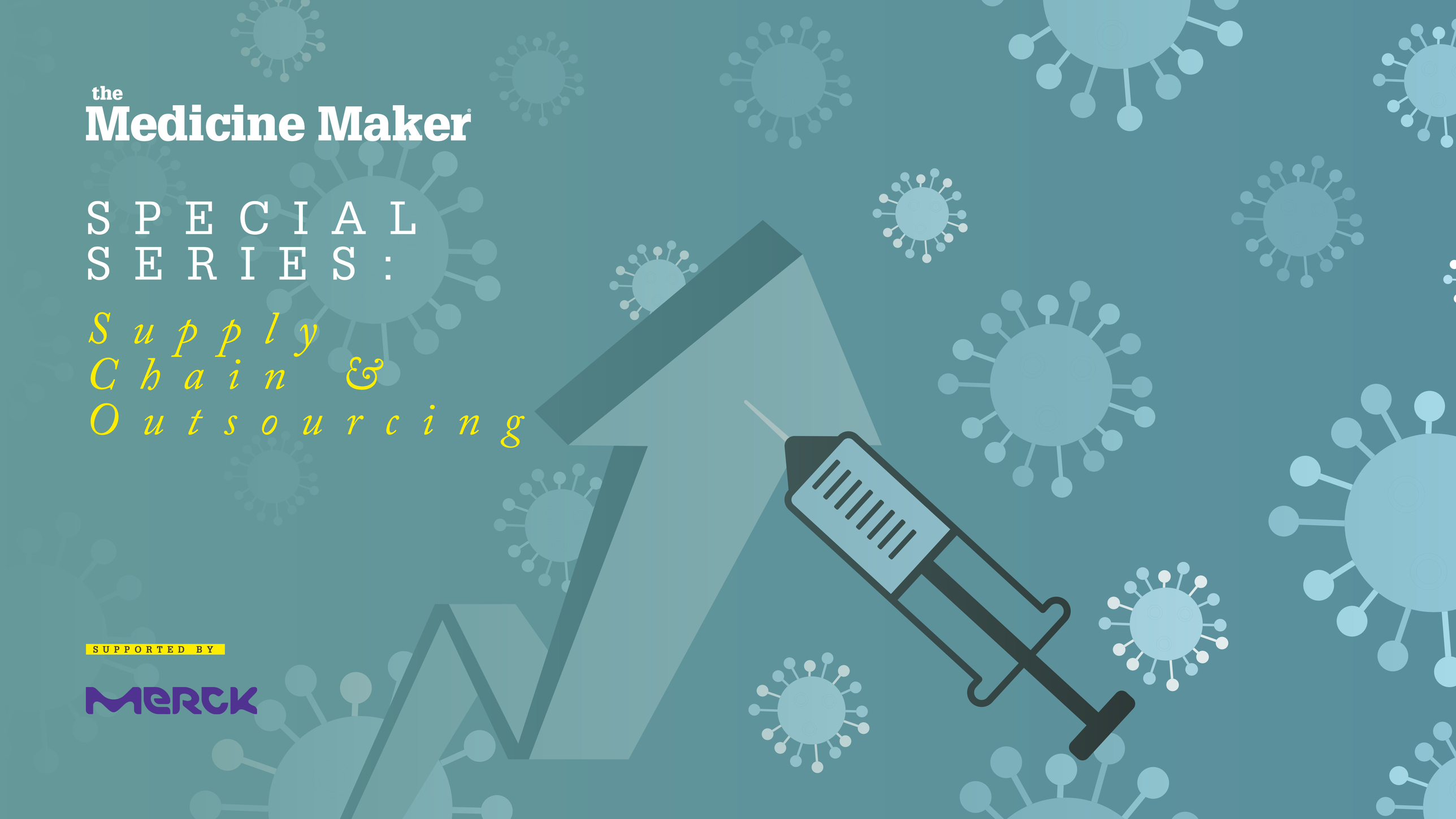
the Medicine Maker

# SPECIAL SERIES:

## *Supply Chain & Outsourcing*



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IN MY VIEW

# Securing Supply: Best Practices for Critical Raw Materials

COVID-19 has taught us that unexpected events can cause significant supply chain disruption – and there's no better time to consider secondary and tertiary sources.

