

Future Proofing Bioprocessing from Upstream to Downstream

Case studies on how to
implement future proof
bioprocessing systems
in a constantly evolving
biologics landscape



Author Bios



Phil Sanders
Biotech Chief Innovation Officer
[Agilitech](#)

In his role as Biotech Chief Innovation Officer at Agilitech, Phil Sanders leads the company's quest to deliver state-of-the-art technology, engineering and automation services to the biotech industry, supporting the advance of science and medicine to solve health problems and make lives better.

Phil oversees all areas for the group, from business strategy, research and development, and quality control processes, to strategic partnerships and commercial operations.

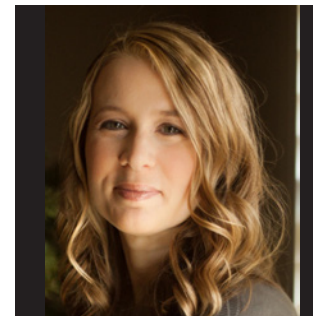
Phil has over 30 years of experience in process engineering, automation, and systems integration, with specialized expertise in the biotech industry, including related FDA and other regulatory requirements that Agilitech customers must adhere to. Before joining Agilitech, Phil served in senior management positions at both startups and industry-leading companies.



Dennis Hodgson
Director, Biotech
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Dennis Hodgson is Director, Biotech, at Agilitech, providing technical leadership for new product development, as well as custom configurations of Agilitech's biotech products and systems to meet the unique and specific needs of each client – today and in the future.

With over 16 years of engineering/manufacturing experience working at preeminent global companies such as Genentech, Novartis Pharmaceuticals, and Boehringer Ingelheim, Dennis is well versed in all functional areas of biotech process design and engineering. He also has broad experience with bioprocess system integration, automation and process optimization, and is proficient with multiple market-leading automation platforms such as DeltaV™ and Rockwell Automation®.



Brandy Sargent
Editor-in-chief
[Cell Culture Dish](#) & [Downstream Column](#)

Brandy Sargent is the Editor-in-chief and frequent author of The Cell Culture Dish and The Downstream Column. She has worked in the biotechnology industry for over twenty years, first in corporate communications and public relations, then in technical sales and marketing, and most recently as a writer and publisher. She strives to introduce topics that are interesting, thought provoking, and possible starting points for discussion by the biomanufacturing community. She has been fascinated by the different applications of biotechnology since she first started working in the industry and continues to be fascinated as the industry evolves.

Introduction

Design for Now with Flexibility for the Future

The biopharmaceutical industry continues to grow and expand at a tremendous rate. This includes innovation into new therapeutic modalities such as novel protein-based therapeutics, and cell and gene therapies. These advancements have pushed the industry to evolve to meet continually changing demands and challenges, recently including responding to a worldwide pandemic and the resulting supply chain shortages.

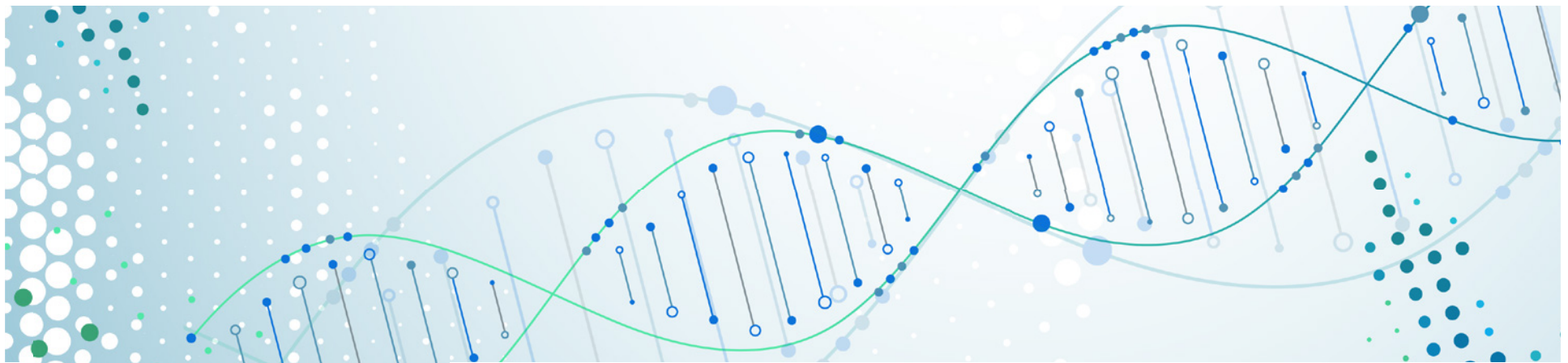
In this eBook, we look at current industry trends that are driving changes in manufacturing as well as novel solutions to challenges that we still face. Industry trends include increased implementation of single-use technologies, shifting demand for manufacturing capacity, the need for flexible manufacturing facilities, adoption of new enabling technologies, and the increased use of automation.

We examine novel approaches to help companies evolve their manufacturing with future-proof bioprocesses and flexible systems that enable companies to respond to changing priorities, new opportunities, and increasing demands. These solutions are illustrated using real-world examples of how companies have addressed challenges with the flexibility required to meet future needs as well.

Case study highlights include:

- Leveraging multiple vendors to reduce supply chain constraints.
- Increased collaboration between biopharmaceutical companies, suppliers, and regulators.
- Obtaining fully customizable fit for purpose solutions.
- Moving to brand-agnostic systems to allow companies the flexibility to use components from different vendors and brands.
- Designing processes that are future proof by addressing both short- and long-term manufacturing goals.

We will look at specific real-world examples of upstream and downstream processes that incorporate equipment that is easily tailored to specific needs, reconfigurable, and able to evolve with the workflow to incorporate technological innovation and address changes in supply or demand. We also present equipment and operating systems that are brand agnostic, which enables scientists and lab technicians to create fully customizable processes and operations that fit their production needs. It is the authors' hope that you will find information that will help you ensure that your processes are designed not just for now, but also with an eye for the future.



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Staying Ahead of a Constantly Evolving Biologics Industry

The biopharmaceutical industry has been growing and expanding since the 1980's. Early biopharmaceutical manufacturing using CHO cells looked much different than biologic production today. Processes were seriously inefficient by today's standards with much of the work being done using manual and open processes. In contrast, current commercial biologics manufacturing utilizes specialized bioreactors, technologically advanced purification systems, continuous monitoring and automation. These and other bioprocess improvements have enabled the most efficient and productive manufacturing to date and have resulted in some of the most advanced lifesaving therapeutics ever conceived.

While significant advancements have been made in biomanufacturing, the industry continues to evolve to meet new demands. Pressures, such as the advent of biosimilars, a focus on reducing drug costs, and responding to a worldwide pandemic have forced the industry to adapt and respond with new technologies. However, with new advancements often comes new challenges. In this article, we look at some of the current trends and challenges facing the biologics industry today along with innovative approaches to enable companies to stay ahead of the evolution.



Industry Trends

Single-use Technologies

One of the most significant advancements in biologics manufacturing has been the invention and adoption of single-use technologies. Single-use systems continue to be adopted at a rapid rate; as of 2018, they accounted for about 85% of pre-clinical and clinical biomanufacturing and are increasingly being incorporated into commercial manufacturing.¹ Experts foresee this trend continuing with single-use bioprocessing systems continuing to replace commercial-scale stainless steel-based manufacturing, both at commercial manufacturing and clinical scales.²

Single-use technologies owe this increased adoption to several key advantages including reduced risk of contamination, increased efficiency, reduced personnel requirements, less validation time, decreased cost for cleaning and sterilization, and shorter batch changeover time. However, challenges also exist including supply chain shortages, lack of flexibility within a platform, lack of standardization of equipment and consumables, and control system incompatibility.

