



Looking Back and Moving Forward in the Fight Against SARS-CoV-2

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The unprecedented global crisis brought on by SARS-CoV-2 has affected all aspects of life and business. This includes the pharmaceutical industry, where existing trends that were driving incremental changes prior to the pandemic have been accelerated to meet the demand for SARS-CoV-2 vaccine production and delivery. A recent **study by BioPlan Associates** takes a closer look at the impact of SARS-CoV-2 on bioprocessing, specifically the near- and long-term changes resulting from the unexpected demand on the industry's resources.

With so many lessons learned from these changes, the industry has an opportunity to apply them going forward so that we can move toward a future where flexibility and adaptability forge a path toward consistent and reliable supply in a post-SARS-CoV-2 environment. In a recent **roundtable discussion** conducted by Life Science Connect, a panel of experts offered their insight on what challenges they have seen come to the forefront during this crisis and what they believe we can learn from them going forward.

Panel of experts



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What are the biggest industry challenges in scaling rapidly to meet demand, and have these challenges changed because of SARS-CoV-2?

Brandon Pence

It's an interesting time in our industry, and I believe this question is something we could take all hour to discuss. When I step back and think about the challenges that we're facing right now, capacity constraints continue to be on the supply side and on the manufacturing side, and I think the SARS-CoV-2 environment has intensified that. The involvement with the contract development and manufacturing organizations has been a critical piece in our response to the SARS-CoV-2 outbreak. The challenge is finding the right way to transfer processes to those sites and the products that go into them, then communicating effectively across that manufacturing network so the suppliers have the real view and version of what is needed from a supply side and we're balancing our supply to the various sites in that manufacturing network

effectively. At the end of the day, what we're trying to do is ensure the right level of production and processes get put in place across the full network to ensure that we're making progress on the vaccines or therapies that are being developed in a SARS-CoV-2 world. That diversity of the manufacturing network has become an intensified challenge in a SARS-CoV-2 environment.

One of the reflections I've had over the past 9 or 10 months is that there has been an impressive response across the entire industry to move with such speed and at such scale to not only continue with our commercial manufacturing of existing vaccines and therapies but also to rapidly develop new vaccines and therapies that could be utilized in this fight against SARS-CoV-2. The other part that I think plays a big role in overcoming some of the challenges is new technology development. Two of our front-runner vaccines in the world of SARS-CoV-2 are using mRNA technology, which is a new application in the sense that we don't have human vaccines from mRNA technology out there today. Yet, within 10 months, we've gone from concept

to completing Phase 3 clinical trials and moving toward the Emergency Use Authorization. And I think that the role technology plays in overcoming industry challenges is one that we've often talked about in years past but has certainly taken a much bigger spotlight in the SARS-CoV-2 environment. Chris Murphy can offer his perspective on challenges on the manufacturing side.

Chris Murphy

What I would home in on here is these new modalities. These modalities were being developed to treat rare diseases and cancers, where a billion plus doses were not needed, as Brandon Pence pointed out, in the next nine months or so. And I think scaling up, of course, is the challenge. When you look at the technologies that we're using to make these and the technical expertise in the industry to support the manufacturer, validation, and testing of these molecules, it's all unique. I see two elements to this: the first is just simple constraints on facilities that were designed to just manufacture smaller batches in support of smaller patient populations, and the second is the race for talent and expertise. You need capacity that can support larger-scale manufacturing of the new molecules for vaccines but also the talent to know how to manufacture and make them.

What factors enable a SARS-CoV-2 vaccine and biotherapeutics manufacturer to get to trials as quickly as possible?

Eric Langer

We've been looking at this industry for 30 years, and one of the common themes we've found over that time, although it's especially consistent today with this pandemic, has been the importance of human capital. And what I mean by that is the nature of biopharma. We could look at it from a technical perspective or an operational perspective—in terms of the industry structure, its suppliers, and the collaborative nature of the industry. But what I think really has been shown during this pandemic is the dedication of the people involved. In industry, you think it's going to be an operational factor, but what we found in that analysis and many others is that it's really about the people and the shift and the dedication we found to do the right thing.

Kate Torchilin

In terms of just human spirit and human collaboration, it also goes beyond individuals in having agencies, networks, and various organizations participate and collaborate as well, starting with regulatory agencies that are green-lighting a lot of those reviews and approvals. It's a much faster pace for recruitment networks to make sure that global clinical trials are enabled across many countries at the same time. In traditional therapeutics development, that takes much more time and a lot of effort to set up. And then on the pandemic side, we see clinical trials across all continents happening very quickly. We're also seeing a lot of creative collaborations between innovative companies and contract manufacturers and vendors, such as Thermo Fisher Scientific, which are enabling a local presence for manufacturing, production, delivery, and logistics of materials needed for clinical trials at the very fast pace and at the global scale.