As demand for biopharmaceuticals continues to increase, expanding manufacturing capacity to maximize productivity is key. However, increased production capacity necessitates more raw materials.

Though meeting scale-up needs or increasing sales volume may be possible with a single supplier, finite capacity or limited availability can make it difficult for the supplier to meet high demands for raw materials. As a result, many biopharma manufacturers are beginning to leverage secondary and tertiary suppliers of critical raw materials, such as cell culture media. In fact, qualifying additional suppliers may be essential for manufacturers to simply maintain capacity in the event of unforeseen circumstances. For example, halts in production due to failed inspections or facility shutdowns can directly impact the availability of critical raw materials. Global issues – such as SARS-CoV-2-related supply interruptions and shipping constraints – can also limit supply. Whether a manufacturer is looking for a supplier to increase its output or as a secondary source in times of need, securing multiple suppliers is a crucial step in keeping production on track.

When it comes to securing suppliers, manufacturers must successfully qualify the supplier and confirm they can meet their requirements. Ideally, this should be done proactively ahead of a critical need.

## What to look for in a potential supplier

The first step in selecting an additional supplier is identifying those that can support your specific requirements. If you are looking for a media supplier to manufacture your media formulation, this may mean that you need one who can source the 100 components that make up your formulation and manufacture it in-house. Conversely, you may be looking for a supplier who can supply a small number of specific raw materials so you can manufacture your own medium. Understanding your requirements will streamline the selection of a secondary supplier.

Working with a media supplier who has qualified multiple sources is also an ideal approach to improve access to critical raw materials. Global suppliers typically procure raw materials from several different sources, creating secondary and tertiary supplies of their own raw materials in-house. For instance, a supplier would have a primary supply of a critical raw material, such as trypsin, but would also have qualified additional suppliers in case of a problem with their primary source – such as low quality or supply interruption. The materials from all these suppliers would have undergone the same testing to confirm quality and establish redundancy.

Considering the origin of your media supply is also important when selecting a supplier as it can help alleviate supply concerns while maintaining production. For instance, does a potential supplier have one facility that produces one of your critical raw materials? Or is it redundantly manufactured at multiple facilities across the globe? The latter helps safeguard the supply of your critical raw materials, even if supply shortages or shipping challenges occur.

A growing industry combined with potential instabilities in global markets means that media suppliers are also acutely aware of how important it is to be able to supply products confidently and continuously. As such, many suppliers are investing in expanding capacity and volume to meet this demand, ranging from large investments (for example, construction of new facilities with increased capabilities) to more minor investments (for example, improving internal processes). Ultimately, these improvements are helping to increase the volume and reliability of raw material supply to meet increasing demand.

## After a supplier is selected, how do you qualify them?

Though the qualification process for new suppliers may differ depending on the specific needs of a project, process, or company, several key steps help streamline the process.

i. Confirm quality. First and foremost, when qualifying a new supplier, you need to confirm the quality of the products you are procuring. You'll want to ensure your media supplier strictly follows its own best practices and has an established standard operating procedure to confirm the quality of their raw materials.

Though suppliers have their own qualification requirements, it is still important for you to confirm this quality. Establishing your quality audit process is important; your specific requirements may differ from other companies.

ii. Confirm that specific processes or protocols are followed. After confirming the quality of the raw materials provided by a secondary media supplier, it is also important to confirm that any required processes or protocols are followed. For specific raw materials, this may range from confirming segregation of animal origin and animal origin-free products in-house to confirming the milling techniques used to create dry powder formats. If you are qualifying a supplier for the manufacture of your formulation, it is important to audit and qualify the specific manufacturing process, as well as the raw materials. Walking through how your medium will be manufactured in-house during a site visit is recommended. Such visits can be an important step in alleviating any concerns and confirming the techniques and equipment used are standard and appropriate for your needs. Finally, though site visits are important, virtual site visits have been gaining popularity as a suitable alternative.

iii. Confirm the accuracy of your products. Whether you are qualifying the production of a complex formulation from your secondary media supplier or a handful of critical raw materials, it is also important to test the products and confirm their identity. For many manufacturers, a documentation packet, such as a certificate of analysis, may be sufficient. However, depending on your requirements, a more in-depth audit of finished goods may also be necessary before qualifying a new supplier. Identity testing multiple lots of a medium formulation or going through individual raw materials, pulling batch records, and analyzing the documentation to confirm quality may be important to qualify your product.