Shifting Demand for Manufacturing Capacity

Changes in product manufacturing demand also require adjustment to process and scale. As a result, biopharmaceutical companies are seeking manufacturing that is easily scalable. Single-use systems and scale-out approaches to manufacturing have enabled this movement. There is no doubt that these strategies will continue to be in high demand. The COVID-19 pandemic has been an excellent lesson as to the importance of being able to significantly increase manufacturing capacity rapidly. We are also moving toward new therapeutics that require smaller volumes, such as cell and gene therapies. Experts also predict, an "increase in the number of biopharmaceutical products marketed, with a focus on developing smaller markets, personalized products, and biosimilars."²

Flexible Manufacturing Facilities

Spearheaded by recent developments in medical research, and in personalized medicine and gene therapy in particular, biotech facilities are shifting from high-volume productions to multi-batch production of smaller-scale product.³ Where stainless steel is conducive to large-volume production, a desire for increased flexibility has created a demand for smaller, more agile processes enabled by single-use systems. The result has been fewer product-dedicated facilities² and an increase in facilities that run smaller manufacturing lots with several different products.



Adoption of New Enabling Technologies

Processes frequently change because of new enabling technologies. The advent of single-use systems, perfusion culture, as well as better analytical tools and sensors are just a sampling of the technologies that have changed bioprocessing over the past decade. This trend will most certainly continue with increased adoption of continuous processing, including upstream perfusion and continuous chromatography for downstream processing as technology and experience increase.²

Implementing these improvements is not often straightforward. Bioprocesses are not always built with the kind of flexibility that allows them to quickly adapt to improvements.³ Change can be difficult and there is sometimes a perception that the cost and lost time associated with new workflows, qualification of new components, and technological investment may not be worth the effort. However, employing innovative technologies as well as the ability to evolve and do so quickly is key for speed to market, meeting quality attributes, and cost-effective manufacturing.

Increased Automation

Increased automation reduces the need for sampling by incorporating in-line monitoring, control, and data collection into the bioprocessing equipment to maintain closed and aseptic environments.² Yet, increased data collection necessitates a way to balance the need to improve processes through automation and integration, while also investing in human resources to properly analyze data and make sure the company stays compliant to industry audit regulations. Current lab systems often produce data output in non-user-friendly formats that are burdening scientists with data conversion or making them increasingly reliant on data analysts before they can do meaningful analysis. While automation software is designed to streamline processes, few have the robustness to support a complete lab bioprocess and its eventual scale-up at cGMP manufacturing levels.³

Novel Approaches to Meet Evolving Industry Demands

The best way to ensure efficient biomanufacturing is to future-proof bioprocesses with flexible systems that enable companies to respond to changing priorities, new opportunities, and increasing demands.

Leveraging Multiple Vendors to Reduce Supply Chain Constraints

The industry is currently experiencing significant equipment and raw material shortages, largely due to the impact of the COVID-19 pandemic, but also due to an increase in single-use product demand.³ However, some materials are prone to shortage, and were difficult to source prior to the pandemic. There is a worldwide shortage of some of the key high-purity polymers causing increased lead times for certain consumables.⁴ In a recent survey conducted by BioPlan Associates, 75% of biopharma respondents and 70% of supplier respondents listed shortage of single-use systems and other supply issues as a top concern in bioprocessing post COVID-19.⁴

As a result, end users can face long delivery times sometimes up to fourteen months for certain consumables.⁵ Frequently vendors can deliver equipment within a few months, but without the consumables, the equipment is not usable. End users, particularly smaller companies, have also experienced slow response times for service request quotes for single-use systems due to required supplier support for COVID-19 vaccine and therapeutic production.

Furthermore, many equipment vendors have single source supply chains because of their proprietary solutions; this also impacts the ability to increase supply quickly, as does facility and workforce constraints.⁵

Supply challenges can be addressed in the near term by providing equipment designs that are less proprietary and more open or agnostic. This way multiple vendors can be leveraged to provide a solution, thus permitting quicker deliveries. Customers may want to carefully consider this before they get locked into a proprietary solution that creates a single source of supply, especially for consumables. Agilitech, a provider of single-use technologies, looks at multiple vendors to provide best-in-class components for specific applications. Not being tied to a specific component or vendor allows Agilitech to create solutions that are best in class and truly fit it for their customers' unique processes. It also enables shorter delivery times for equipment and consumables.

Collaboration

A key tool for ensuring that a process is flexible and adaptable is through collaboration. There needs to be good communication between the biopharmaceutical companies, suppliers, and regulators to ensure that the industry can be nimble in responding to internal and external changes. A good collaboration can also create a process that exactly fits the purpose for which it was designed. For instance, Agilitech works with customers to co-design process-based solutions that meet their exact requirements. This front-end planning and collaborative design process is typically no more costly than other available products, while providing significant benefits to the overall workflow.

Another area where collaboration is key is in implementing increased automation. Agilitech leverages a strong engineering background to approach automation problem solving with customers from a process optimization perspective by looking at the whole as well as the parts. With broad automation experience on DeltaV™, Rockwell Automation®, and other leading platforms, Agilitech works with customers to understand their pain points and find a solution using the existing hardware and software components that they have. This helps to ensure ease of process transfer for a growing company and offers a flexible platform for customizability. Users can also make system modifications on their own if they have the resources to do so. Agilitech's flexible approach to automation and bioprocess control also enables seamless integration of equipment from different manufacturers and helps to eliminate the islands of automation that are often found in biotech laboratories.

Fully Customizable Fit-for-purpose Solutions

One of the major challenges to flexibility in facilities and in the manufacturing process is technological incompatibility. While customizability of a platform process is the primary goal, the reality is that customizing an existing platform has limitations.

Market-leading suppliers offer a range of competitive single-use systems with some flexibility within their platform of products. However, full flexibility of these products is often limited: they are flexible in that they are single use, facilitating quick and sterile batch changes between production runs, but the instruments themselves are not always adaptive to unique process needs and typically do not integrate products and/or components outside of brand.

There is a need in the industry for more flexible solutions that can be tailored to specific bioprocessing needs, as well as solutions that can adapt and evolve as process requirements change. Agilitech offers a different approach to flexibility by providing systems that can be tailored to specific needs and integrate fit-for-purpose workflows.

Move to Brand-agnostic Systems

Brand-agnostic systems provide end users the freedom to work with the companies and products that best meet a workflow need. This approach can also help mitigate supply chain issues, as process equipment can have the flexibility to use components from different vendors and brands.

Agilitech provides brand-agnostic systems that can be reconfigured to use filters, sensors, and other components from virtually any manufacturer brand. For example, customers can use their preferred filter brand with their preferred sensors along with a custom-configured flow path. This enables them to fully customize their bioprocess while minimizing the equipment operation/maintenance learning curve and their spare parts inventory. This adaptability also means that users become co-designers of their equipment and that they can continue to evolve their instruments according to changing needs and evolving technology.

Agilitech is not limited to the same supply chain constraints that other vendors are; if there is an issue with delivery of a specific component, they can pivot to a different vendor with quicker delivery times without any effect on the design or the delivery of the system. This approach allows customers who have long-term relationships with specific vendors to leverage that relationship for better pricing as well as eliminating the need to maintain several different components in their onsite inventory.

For automation, it is critical to create solutions based on open architecture control systems. This means the systems are not proprietary and can be supported by the end user's in-house automation team. This also provides customers the flexibility to go from a standalone control capability to a distributed control architecture in the future, which is important as a company grows and begins to scale up. It also enables the move from manual to fully automated control.

Future Proofing Process Design

Future proofing a manufacturing system ensures that it evolves with the industry. To do this successfully, it is important to understand the short- and long-term manufacturing goals, as well as current constraints. It is also key to reduce capital spending up front and allows companies to purchase only what they need at the time, but with the building blocks required to grow the system as the company grows.