Murphy

To add one thing, I do think that even though these modalities, such as mRNA or adenovirus, are certainly new from a vaccine approach, or at least some of them are, as Kate just pointed out, they have been tested in very sick people for many decades. What's helping accelerate these trials is that the safety profile is very high, so I do not think the regulators are cutting corners. In fact, they are reflecting on the rich history of these trials, where these vaccine approaches have already been demonstrated to be safe. I think that's going to be important for the general public to understand. This wasn't just something invented in the last nine months; many people have already been treated with this type of technology.

What current challenges are manufacturers facing with regards to supply issues affecting SARS-CoV-2 vaccine and biotherapeutics manufacturing?

Langer

When we did our white paper analysis and spoke with 25 bioprocessing professionals and senior decision-makers, the number one concern among 75% of the participants was fear of shortages. Pre-pandemic, the answer to this question was a lack of communication when working with suppliers or service providers. A fear of shortages can create panic solutions that aren't necessarily warranted. What we've evaluated here is that, if a shortage is possible, many end users are going to look at this in terms of worst-

case scenarios, so they're going to make decisions based on that, which they may have to do. If the problem is not as acute as it may be, then the solution could come with better communication between the supplier and the end users regarding those potential shortages. Otherwise, the end users are just going to respond to worst-case scenarios, and that's not necessarily optimal.

Pence

To touch on your comment there, as it relates to fear of shortages, I think that's a very real thing. We're seeing that in the industry now, which, in some ways, is a factor or a function of a year ago. We had a very healthy pipeline of biologics and vaccines that were being manufactured for commercial applications, and a very robust clinical pipeline, and a lot of supply was going into those things. And then we toss in SARS-CoV-2 and the industry's response to that. It's not that we want to shut down or not progress on our clinical trials, or halt our commercial supply of existing vaccines and biotherapeutics, but we have to balance that. As we start to make decisions based upon supply going into SARS-CoV-2 applications or non-SARS-CoV-2 applications, the optimal way for us to do that is to enhance our communications to understand exactly what the application is, what is needed, and when it is needed, so that we can plan accordingly. If we get into panic buying and safety stocks and materials, it only exacerbates the problem that we're facing as an industry. There's always been this mentality of concern around securing our supply and protecting our supply chain, and I think that's a very valid concern and something that is top-of-mind for most in the industry. But I think, in the current environment, businesses on the supply side and manufacturers on their side are recognizing that, if we enhance that communication and increase the transparency and the visibility, we are able to balance supply much more effectively.

How can suppliers mitigate concerns related to these supply issues, and what critical supply changes need to be made for the future of vaccine and biotherapeutics manufacturing?

Williams

The state of the single-use industry has evolved over time and, in my opinion, with far too much customization. We've over-designed and over-engineered a lot of the single-use bioprocess containers and transfer assemblies. As Chris Murphy mentioned earlier, a lot of the processes

we use for manufacturing are still very manual and labor-intensive because of the customization. The general trend for the industry as we mature is that we need to have more standardized solutions that will lead to more opportunities for automation. That will take the labor intensiveness away, which can help lead to rapid scale-up. Thermo Fisher's approach has been to build a more robust and mature end-to-end supply chain, which is in three parts: (1) what raw materials are coming in, (2) what is our manufacturing conversion, and (3) what are the post-manufacturing steps?

When thinking about the raw materials coming in upstream, we look at redundancy of supply of those materials, so we have redundant suppliers for film and for tubing. Specificity of raw materials by end users has driven us into some corners, and we've all paid the price for that in lead times across the industry. The second part is rapidly expanding our capacity globally to where we now have full manufacturing capability on three different continents. Part of that is to get closer to our customers. This allows us to move a lot of material around but also to provide redundancy, in case something happens to one facility for whatever reason. And we've all seen it happen in the single-use business across the suppliers. The last part we think about is post-manufacturing. When it leaves our facility, it must go through radiation, and that's been an interesting challenge. In the industry, we try to look for redundant radiation suppliers, but in addition to that, because of a global pinch on these types of facilities, we've been pushing more for alternate radiation technologies for different types of assemblies to "de-bottleneck" some of those critical gamma facilities. The last piece is that we must push more for harmonization. Thermo Fisher is building a harmonized network so that all of our systems and suppliers are the same, regardless of which facilities they're coming from, which helps mitigate the supply risk for everyone.