iv. Confirm site-to-site equivalency. Site-to-site equivalency should be clearly demonstrated by media suppliers. Oftentimes, equivalency begins with procedures and practices around the supply chain and includes processes for quality management system alignment and harmonization, manufacturing, and equipment equivalency. Batch testing across the network should also be performed by manufacturers to confirm equivalency. Equivalency documentation or an audit may be sufficient to accept a material produced at multiple sites. Conversely, you may require multiple batches of a given product to demonstrate that the same product being manufactured at different sites performs equivalently in your process. Site visits may also be performed to confirm equivalency within a global network.

v. Confirm supply chain reliability. Though this is not strictly a necessity, when it comes to the qualification process, confirming the reliability of your new media supplier's supply chain is advisable. Evidence of a dependable supply chain should be provided upfront alongside discussions of any specifics of what will be provided. Though you may have already done this with a primary supplier, confirming with a secondary or tertiary supplier is just as important – whether they will be supplying raw materials in tandem with your primary supplier or only when the need arises.

vi. Establish transparent communication. Establishing a transparent communication system to share data is critical – from being alerted to supply updates or changes to any necessary quality documentation or paperwork. Ultimately, these systems can help keep things running on schedule and identify any potential issues.

## Do not wait until it is too late

Given the increase in global demand, it has never been more important to consider whether qualifying additional suppliers is necessary to support the uninterrupted production of your essential biopharmaceutical products. Proactively qualifying additional media suppliers ahead of a critical need can mitigate the risk of costly delays to your process – all while supporting your ability to provide life-changing therapeutics to the people who need them most.

*Michelle Ferreri, Director, Custom Products, at Thermo Fisher Scientific Biologicals and Chemicals Division.*

IN MY VIEW

# The Early Bird Gets the…

All decisions have a ripple effect throughout your cell sourcing supply chain; you must adopt a commercial mentality right from the start

When it comes to your supply chain for cell sourcing, you must embrace a commercial mindset whatever phase of development your cell or gene therapy is in. And that means starting with the end goal in mind and working in reverse. Why is this important? With the anticipated trajectory of cell and gene therapy development and approvals, you need a resilient cell sourcing infrastructure from the start, including suppliers that can meet your long-term demand.

What does this mean in practice? Let's look at each step of the supply chain in reverse starting with the patients who will receive the therapy. First of all, you need to think about your indication. The supply chain for a cell therapy treating a rare disease has far different needs than one that will be delivered to thousands of patients a year. Equally important is where the patients will be treated. Here, I'm specifically referring to the country where the therapy will be delivered. Different countries have different regulatory requirements for starting material collection and manufacturing. If you expect your therapy to have international distribution, you need to think beyond where your initial clinical trials take place. This is particularly important for allogeneic therapies (where the same starting material may be used to create therapies for multiple patients).

Consider the following scenario. You collect starting material for your allogeneic cell bank in a manner that is compliant with FDA regulations in the US. Later, you decide you want to distribute your therapy in Australia. The US and Australia have different regulations when it comes to donor screening and product testing for use as allogeneic cellular source material. The differing regulations could render your FDA-only compliant material ineligible in Australia.

You can avoid this by thinking about distribution — and varying global regulations — from the start.

Next, what type of cells will you use as your therapy starting material? This decision impacts how you transport the material. Some cell types are very sensitive to cryopreservation so fresh shipments are necessary, but regardless of method (cryopreserved or fresh), you need to keep an eye on your vendor and make sure they know what they are doing when it comes to moving time-sensitive starting material or cell therapies around the globe. Numerous obstacles can stand in the way of a product delivery – from weather delays to a global pandemic… You need to make sure your vendor is up to the job.

The decisions you make upfront, such as fresh versus cryo, will also impact which apheresis centers can collect for your therapy. Different centers have different cell processing capabilities. And that's also true for capabilities beyond cryopreservation, which is why you need to determine the requirements for your protocol as early as possible; not doing so will cost you development time — and your ability to scale up collections quickly.

Finally, for allogeneic cell therapies, you must know the donor attributes that are critical to the safety and efficacy of the end product as you develop a cell bank that can meet the needs of future patients once your therapy is commercially approved. The more requirements you put on donor characteristics, the larger your donor pool needs to be. Each donor attribute eliminates some portion of the donor population – and the size of the donor pool you need may surprise you. Therefore, it is essential to ensure that the supplier you select to provide allogeneic starting material has a donor pool large enough to meet your needs –especially as you scale.