Conclusion

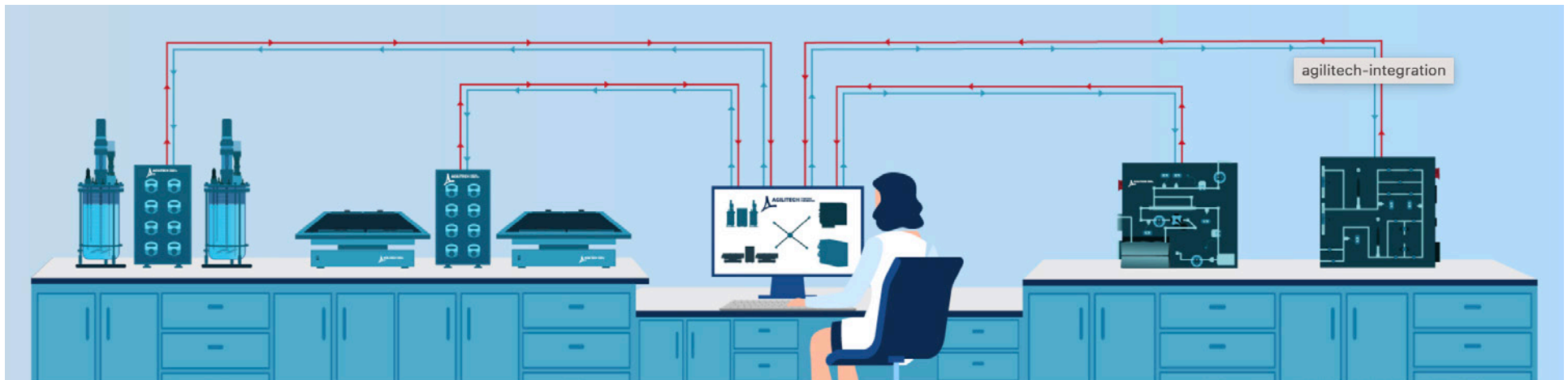
Full flexibility requires equipment that is easily tailored to specific needs, reconfigurable, and able to evolve with the workflow to incorporate technological innovation and address changes in supply or demand. It also means having instruments and operating systems that are brand agnostic, which enables scientists and lab technicians to create fully customizable processes and operations that fit their production needs. This will allow scientists to not only design their “dream process,” but also frees them to forge partnerships with a variety of vendors and suppliers to optimize their engineering process, both efficiently and cost-effectively.

It is important for today’s providers of single-use and other bioprocessing technologies and services to focus on understanding and accommodating unique customer needs to provide solutions that are truly fit-for-purpose with the flexibility required to adapt to future stresses or demands on the process.

In the following articles, we will look at specific solutions and case studies in upstream and downstream bioprocesses. We also present best practices for creating a holistic upstream and downstream process, thereby reducing the impact of process silos.

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Flexible Single-use Filtration Skid with Multiple Application Capability

The Agilitech multipurpose filtration system enables a new level of flexibility. The compact, single-use system can be adapted to virtually any commercially available external filtration system and the skid design allows one skid for multiple applications – sterile filtration, depth filtration, and virus filtration.

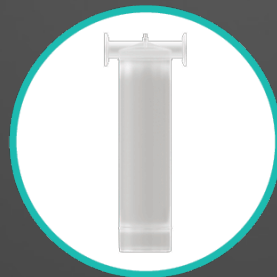
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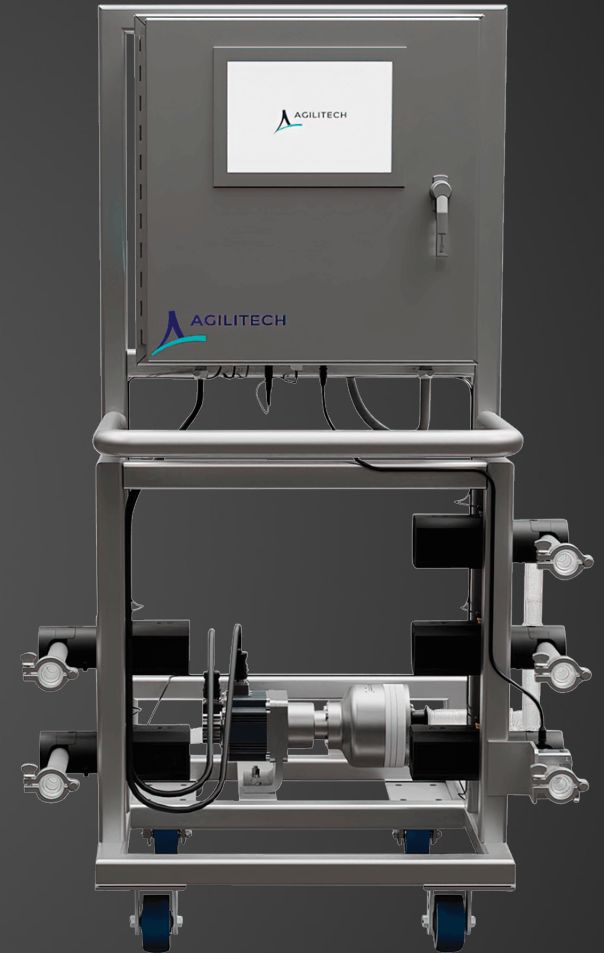
Virus
Filtration



Depth
Filtration



Sterile
Filtration



Future Proofing Upstream Bioprocess Operations

In the early days of upstream biopharmaceutical manufacturing, processes looked much different than biologic production today. Most early manufacturing runs were conducted as batches and ran for seven days with yields around 100 mg/liter. Then bioreactors began to be used and run times moved to 10-14 days with media and nutrients being replenished during the run. Now commercial biologics manufacturing utilizes specialized bioreactors, media and nutrients, and cells are monitored continuously.

As we look toward the future of upstream bioprocessing, the industry needs to remain mindful of the next wave of process advancements and manufacturing challenges. The goal is to design systems that are future proof and can handle advancements and any potential setbacks. It is also important to design fit-for-purpose systems that are tailored to an end users' specific needs, are easily reconfigurable, and can evolve with the workflow to incorporate technological innovation and respond to changes in supply or demand.

In this article, we will look at a few examples of how, with careful design, upstream bioprocessing solutions can be flexible, fit-for-purpose and future proof.

Addressing Supply Chain Constraints

The industry is currently experiencing significant equipment and raw material shortages, largely due to the impact of the COVID-19 pandemic, but also due to an increase in single-use product demand.¹ However, some materials are prone to shortage, and were difficult to source prior to the pandemic, including some key high-purity polymers.² As a result, end users can face long delivery times, sometimes up to fourteen months, for certain consumables.³ Furthermore, many equipment vendors have single source supply chains because of their proprietary solutions, which also impacts the ability to increase supply quickly, as does facility and workforce constraints.³

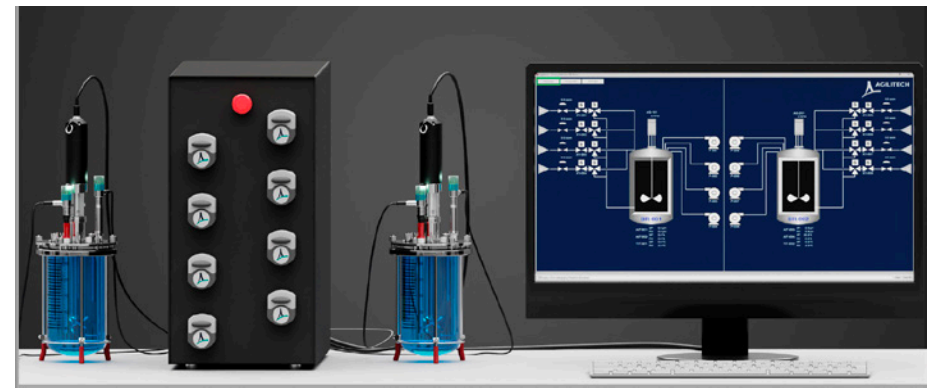
Supply challenges can be addressed in the near term by providing equipment designs that are less proprietary and more open or agnostic. This way multiple vendors can be leveraged to provide a solution, thus permitting quicker deliveries. Brand-agnostic systems provide end users the freedom to work with the companies and products that best meet a workflow need. This approach can also help mitigate supply chain issues, as process equipment can have the flexibility to use components from different vendors and brands.

