://www.watson-marlow.com/gb-en/news/asepco-facility/>