I worked with our team on an analysis of frequency data for different genetic types within our donor registry to learn the starting pool size needed for 10 qualified HLA-matched donors for a therapy. In the case of the fiftieth most common HLA genotype for donors who self-reported being Hispanic or Latino (which may not seem common but is out of 462,000 genotypes), the donor pool would need to be over 600,000. And, that's before taking other demographics, such as age or sex, into account.

I hope I've persuaded you of the extreme importance of keeping future commercial scale in mind. By adopting a commercial mindset, you can think about your potential needs from a clinical and commercial standpoint from the very beginning. And that's the mindset you need to help set your therapy up for success.

*Joy Aho is the Senior Product Manager at Be The Match BioTherapies.*

## Manage the Relationship

Outsourcing partnerships aim to reduce costs and improve efficiencies, but they can rapidly fall apart if you overlook the human elements.

Outsourcing certain services to competent business partners is often essential to securing value in drug development. The idea behind outsourcing is to reduce costs and increase efficiency by hiring experts who can do the job in less time, with less costs, and to a high standard of quality. It sounds straightforward, but management conflicts and mistrust in the relationship – commonly encountered in outsourcing partnerships – can counteract these goals. Relationship management is incredibly important in the outsourcing relationship and I believe that the industry must learn to set adequate performance metrics that not only reflect milestone achievements within a set timeframe, but further extend to measure the quality of the work in terms of issue management and efficiency.

According to Jean Toth-Allen, "Quality is characterized by the ability to effectively and efficiently answer the intended question about the benefits and risks of a medical product (therapeutic or diagnostic) procedure, while ensuring protection of human subjects" (1). Quality is the main goal in our industry. Quality is constantly at risk during drug development and when conducting clinical trials, whether managed in-house or outsourced. However, there are methods and techniques that can address these risks – and these should be agreed upon at the start of a contract services relationship. In particular, teams need to be supported in dealing with the real-life challenges and issues that emerge during the course of the relationship. I specialize in clinical trials – here, the human element is vital. All issues in clinical trials are usually directly or indirectly related to human interaction. Unfortunately, I find that this element is often neglected and left to the individuals managing the contracts to attend to without sufficient support. These individuals may not have any experience in relationship management, or may be ill resourced and overworked (increasingly common in today's economical environment), which leads to relationship management falling between the cracks. This major deficiency must be addressed at both the sponsor and service provider ends. Long-term strategic partnerships seem to better deal with relationship management aspects because of the commitment and mutual risk sharing. But not all companies are able to form (and sometimes do not require) long-term relationships.

Outsourcing, whether short or long term, must be seen as a relationship between human beings that do not always share the same values, culture, visions, objectives, and practices. One party fills the other's gap, but for the piece to truly fit the puzzle, the various differences need to be thoroughly identified, discussed and aligned. Falling short in giving the human element of the relationship due attention and care will inevitably lead to delays, inconsistencies, and relationship failure, which will damage the outcome in one way or another.

The industry is not aligned on vendor management expectations outside of deliverables and milestone definitions. In my view, we need an industry tool that addresses and defines the key aspects of the sponsor/contractor relationship required for success. Ideally, such a tool would include clearly defined issue resolution scenarios and escalation paths for CRO performance problems (vendor managers must be involved and trained accordingly). A strong structure must also be in place to encourage a shift in mindset related to vendor oversight – namely, a solid multiple level governance system. In addition, sponsor in-house teams must be trained on managing outsourcing partners on a cooperation level rather than just focusing on deliverables and timelines. The overall aim is to educate companies about the important role that human factors play in the success or failure of outsourcing.

*Muna Kugler is Global Strategic Sourcing Manager, Idorsia Pharmaceuticals, Switzerland.*

REFERENCES AVAILABLE ONLINE

FEATURE

# So, You Want to Become a CDMO…

Looking to pivot your business model to a CDMO service offering? Here's what to keep in mind.