Agilitech provides brand-agnostic systems that can be reconfigured to use filters, sensors, and other components from virtually any manufacturer brand. As a result,

Agilitech is not limited to the same supply chain constraints that other vendors are. If there is an issue with delivery of a specific component, they can pivot immediately to a different vendor with quicker delivery times without any effect on the design or the delivery of the system.

Case Study – Avoiding Supply Chain Delays with a Brand-agnostic Approach

Recently Agilitech has had to work with several customers to overcome the challenge of supply chain shortages. In many instances, customers are requiring specific timeframes for needed equipment and Agilitech will search for and locate different components that could be substituted to meet deadlines. Specifically, one customer was looking to purchase a depth filtration skid that was 30 to 40 weeks out on delivery. Working with a different platform, Agilitech was able to cut that delivery time in half and still meet all the requirements that the customer had for delivery. It is important to look at what is happening in the industry and which components are causing delays, then anticipate shortages and pivot to other suppliers or product types to meet timelines.



Flexible and Compact Stir Vessel Bioreactor System

The Agilitech benchtop bioreactor system is adaptable to microbial and cell culture configurations. With a brand-agnostic design, it offers the flexibility of choosing your own vessel configuration, preferred sensors, as well as the automation and control platform.

Another example was when a customer had a system that was specified for a certain type of programmable logic controller (PLC) components. By the time that the purchase order was issued, the lead time on these components had exploded. Agilitech was able to substitute different PLC components that met all specifications and were available to meet project timelines. This required Agilitech to quickly re-design the internal enclosure components and connections, which they completed in time to meet overall project deadlines.

Managing Technology Incompatibility and Platform Limitations

One obstacle to creating a fully optimized workflow is technological incompatibility. While customizability of a platform process is often the primary goal, the reality is that customizing an existing platform has limitations.

Market-leading suppliers offer a range of platform systems with some flexibility within their platform of products. However, full flexibility of these products is often limited as the equipment itself is not always adaptive to unique process needs and typically do not integrate products and/or components outside of brand.

There is a need in the industry for more flexible solutions that can be tailored to specific bioprocessing needs, as well as solutions that can adapt and evolve as process requirements change. Agilitech offers a different take on the platform approach by providing systems that can be tailored to specific end user needs and can easily integrate into fit-for-purpose workflows. It might seem like this level of customization would be cost-prohibitive, however front-end planning and collaborative design is typically no more costly than other available products, but provides significant benefits to the overall workflow.

Case Study – A Fit-for-purpose Solution

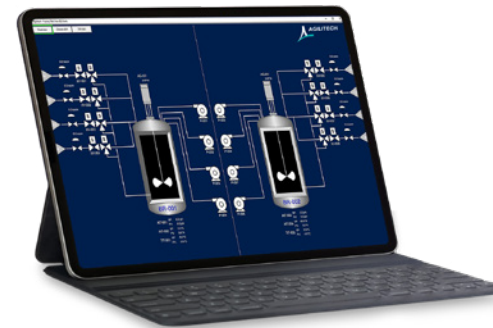
In this case study, a fit-for-purpose solution was developed for a customer. The customer's existing process consisted of feeds using theoretical volume calculations based on the peristaltic pump, thereby assuming that each revolution of the pump equates to a certain volume and then tracking the revolutions.

What the customer needed was a more accurate picture of the amount of each feed going into the process. They wanted each of their feeds to be on an individual load cell scale so that they could measure the weight of each feed bottle before and after to calculate total feed volume.

At first, the customer discussed their interest in putting four bottles on one scale and then delineating how much is being used at each bottle. This was possible, provided they were not planning on running the pumps at the same time. However,

they wanted to be able to run the pumps simultaneously across multiple bottles. Agilitech then developed a system of eight load cells, four for each bioreactor, with a bottle holder on each load cell that could hold the specified bottle sizes. Four load cells for each bioreactor are tied into a single weight transmitter that is able to delineate the eight signals and send them in one condensed cable over DeviceNet™ to their existing data collection solution.

Once the solution was identified, Agilitech needed to provide this in a compact system to conserve limited bench space. This resulted in placing the system on a stand above the pump towers, allowing the entire system to sit above the bench and leaving it open for other work.



Automation and Control

Bioreactor system controls with flexibility to support manual operation to full batch control are key to a future-proof process. Agilitech delivers systems with DeltaV™, Rockwell Automation®, Inductive Automation Ignition®, Wonderware®, or other control system based on customer need. An easy-to-use controller interface offers added convenience by bringing the most commonly used functions and data to the top layer of the screen.

Designing a Workflow Now and for the Future

Future proofing a manufacturing system ensures that it evolves with the company. To do this successfully, it is important to understand short- and long-term manufacturing goals, as well as current constraints. It is also key to reduce capital spending up front while allowing companies to purchase only what they need at the time, but with the flexibility to grow the system as the company grows.

Case Study – Future Proofing a Switch to Automation

In this instance, the customer was using depth filtration in their current harvest process and this was a process they ran manually. The customer needed to run up to three filter trains in parallel. They would wait for one filter to clog, then they would transition to the next one and so on.

In addition, the system was originally designed with three inlet valves to determine which solution is being pumped, but with the new desire to run three filter trains, they needed more granular control of the destination. So, the three inlet valves were repurposed as outlet valves.

Another custom feature of this project was the customer's desire to run multiple size tubing ID's with the skid. Agilitech designed the skid to be able to swap between 1-inch and 3/4-inch tubing at the valves and sensors.

By using Agilitech's multipurpose filtration skid, originally designed for downstream operations, and configuring it to fit this specific process, the customer was able to move their depth filtration process from a completely manual process where operators were manually controlling pump speed, monitoring flows, and pressures to a system that was fully automated. The Agilitech solution provided an automated system from flushing to filtration to post-use flushes and filtrate and blowdowns.

Because the customer is a CMO running multiple products through their facility each year, they needed a solution that would be applicable for the current product and flexible enough to handle any other filtration systems that they could envision using in the future. Agilitech designed the automation component to be quite flexible to accommodate any future products as well.

Conclusion

A common theme across all case studies was collaboration. There needs to be good communication between the biopharmaceutical companies and suppliers to ensure that the process created exactly fits the purpose for which it was designed, that the process is future proof and able to evolve with the company, and that the required equipment and consumables will be able to be timely sourced even during supply chain shortages.

Agilitech utilizes a project implementation process that encourages and supports this collaboration. The process of creating a 3D model and design prior to the proposal phase requires customers to be involved early. This involvement continues after the project starts by engaging customers in the review of functional specifications, graphics and dry software runs prior to factory acceptance testing (FAT) to ensure all needs are met. Instead of issuing a purchase order and waiting to receive updates on the status of delivery, with Agilitech customers are partners in the process ensuring that they receive the exact product that meets their needs.

