

Upstream and Downstream Processes — A Holistic View



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. Throughout his career, he has successfully guided cross-functional teams from operations to R&D, driving organizations to success by mentoring and motivating others to produce results while minimizing risk.



Dennis Hodgson
Director, Biotech
[Agilitech](#)

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®.

Dennis' vast expertise and understanding of the ever-changing arena of biotech research and development, as well as biopharmaceutical manufacturing are sought after by both internal colleagues and clients alike.



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.

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.

Dish@CellCultureDish.com | CellCultureDish.com | DownstreamColumn.com



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.

info@agilitech.bio | Agilitech.bio

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