The CDMO industry is fragmented with a vast number of companies occupying broad positions. CDMOs offer an array of services to help innovators accelerate products to market and assist in drug development – whether in the manufacture of drug substances or the formulation of drug products. In between these broad lines of division, there are numerous other disciplines, such as analysis, and other specialized services. Some companies market themselves purely on their niche capabilities, offering discrete and transactional services; others look to provide integrated services and collaborative development partnerships, effectively acting as extensions to the innovator's in-house team. No matter the nature of the company and the services it offers, the focus of a CDMO is to be customer-orientated and to deliver the best possible outcomes.

For an innovator company, the focus of R&D is science driven: discovering new chemical entities (NCEs) to target a disease and delivering treatment in the most efficacious way. Resources are centered on internal scientific excellence; business targets are set internally on project milestones and delivering the product portfolio.

The core competencies of a CDMO must be broader than that of an R&D company, whose value and unique selling points lie in invention and innovation. A CDMO must have the ability to take a molecule and, irrespective of disease target, develop and progress it towards becoming a treatment. The journey will be unique for each molecule, but the experience of other projects, and a wide range of cross-

functional skills offered by a CDMO, are crucial for the successful development of a drug product.

## Why become a CDMO?

The rewards and benefits of being a CDMO can be viewed in different ways. From a business point of view, the risk profile to the business is very different compared to an R&D company spending money on internal programs. For smaller companies, potentially with a limited number of promising candidates, the need for one of them to be successful determines the entire future of the company. And the number of successful projects in this industry, as we all know, is not as great as the number of projects that fail. By being a CDMO, the ability to work with a broad range of clients and having a diverse revenue stream reduces a company's financial exposure.

Additionally, there are personal benefits and rewards. For example, scientists working in a CDMO environment have the opportunity to broaden their experiences by progressing a number of projects with various therapeutic indications. Science provides the opportunity to be creative, and working on diverse projects is a very different experience and role than working on a single project for a prolonged period of time. A CDMO's strength is in the motivation and knowledge of its scientists; and the greater exposure they get in solving challenges and overcoming problems, the more experience they gain for future projects.

The satisfaction that can be achieved as a company that is part of a successful drug launch is also a factor that cannot be overlooked or overemphasized. As a CDMO, working on projects at various stages throughout their development, and to enable a molecule to become a treatment, is highly motivational for all staff. Success breeds success, and so, as the number of products launched increases that have been worked on by a CDMO, there is a sense of pride that comes with having a positive impact on a broader patient population. This not only enhances the reputation of a CDMO but increases its appeal to innovators.

But how do you, as an innovator company, change your business strategy to become a CDMO? And what are the differences that you must make during the transition? What should your main priorities be and how will you measure success?

The most important consideration is understanding what needs to stay the same. The same excellence in science and focus towards what is important does not change, and there will always be a patient at the end of every project. There will be a customer contract in place – but the final customer and ultimate goal will always be to meet patients' needs.

It is vital that you keep scientific excellence at the core of your business: talent, expertise and experience is what attracts customers to working with partners. In my experience, this the most important selling point for any CDMO: mediocre services do not cut it.

From that core, the individual layers of service, procedures and values can be built up to create an offering. Some will be similar to undertaking internal R&D, but others are very different. You need to weave all of these layers together to create a positive "customer experience" that allows you to differentiate your company within the market.

## Deciding on your structure

A good first step is to define the CDMO process and the company structure; roles and responsibilities should be well defined, so it is clear who is accountable for each step. The expectations of "what good looks like" need to be clarified, and a feedback mechanism should be established to assess progress in a transparent and honest way – in fact, this is crucial given the importance of customer service in a CDMO business model.

Put simply, the CDMO end-to-end process can be split into six distinct phases: i) customer engagement (pre-quote), ii) quoting, iii) ready to execute, iv) project execution, v) project close out, and vi) customer feedback. By going through this cycle multiple times with

a continuous improvement mind-set – and based on a foundation of quality and regulatory compliance – you'll soon have the foundations for your service provision. A CDMO also obviously needs a business development team to engage with potential customers, but operationally, the company needs to be in a position to be marketed effectively; you need the capability to handle multiple (and likely diverse) projects simultaneously – each to the highest standards. In other words, your internal processes need to be fit for purpose so that you can please your customers.