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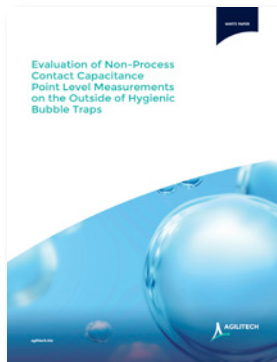
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Further Reading



Single-use Mixers - Ensuring the Customization, Scalability and Supply Required for Success

This podcast discusses the benefits of single-use mixers, dealing with supply chain concerns, ensuring scalability, and tailoring a mixer to meet specific process needs. [Listen here](#)



Evaluation of Non-Process Contact Capacitance Point Level Measurements on the Outside of Hygienic Bubble Traps

This white paper examines the challenge of gas bubbles in process fluids and buffer solutions. It discusses addressing the problem with a non-contact probe for point level control in hygienic bubble traps. [Download](#)



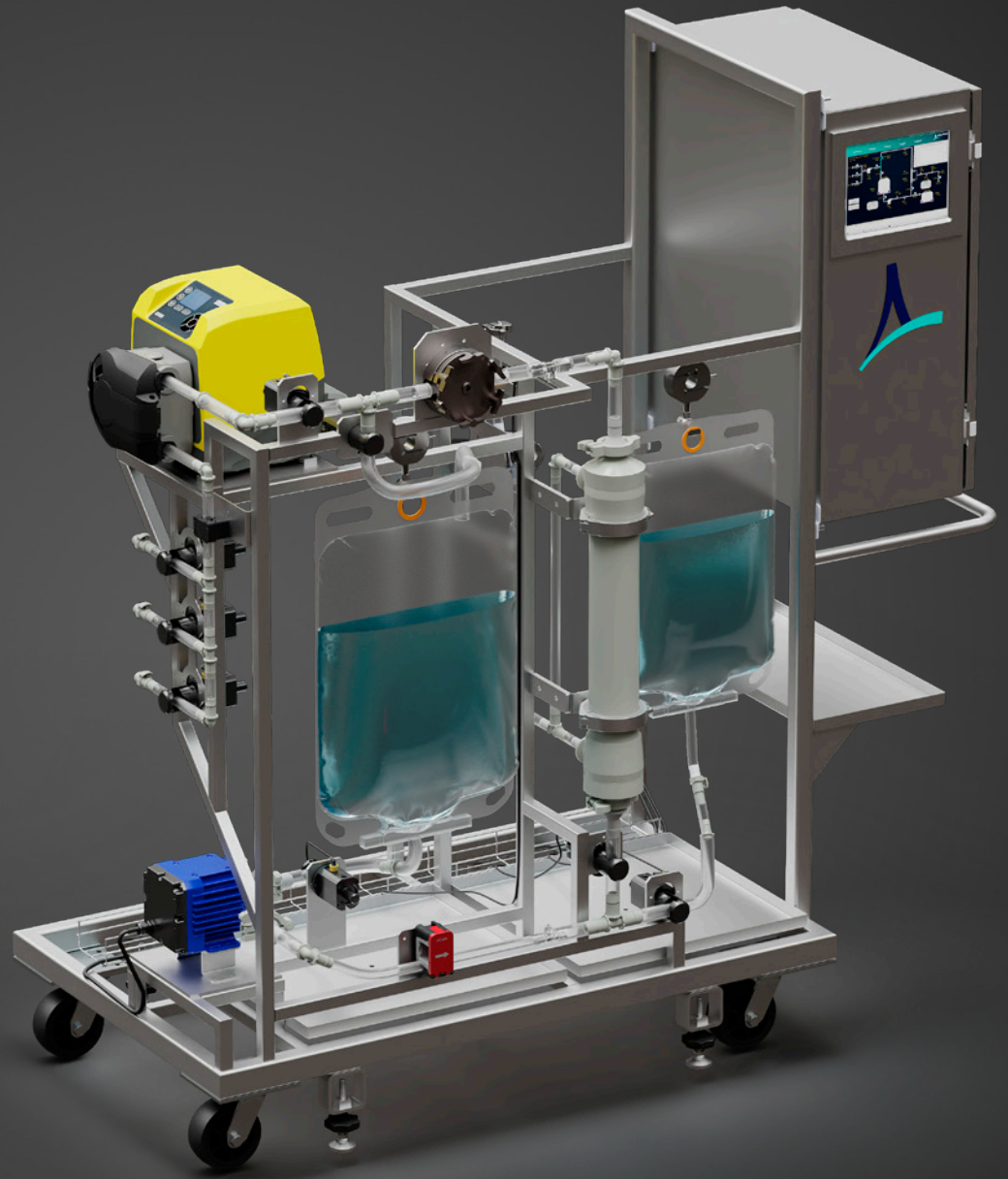
Future-proof Bioprocesses: Flexible Single-use Technology that Adapts to an Evolving Industry

This article looks at best ways to future-proof bioprocesses and using flexible systems that enable companies to respond to changing priorities, new opportunities, and increasing demands. [Download](#)



Fit-for-purpose Single-use TFF Systems

Agilitech's unique system design and brand-agnostic approach provides complete flexibility to meet exact process requirements to maximize throughput and minimize processing time. The system features best-in-class components to optimize performance. [Learn more](#)



Future Proofing Downstream Bioprocess Operations

Historically, downstream bioprocesses have been simpler than upstream bioprocesses. They were more manual and Protein A columns permitted a simple and effective purification solution for monoclonal antibodies and protein-based therapeutics. More recently, upstream bioprocesses have undergone significant improvements in process and subsequently yield. These improvements in upstream created bottlenecks in downstream as the systems in place were not prepared to adjust to changes in both the starting material from upstream and yield. As a result, downstream bioprocesses have had to evolve to meet the needs of these new challenges by incorporating technology advancements such as single-use technologies, improved chromatography solutions, continuous processing, advanced buffer management systems, increased automation, and many others.

The future of downstream bioprocessing will require additional improvements and the industry will need to stay aware of changes in upstream bioprocessing that will have an impact on downstream bioprocessing. While it is not always possible to anticipate every need in advance, the goal should be to design downstream systems that are flexible and can be adapted to meet the needs of future advancements and challenges. Part of the solution is ensuring that systems are fit for purpose to begin with and then from there are easily reconfigurable, allowing the workflow to evolve and integrate beneficial new technologies.

In this article, we look at some examples of how downstream bioprocessing solutions can be designed for flexibility, fit for purpose, and to be future proof.

A Workflow That Can Evolve

It is important when designing solutions for now that companies also consider future needs such as changing process requirements, scalability, and potential improvements. Future proofing a manufacturing system requires a good understanding of both short- and long-term goals for the process as well as current issues that need to be resolved. With forward looking planning and design, companies can purchase only what they need currently, but with the supports in place to adjust the system as needed.

Case Study – Future Proofing by Solving Current Problems while Considering Future Needs

In this example, Agilitech met with a client that was running their current process through a hollow fiber TFF filter for microfiltration, but because the starting material was so viscous, they could not use dead end filtration. Instead, they were using tangential flow filtration, which allowed them to ease the material through the system.

To future proof their system and allow them to process more material with the same unit, Agilitech created a custom skid that could run one or two hollow fiber filters in parallel. The company's current needs and processing material only required one filter, but they anticipated their volume increasing and wanted to be able to run faster outputs or larger volumes without increasing the overall processing time. Agilitech configured a system that could support a second filter in parallel to address future increases in volume. With this solution, they would be able to easily make the changes themselves by just installing the appropriate tube set and changing some parameters. These features ensured that the company could future proof their system to be able to grow and adapt to the specific process requirements for their five-year production target.



Flexible Single-use TFF Systems

Agilitech tangential flow filtration (TFF) systems range from benchtop size to up to 100 LPM and feature a unique brand-agnostic design that can be tailored to meet a customer's specific needs. The fit-for-purpose design offers options and possibilities for every facet of the system including preferred brand filter and customizable bags, to the automation and control platform.

Managing Supply Chain Delays

Supply chain delays are plaguing the industry right now resulting in significant equipment and raw material shortages, largely due to the impact of the COVID-19 pandemic, but also due to an increase in single-use product demand.¹ Some of these materials are prone to shortage; this includes some key high-purity polymers.² As a result, end users can face long delivery times for certain equipment and consumables³.

A more open or agnostic approach to equipment brands can address supply challenges by permitting more flexibility when sourcing products from vendors. This allows customers to search for the quickest delivery and best pricing across a range of products and vendors rather than being tied to one specific solution.

Agilitech's approach is to provide brand-agnostic systems that can be reconfigured to use components from different manufacturer brands. As a result, Agilitech is not limited to the same supply chain constraints that other vendors are; if there is an issue with delivery of a specific component, they create a custom solution or can move to a different vendor with quicker delivery times without any effect on the design or the delivery of the system.