Torchilin

The assurance of supply and making sure we can support substantial demands as well as spikes in the future comes with first having enough footprint, capacity, and raw materials. It also requires a supply chain that is reliable enough to bring the raw materials on-site for manufacturing. And then, with that in mind, having a footprint with enough room to support the ongoing growth as well as spikes, such as what happened to the industry with SARS-CoV-2. So, how do we invest in placing those capacities across the globe? How do we form strategic relationships with raw material suppliers so that we can consistently and reliably have a supply

chain and assurance of supply? Once we've done that, how do we make sure that we can support manufacturing globally in several different locations? That absolutely necessitates harmonization and making sure that whatever we manufacture in different parts of the globe can be scaled consistently. And from a standpoint of contract manufacturers or companies manufacturing vaccines and biotherapeutics, how do they do the same? You must be extremely agile and nimble in order to substantially increase volumes of manufacturing. These companies are beginning to look at outsourcing as part of their manufacturing, such as large-volume buffer production, which might not be needed at every location. Vendors like Thermo Fisher are beginning to think through and invest globally to support outsourcing of non-core capabilities so that we can guarantee on time deliveries to support vaccine manufacturers and biologics manufacturers globally.

What would you say is the number one way that manufacturers and suppliers can collaborate to make a substantial difference in the future of vaccine and biotherapeutics production?

Torchilin

If I were to have one big wish for myself, it would be partnering early, because we want innovator companies to develop new vaccine platforms as well as biotherapeutics. For that to bear fruit across the globe and large populations, it must be reliably scalable and manufacturable, and we, as an industry, must be able to support large-scale assurance of supply and manufacturing. The earlier the innovator companies developing those platforms can partner with organizations that can support manufacturing and scaling of those processes, the better it will be overall for our human health globally.

How can we, from the very early days when the new platform is being designed, partner in a way that allows us to think through what needs to happen to scale that process? How do we think about raw materials and the bill of materials that go into those new platforms so that we don't end up with something that's so esoteric or hard to procure large-scale that it impacts its scalability? How do we think through the process so that it can reliably produce high yields for vaccines and biologics, so they are not cost prohibitive once they're manufactured? How do we design a process so that, once a product is approved, it can be manufactured and distributed globally? Much of this

is engineering by design, and the earlier we can partner with manufacturing companies and innovator companies to think through those elements, the better it will be for everyone.

Pence

When it comes to how manufacturers and suppliers can collaborate to make a difference, one of the things that jumps out at me is the phenomenal speed at which the industry has responded this year. I can't imagine that once we get in front of the SARS-CoV-2 pandemic that we'll go back to the ways we worked previously. For us to continue to have a lasting impact on vaccine or biotherapeutics production in the future, we have to work together more seamlessly, which requires integrating our development on the supply side with the clinical pipeline development on the manufacturing and innovator side.

Chris Murphy mentioned earlier in the discussion that some of the processes and tools that we utilize right now are decades old. The rate of innovation and the way innovation then gets qualified and implemented into new manufacturing processes for either existing or new biologics modalities has to change. We must work more closely together as an organization from the supply side with our customers to understand what their needs are, what's working, and what's not working. And then the customer side has to look at this and find ways to bring in new technologies, new supply channels, and additional logistics services more effectively. Going through the processes for years and qualifying new technologies before they ever get utilized doesn't work, as we're seeing today. We must find a way to work more effectively and more closely together, and both sides have a responsibility to make that happen.

Langer

Partnering is a loaded word, and there are so many good ways this could be done. The challenge is defining what it is we want to get out of something, such as standardizing solutions. Everybody wants to standardize, but they all want to standardize on their platform. How do we collaborate to ensure that we're using a beta tape and not a VHS? In terms of partnering, that's critical, especially in areas like cell therapy, where new technologies are emerging out of academic labs and neither side is 100% sure what a solution is going to look like. The challenge is: how do you work out a partnership in an environment where things are not fully solidified?

One example that's been going on for years in this industry segment is that people always want to have their cell culture media optimized. In the past, companies would offer a cell optimization service and those cell optimization services would come at a price. Then you get locked into somebody's formulation for 20 years, and that kind of collaborative partnership didn't work. What could work, though, is when you think about a partnership, it is sort of a marriage, and some people have said a marriage and a partnership needs to be a situation where both parties give 60%. Obviously, the math shows that everybody's going to have to give more than they think for a partnership to truly work. That is probably how a collaborative environment is going to have to work during SARS-CoV-2. After SARS-CoV-2, when we move back into the normal environment, the question of collaborations and ensuring we're ready for the next pandemic is going to require a little bit more stamina and more forethought on the part of both the end users and the suppliers in terms of what they're willing to give.

One area that I think is going to be critical, and we've touched on it already a couple of times, is staffing. We found that 70% of the industry says they're going to be outsourcing more during SARS-CoV-2. That's the number one change that the industry is going to start to undertake, and that goes to the question of whether that is a core business. If it's not, companies are going to start to determine whether it's something they should be doing, because the lack of staff to undertake some of these core business activities is going to start to create bottlenecks. Therefore the only solution, such as in cell therapy, is going to be outsourcing of unit operations and staffing to contract manufacturers. I suspect some of these solutions have not been explored yet. But when push comes to shove and there isn't the human capital to do the job that needs to be done, that's when people are going to start to think of creative solutions that are going to make collaborations more effective.

Watch the full webinar on demand to hear the full discussion among our experts



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Round table discussion:
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