To ensure quality and delivery, you'll need to establish a way of working that is standardized but agile enough to respond to

challenges. In the CDMO world, no two projects are identical. The overall product development approach and processes are well-established in our industry, and governed by long-established regulatory requirements for quality, safety and efficacy of the product. And that does not change in the CDMO environment. What's different? The nuances of interpretation of customer requirements. Each customer may also have their own best practices that can potentially increase complexity. As a CDMO develops and matures, you'll need to have a continued focus on simplification, balancing standard ways of working with adapting to any bespoke needs of a project. You must be able to provide timely and transparent feedback to customers that can let them make the right go/no-go decisions.

## Adapting to the customer

My experience in working within the CDMO space has taught me that it is important to act as an extension of your customers; that's how customers should feel when working with a service company. And though it may sound obvious, for a company changing from a research-led ethos to an external service provider, it can be challenging to adjust to the customer service mindset! Communication – the basis of your relationship with customers – will be one of your most important skills. You must ensure there is unambiguous alignment about the scope of work being requested, you need to be proactive in providing solutions to development challenges (which there will be – I assure you of that!), and you'll have to be responsive, flexible, and available – all while safeguarding the foundation of the company as a contract provider so that the business continues to be stable in the future.

Clear communication brings trust and openness. As a CDMO working on different projects – and in some cases on projects in closely-aligned areas – a clear policy on confidentiality will be paramount; it should be mandated in all employee training and education, and reinforced through everyday working practices. There will be challenging situations. And, at times, there may be difficult conversations to be had with your customer about a project. Again, you must be clear and honest in these discussions. And then you need to mobilize resources rapidly to minimize any disruption to your customer's project plan. You will probably need to think outside of the box and believe a solution is possible.

In a CDMO organization, everyone is a salesperson irrespective of their role; for every customer, every moment and every touch point matters – with whomever they interact. I've seen many occasions where a project's success is defined by technical teams from both sides share insights and solutions that are credible and achievable, demonstrating the CDMO's expertise.

For innovators transitioning into CDMOs, enabling regulatory success of projects may be one of the more familiar areas in which to provide assistance to customers. As an innovator, you'll already have experience in developing products and navigating the regulatory landscape; as a CDMO, you'll have the opportunity to anticipate, determine, and recommend strategies to customers less-versed in the journey, which is very rewarding. Every customer will have differing levels of need, but having the depth of expertise to challenge as appropriate and to suggest alternate paths is important.

## Staying ahead

When choosing CDMOs, companies often look for investment in terms of both innovative technologies and scientific talent. Innovators want to see CDMOs looking forward, anticipating the next trends in their area of specialism. Looking at new equipment and technologies is the easier of the two; you just buy what you need. Your in-house experts, however, will be absolutely core to your business. Indeed, knowledge and scientific talent is the true capital investment, so knowledge retention and creating an environment for career growth in a changing paradigm will be key to the success of your business.

The strength of scientific talent lies in the ability to extrapolate experience and expertise to something new – to harness scientific curiosity for creative problem solving. And it creates huge amounts of value for a CDMO. After all, CDMO scientists are exposed to a much more diverse range of molecules, indications, and technology, which feeds their imagination – but they are also driven by the need to find solutions within a target timeline to deliver the target product profile. Being on someone else's clock creates a different perspective and urgency at times, and for some scientists this is a big step (and change!). Appropriate management and support is vital to ensure the transition can be made successfully – you don't want to lose talent…

While making the transformation, continue to review your processes and practices, and evolve to the current market demands. (Sidenote: Changing your business model a few months before the start of a global pandemic is not ideal – try to avoid that if you can!). A CDMO always needs an answer to "What do we do about this – and how do we get to yes?" The importance of this cannot be understated. Today, the need to adapt and adjust has become both a necessity and a strength during these extraordinary times.

Leadership drives the company. And for success to lead to growth and longevity, you'll need transparent, actionable key performance indicators to ensure accountability with a continuous improvement mindset.

In the highly competitive CDMO industry, I have long held the belief that only excellence is tolerated.

*Sharon Johnson is Executive Vice President for Delivery Managementat Vectura.*

DEPARTMENT

# Supply Chains for Advanced Therapies

We asked the field's greatest minds: "What improvements do we need to see in cell and gene supply chains?"