Case Study – Avoiding Supply Chain Delays with a Custom Brand-agnostic Approach

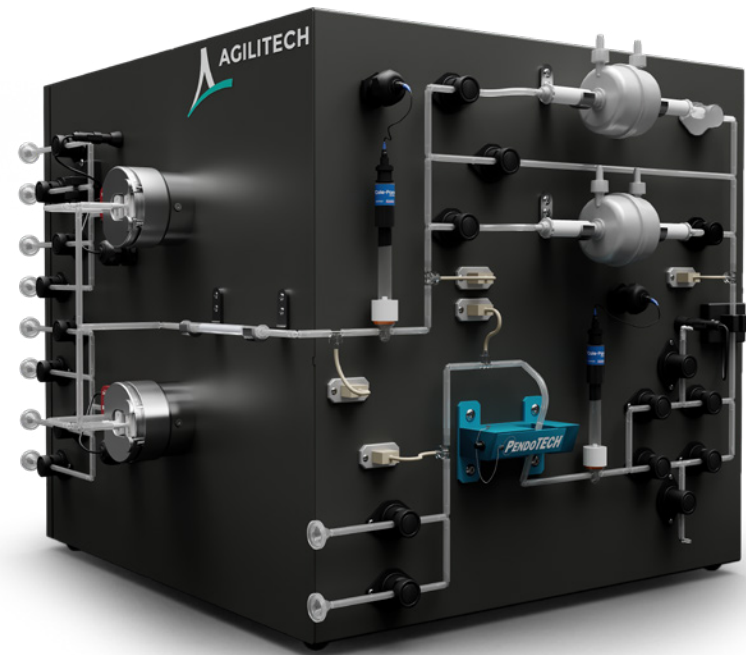
Agilitech worked with a customer that had a specific need that could not be addressed in a timely manner by ordering from another vendor due to supply chain demands and lack of availability. The customer was using a production scale single-use chromatography skid from a different supplier. They wanted to add a lab scale size single-use chromatography skid that would match as closely as possible their current production size skid. However, when they purchased a lab scale skid from a different vendor, they found out that it would be a month or two for delivery and that the new skid was not single use. This made the new system very different from the one used in manufacturing and resulted in the need for a custom solution in order to be as close as possible between process development and manufacturing.

They asked Agilitech to create a custom single-use chromatography skid to match their production size skid. Agilitech was able to complement the configuration of the other supplier's production skid. This enabled the company to do process development, testing, and other studies at lab scale while matching the same configuration of their production scale version.

Obtaining Exactly What You Need with Fit-for-purpose Solutions

Market-leading suppliers offer a range of platform systems with some flexibility within their platform of products. However, full flexibility of these products can be limited as the equipment itself is not always adaptive to unique process needs and typically do not integrate products and/or components outside of brand. Typical industry practice is to reconfigure these standard systems on the back end to meet specific process needs. However, this approach is typically less effective and ends up costing more.

The industry needs more flexible solutions that can be tailored to specific bioprocessing needs, as well as solutions that can adapt and evolve as process requirements change. Agilitech uses careful front-end planning and flexible design to provide customers with a true fit-for-purpose solution that is tailored to their unique process and that can be adapted as that process evolves.



Fit-for-purpose Single-use Chromatography Systems

With an open system design, Agilitech's single-use chromatography systems provide flexibility to choose preferred brand of column, filters, and other components, as well as the automation and control platform. The chromatography skid is engineered to accommodate optimized column sizes and resin quantities to meet specific process needs and to keep raw material costs as low as possible.

Case Study – A Very Specialized Solution for a Unique Request

In this example, Agilitech worked with a customer that had a number of unique needs for their system. They needed a tangential flow filtration system that could adapt to flat sheet cassettes, 12-inch hollow fiber filters and 24-inch hollow fiber filters. The system had to be capable of handling those very different kinds of filters while maintaining usability and not increasing hold up volumes.

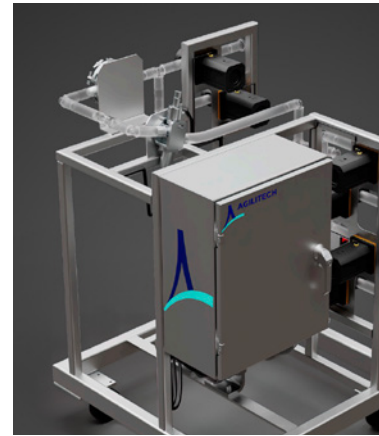
Agilitech knew that they needed to design to accommodate every scale, so that when the client was using the smallest scale filters the system was not cumbersome because it was oversized. Agilitech developed a way to put certain components on a single frame and made the frame movable within the skid boundary, so certain equipment could be moved to where it needed to be to make it most optimized for that configuration. With this skid configuration, the customer could move the permeate and the retentate instruments and valves to a specific position for optimal use for that configuration. This was achieved using linear actuators, so it is also automated. The linear actuators move with a motor that uses predefined set points to move into a specific location.

Case study – A Perfect Design to Address Potential Supply Chain Issues, Future Needs and a Truly Fit-for-Purpose Solution

In this case study, Agilitech worked with a client that is a leader in the discovery and production of enzymes for molecular biology applications. The customer needed a new tangential flow filtration (TFF) system to support production of electrocompetent cells. Their production process depended on accurate tangential flow filtration, an essential step for washing their material before preparing the product for market. The company had outgrown its current TFF system as demand for the product increased. Higher volumes required the client to run their system weekly as opposed to bi-monthly to keep up with production. Frequent processing runs meant increased costs for disposables that were becoming more and more difficult to procure due to supply chain constraints. Furthermore, as a company producing another 400 products, the frequency of running the system was interfering with the production of other biologics. The company was searching for an engineering solution that would maximize their throughput while easing workflow processes to future-proof production.

Agilitech was able to solve their problem by designing a TFF system specifically to meet the company's needs. Simultaneously, Agilitech examined the company's process to identify the core problem. Agilitech found that the company was using a TFF system that was designed for flat sheet cassettes, whereas the client was using

a 41-inch hollow fiber filter. As a result, the company was experiencing problems in their process, specifically high pressure along the filter, which forced them to slow down the flow rate, resulting in extended processing times. Their initial system worked with a 20 L bioreactor that would yield 2 L of concentrate in approximately 6-8 hours. With future goals to double throughput, eventually working with a 40 L bioreactor to yield 4 L of concentrate, the company wanted to ensure faster production times. Additionally, there were problems with accuracy in the diafiltration process. The nature of the company's product meant they were working in microsiemens, but the sensor of their diafiltration skid was scaled to millisiemens for conductivity. This made it difficult to determine when the diafiltration was complete and was impacting their product volumes as they took off samples to confirm their results.



Automated Single-use Inline Dilution System

The Agilitech inline dilution system automates buffer preparation and delivery to overcome bottlenecks and improve downstream bioprocess efficiency by eliminating manual labor and buffer storage capacity issues. Fit-for-purpose options allow the system to be adapted with additional inlets and pumps and the brand-agnostic system design enables use with preferred automation and control system.

The solution required Agilitech to investigate filter options with WaterSep Bioseparations Corp, the hollow fiber manufacturer that was supplying the company with their filters. Agilitech determined that a 24-inch hollow fiber filter would be more effective than the original 41-inch filter; its wider diameter would provide more surface area and channels for improved processing. Where the client originally sought a solution for adjusting their TFF system to handle a small filter, Agilitech understood that the problem was about upsizing the filter.

Keeping in mind the client's priority to future-proof their system, Agilitech also provided them with a pump that could handle flow rate requirements for multiple size filters, to allow for future upsizing. The result, Agilitech adapted its standard TFF system to allow for much higher flow rates, at high pressures, without stressing the system. Agilitech and its customer are expecting much higher throughput volumes, and faster concentration and diafiltration processes. Whereas the customer's original TFF system was running 800 mL/min in feed flow across the filter,

the Agilitech system sets a new target of 19 L/min for a cross flow rate. Adjusted for degradation of flow based on cell material, Agilitech still estimates cross flow within the 5-10 L/min range.

The Agilitech TFF system not only allows the customer to reach their priority goal of increasing throughput, but also allows for more automation. Agilitech provided a tailored, user-friendly operating system that can be easily transferred to an operator, freeing up the time of the company's lead expert.

What's more, Agilitech's brand-agnostic engineering solutions have the additional benefit of allowing the company to order single-use components from different suppliers, an essential design feature to ensure agility in the face of potential future supply chain problems.

Conclusion

These types of process problems are somewhat typical for the biotech industry. Many of the single-use technologies currently on the market offer some degree of customization; however, there are typically limits to how much the solution can be tailored to the specific needs of the customer. Biologics manufacturers often must fit their process to the available technologies instead of the technology meeting their exact needs, often resulting in a technology solution that is sub-optimal for the process. Companies seeking to customize their systems to fit their process also find themselves piecemealing different components to achieve their production goals. When problems arise, they face resistance from their supplier's support teams as

they have used equipment in non-standard ways. For Agilitech, the engineering challenge with this customer was about not only designing a fit-for-purpose solution that was exactly what the client needed, but also about reframing the problem.

It is important for customers to remember that there are companies who can engineer a true best fit solution. Don't be afraid to ask for an engineering challenge that might initially seem daunting.

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3. Sanders, P., & Sargent, B. (Oct. 28, 2021) Addressing the increasing demand for single-use technologies and supply chain shortages with future proof systems. Accessed September 1, 2022 : Retrieved from <https://downstreamcolumn.com/addressing-increasing-demand-single-use-technologies-supply-chain-shortages-future-proof-systems/>.

Further Reading



Achieving Peak Flexibility – A single-use filtration skid with multiple application capability

This article looks at a multi-purpose filtration system that enables a new level of flexibility. The compact, single-use skid can be adapted to virtually any commercially available external filtration system and it can be used for multiple applications – sterile, depth, and virus filtration. [Download](#)



Biologics manufacturer seeks to optimize its tangential flow filtration system to process more biomaterial at a faster rate

This case study looks at how Agilitech adapted and optimized its TFF system for a leading biologics manufacturer. The future-proof TFF system is uniquely designed to accommodate two different filter sizes, meeting current and future throughput needs. [Download](#)

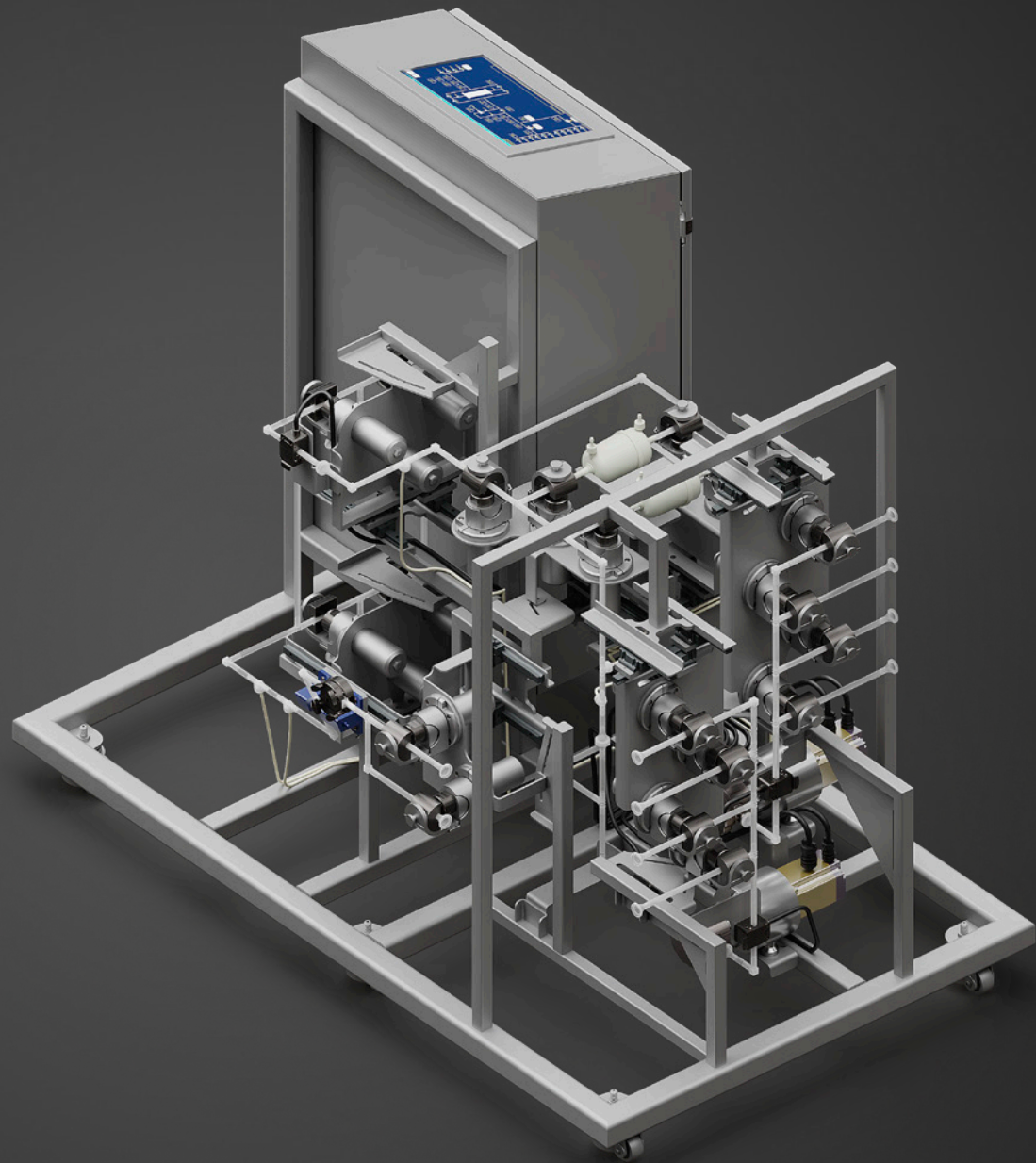


Addressing the increasing demand for single-use technologies and supply chain shortages with future proof systems

This podcast discusses the increase in demand for single-use equipment and consumables and the resulting supply chain shortages. We also talk about how to address these issues by incorporating strategies like being brand agnostic and designing future proof systems. [Listen here](#)

Future-proof Scalable Single-Use Chromatography

Agilitech's unique scalable chromatography system can be adapted to accommodate two different size tubing sets — all with the same skid. Transition between 1/4-inch and 1/2-inch tubing by simply switching out the tubing set and relevant components, rather than having to procure a whole new skid. This enables rapid scale-up or scale-down of processes on site and with the company's existing team handling the transition. [Learn more](#)



Upstream and Downstream Processes - A Holistic View

Not everyone has the luxury of building from the ground up. How do you create a unified system between upstream and downstream with existing equipment and processes? And if you have the ability to build from the ground up, how can you ensure that your design is future proof? We spoke with Phil Sanders, Biotech Chief Innovation Officer from Agilitech, to develop a set of best practices for creating a holistic process from upstream to downstream.

Create a Growth Plan with Scalability Built In

When companies are developing their process, it is easy to have a more myopic view of focusing on what is needed right now. Unfortunately, from a planning perspective this is very difficult because what is needed now often doesn't work as companies need to scale up. When Agilitech works with customers, they ask customers to help them envision what their needs will be 3 years from now, 5 years from now, and at full commercialization. These answers are critical for decisions that companies will make right now. Because speed and cost are two driving factors, especially at the beginning of operation, companies often look for what is available now and what is the most cost-effective option. However, later they may learn that the process that they have created can't scale up or can't meet other process or quality related requirements. At that point, companies frequently wish they would have made different decisions earlier that took future needs into consideration.