Miguel Forte of Bone Therapeutics says:
*"Tech and talent – you can't have just one."*

The supply chain is the route by which well characterized and functional cell and gene therapy products reach patients. It plays host to products ranging from very challenging (and now mostly outdated) single-patient, autologous therapies to large-scale cryopreserved allogeneic products for multiple patients. In all cases, three aspects remain critical for a successful supply chain – technology, process control, and readiness to manage the unforeseen.

We continue to see great developments in the technologies that enable the supply chain, but improvements are still needed. These include wider and less stringent cryopreservation requirements with the possibility of reduced necessity for lower temperatures and increased flexibility with local and point-of-care storage options.

Tight control and management of the supply chain process is vital for the quality of the product, and a general readiness to manage exceptional and urgent unforeseen circumstances remains critical. Well adapted processes and suitable operator talent are still necessary assets for a successful supply chain. It should work smoothly and mechanically but enable quick reactions to inevitable surprises.

In the near-future, more patient bed-side manufacturing technologies will be considered and developed and "micro supply chain" options will be needed. This area will certainly see growth.

Overall, it is always about the interface between the technology and talent and experience of the operators. We will need to develop both.

Joy Aho of Be the Match BioTherapies says:
*"It starts at the start."*

With the continual growth in the development of allogeneic cell and gene therapies, the sourcing of allogeneic cellular starting material is becoming an increasingly critical component of the cell and gene therapy supply chain. As these therapies continue to move into later clinical phases and approach commercial approval, there are many important considerations to ensure scalability and consistency in supply.

The industry needs a better understanding of optimal donor characteristics for these emerging cell and gene therapies. Many groups rely on a small number of "super donors" – smaller sets of donors whose donated material has been used successfully in manufacturing – to support their starting material needs. This is unlikely to provide a long-term solution for later clinical phases and into commercial approval, especially for the large indications being targeted by many of these therapies. For the sake of future scalability, it will be important to better understand and more easily test for these characteristics upfront.

Greater clarity and consistency in starting material testing needs would also greatly benefit current supply chains. For developers planning to distribute their therapies globally, differing regulatory requirements across the globe have led to complex testing needs for cellular starting material. In general, as seen with autologous therapies, finding areas to standardize around starting material collection without impacting critical quality attributes for a particular therapy will be essential to ensure scalability for manufacturing allogeneic therapies and access to the patients in need.

Bill Vincent of Genezen says:
*"Brace for impact."*

When predicting challenges that the cell and gene therapy industry would face in 2022, it was no surprise that many drug developers consistently identified supply chain issues as a big area of concern. In the years leading up to 2020, the global viral vector manufacturing capacity had expanded in response to increased demand for these advancing technologies. The onset of the COVID-19 pandemic then magnified the supply burden that manifested.

Increased demand for vaccine manufacturing supplies was seen worldwide, in parallel with supply transport and delivery disruptions. Additional issues stemmed from the reduced availability of raw materials, like fetal bovine serum (FBS), used in the upstream processing of many biologics.

With some items subject to a one-year lead time, developers and manufacturers came under further pressure to increase stockpiles or find alternative suppliers to prevent disruption. This challenge persists to date and is particularly prominent for projects at clinical phases, where speed is of the utmost importance for success.

Although those in the cell and gene industry are hopeful that supply issues will be resolved with the world coming out of COVID "lockdown," the impact of future global events will never be easy to predict – from natural disasters to new pandemics or conflicts. However, we can foresee that continued high demand for COVID-19 vaccines and growth in the cell and gene market will only add to future supply challenges.

To overcome these issues, a growing burden will be on suppliers to invest in manufacturing capacity and offset this bottleneck. By making all the necessary technical, quality, and safety information easily accessible, as well as being proactive in identifying potential solutions, suppliers could further ease the difficulties biopharma manufacturers face. If major suppliers do not adapt quickly, we can expect alternative competitor vendors to fill the void.

Jessica Madigan of BIOVECTRA says:
*"Prioritize plasmids."*

Perhaps the biggest supply issue for cell and gene therapies is a lack of reliable sources of GMP-grade plasmid DNA. The supply of pDNA – and, therefore, mRNA – is constrained by both manufacturing issues and short supply of consumables and starting materials. These constraints result in at least year-long lead times for pDNA made under GMP conditions.