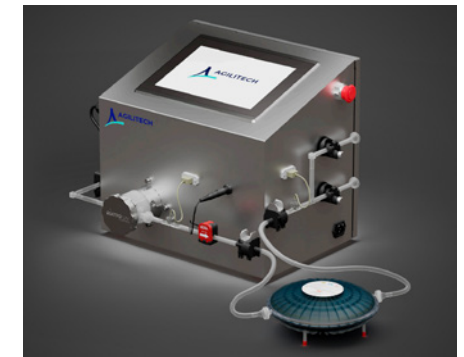
One thing that Agilitech is helping customers with is bringing a holistic view. For instance, even if the project is related to upstream, it is important to think about what is the downstream going to look like. What will it look like in a process development environment, how about a manufacturing environment? Thinking about the scalability earlier in the process allows room to build scalability into the design for the future.

It is common in an industry that is always pushing for speed and efficiency to think about what must be produced now, but later customers often realize that they have wasted a tremendous amount of time creating a process and buying equipment that will ultimately need to be replaced for something that is more scalable or flexible; therefore, off-the-shelf is not always the best solution, even if it serves the purpose in the moment.

Don't Get Locked into a Proprietary Solution – Remain Brand Agnostic

It can be tempting to lock into a single brand or a proprietary solution for your process needs from a convenience or discount standpoint. However, there are several reasons why you may want to remain brand agnostic.

Locking into a single solution may limit the process in the future. Often locking into a platform that works now results in limits on equipment size and volume that require redesigns that are costly and time consuming. A brand-agnostic approach allows companies to create a process that is flexible where all equipment works well together and communicates well across the entire process.



Agilitech Single-use Multipurpose Filtration Systems are Redefining Flexibility

The benchtop option (up to 3 LPM) and larger system (up to 90 LPM) both adapt to virtually any external filtration system. They can be used for multiple applications including sterile filtration, depth filtration, or virus filtration. Fit-for-purpose options permit reconfiguring the flow path to add more inlets, outlets, and more.



Single-use Mixers for All Bioprocess Mixing Steps and Scale

Agilent single-use mixers provide flexibility in scale with 7 models from 10 L to 650 L. The brand-agnostic design enables single-use bags to be customized to meet specific application requirements, including inlets, outlets, and sample ports. Analytical measurements such as pH, conductivity, and dissolved oxygen can also be added.

Proprietary software can be extremely limiting in scalability and working with other systems, particularly between upstream and downstream. Companies can find themselves in a situation where they must add another control system to expand their process for a more scalable solution.

Proprietary solutions can also impact support and whether updates and changes can be done in house or if outside help assistance is required. For instance, when using proprietary solutions, customers often find themselves relying on a specific company to provide product assistance and repairs; if customers remain more agnostic, it allows for much of this work to be done in house.

Early investment in a proprietary system often ends up being wasted because the right platform is not chosen for the long term and a proprietary solution may not permit easy substitution of another brand equipment.

Plan for the Automation Environment

Increased automation continues to be an important trend in biologics as it enables increased process optimization, implementation of Process Analytics Technology (PAT) approaches and Quality by Design (QbD) initiatives, and helps to maintain aseptic, closed manufacturing by automating sampling procedures. When companies are starting out, they are working at a smaller scale than they will be at clinical or commercial manufacturing and many times they are still figuring out their process. This can lead to equipment purchases that save time or money. The problem with this approach is that it does not consider future integration needs or the kind of capability that they will eventually need. If the product is successful and increases in manufacturing need to occur, it will be much more costly and time consuming to make the changes later in the process. For instance, it may cost an extra \$5,000-\$10,000 to set up the SCADA system infrastructure up front, but once in place, companies can add to it as needed and there is an existing framework. Waiting to do this in the clinical or commercial phase will cost significantly more and will likely result in some level of process redesign. This is also an important part of how upstream and downstream process groups will communicate, so building this framework up front will facilitate communications both in process development and eventually manufacturing.

In addition, while using an industrialized platform like DeltaV™ or Rockwell Automation® will cost more up front in comparison with a proprietary automation platform, in the end scaling up on something standardized will be much simpler than using something proprietary. For example, a recent customer in the cell-based protein market decided to employ an industrialized platform for just two small bioreactors, knowing that in the future they can easily scale this system up to meet their needs. They can also replicate this system as many times as needed for manufacturing. Ultimately if a company is looking to manufacture a product at market scale, they will eventually need to automate that platform and will likely use an industrialized platform. Best to start with the industrialized platform and grow from there.

Balance Speed with Designing for the Future

There is an understandable drive to speed the process, especially speed to clinic. Often companies look to how they can get up and operational as soon as possible. However, it is important to balance this desire for speed with the need to plan for the future. It is important to look at the big picture and plan a process that works today and in the future. Saving time now could end up costing time and money later. It is important for companies to work with suppliers who will create a proposal that takes future scale into consideration and will suggest processes that can grow each step toward commercialization. At Agilitech, a proposal is created that shows companies how to build a process that will grow with them, including cost considerations and a scaling plan that lets customers know what their upfront investment is along with estimates for future expansion.

Agilitech sees this issue frequently with tangential flow filtration (TFF) skids — and creates flexibility that enables customers to use different size tubing that meets their needs now and allows for future expansion. Instead of having to purchase a new skid later, it is possible to design one that will be flexible and future proof. It is important to note that companies do not have to sacrifice timelines for these solutions. Agilitech can turnaround a tailored solution like that in six to seven months, which is a typical lead time in the market today. Thus, enabling design for the future while still maintaining very fast timelines.

Leveraging Industry Standards

Another aspect of designing for the future is leveraging all the industry standards that are available. Everything Agilitech builds is to ISA 88 batch standards, which means that different levels of automation can be employed. If a customer wants something that is very manual, there are control modules for valves, pumps, and transmitters that can be built in so that everything becomes a manual operation. However, this also provides the ability to use that platform as the foundation for future growth. Equipment modules or operations can be put on

top of that platform to the point where recipes or batch can be used to control the process. Following good manufacturing processes such as GAMP forces you to examine the process and ensures the development of a functional specification that defines how the unit or process will operate. Using these standards, all specifications are driven to completion before the implementation starts so that everyone is on the same page.

Future Proofing for Emerging Technologies

It is important for cell and gene therapy companies to have solutions that really fit their needs now and in the future. Many solutions are designed for much larger scale operations. Agilitech is working to provide these companies with smaller scale solutions. For example, having a single-use 10 L or 25 L mixer is really important for these companies, they can't utilize a 650 L or 1,000 L mixer. Agilitech offers chromatography skids that are among the smallest units on the market to support these emerging technologies at the scale that they need. At the same time, Agilitech is gaining insight into these processes and thinking about how solutions can be created to resolve other issues that these companies are having, including other products that need to be scaled down to meet their needs.

Transformative Product Design





The Cell Culture Dish and the Downstream Column are online publications designed to provide a community for scientists and others involved in biotechnology. The goal is to share expertise and best practices as well as discuss topics of interest to the community. Articles cover areas important to the application, development and regulatory approval of mammalian cell culture processes and products. This includes biomanufacturing, vaccines, cell culture and purification, regenerative medicine, cord blood stem cells, cellular therapy, cell-based assays, diagnostic antibodies, life science research and related applications.

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Agilitech is a pioneering partner to the biotech industry. The company helps to drive progress by designing and implementing state-of-the-art equipment and bioprocessing systems for biotech research labs through to full-scale production, along with game-changing bioprocess engineering and automation services.

In a fast-moving industry that is constantly evolving, Agilitech has the flexibility and experience to tailor its offerings to the specific requirements of each and every customer. A transformative product design and engineering process is what makes Agilitech single-use bioprocessing technologies unique and ensures that the company's solutions meet the exact needs of each and every customer. Through front-end planning and collaborative product design with end users, Agilitech delivers truly fit-for-purpose solutions to real problems.

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