The industry should adopt established manufacturing platforms that have been through the drug approval process for cGMP plasmid production. For example, plasmid manufacturing has not been designed and scaled to create a reproducible, reliable process for both alkaline lysis and purification. We need a large-scale manufacturing process that can lyse cells as quickly as possible to avoid the buildup of impurities. An optimized lyzing process would lead to higher yields by eliminating the need for additional purification steps with a goal of delivering shorter timelines and reduced manufacturing costs. Since the technology for plasmids and vectors is continuously changing, cGMP manufacturing will need to be flexible and supported by a supply chain and production capacity that can keep pace.

We need to see additional suppliers in the overall supply chain for critical starting materials and consumables to meet the demand of the many manufacturers who have invested in single use fermenters, only to be challenged by months-long lead times for filters, bioreactor bags, and diafiltration cassettes. Another good example of necessary improvements are the anion exchange resins used during plasmid purification to remove host cell DNA, RNA, and proteins. Currently, the best options for high specificity at large scale are low-capacity chromatography resins, requiring large columns and slow cycling times. The industry needs to develop higher capacity ion exchange resins to make purification more reproducible and decrease lead times.

These advances should help relieve the strain on supply that currently bottlenecks the cell and gene therapy market.

DEPARTMENT

# When Outsourcing Goes Astray

"The best-laid schemes o'mice an' men" often go awry – and that can apply to your outsourcing plans. What do you do if your contractor ends up in the regulators' bad books?

Outsourcing is well entrenched in pharma's business models and is a relationship that dates back to the very beginning of the pharma industry. Though some raw materials can be manufactured in house, the vast majority has always been purchased from third parties. And in the last 30 years there has been a surge in the use of outsourcing for all sorts of activities other than ingredients supply. Today, anything and everything can be outsourced including research, development, clinical trials, manufacturing, supply chain, regulatory affairs, business development and more. In fact, I have worked as a consultant at companies where there are barely any permanent staff members. Even the oversight of the contract manufacturing organization (CMO) was outsourced to a third party (me!).

Outsourcing is so common that regulatory bodies have written it into their regulations and guidances (1), and there are conferences and entire magazines dedicated to the topic. I too have spoken and written about outsourcing on numerous occasions. In general, most people focus on the themes of best practice and ensuring success (2-4), and almost all articles assume that if you plan well then everything will go well. But when does life ever go according to plan? As Robert Burns wrote in 'To the Mouse' – "The best laid schemes o'mice an' men, gang aft a-gley", which, when translated and simplified, means that even the best plans often go awry. In other words, you should always assume that something will go wrong – and have a Plan B.

What can go wrong? There are basically two types of outsourcing failures. The first type of failure is choosing the wrong contractor – perhaps incorrect assumptions were made, or the data collected were incomplete or wrong (see 'The CMO Checklist'). The second type of failure occurs after the work begins. Usually it is because something changes, such as a loss of expertise from the contractor company due to staff attrition. In other cases, regulatory incidents may occur that change a "good" CMO into a less than stellar one. When something goes wrong in your outsourcing provider, it is usually out of your control – so much so that you may not learn about them until it's too late. The key is to be constantly aware of the situation and to look for telltale signs. With any luck, due diligence activities will flag up warnings and either eliminate the organization from consideration, or at least allow you to put in place a mechanism to prevent those warning signs from becoming a problem. Sometimes everything goes smoothly and it is only later that problems manifest themselves. But with lessons learned, you will be able modify your due diligence system to prevent its recurrence next time.

## Learning from mistakes

I've worked in or with a number of organizations and mistakes do happen. For example, I was part of a company that had a very rich pipeline and we wanted to develop more products than we had staff or facilities for, so we decided to outsource the development of one of the products. We performed due diligence with a new player in the space and they impressed in all meetings and presentations. Upper management had clearly done development before and the facilities were new with new staff. The contract was signed and we were off! Within a few months, however, it became clear that the development team at the bench were totally inexperienced. And we were locked into a contract where we were paying them to develop our product – but teaching them how to do it, at our expense. We were lucky that the contract was well written and so after the minimal period we exited. Clearly, the due diligence in the site visit left much to be desired.

*"Sometimes everything goes smoothly and it is only later that problems manifest themselves."*

In another example, a newly approved product looked like it would take off, but we had limited capacity and needed extra – and fast. We identified a potential CMO and approached them. The "expensive suits" in upper management met with their equivalents at the potential CMO. (Note that no real hands-on technical people were involved – a mistake). The suits returned with a declaration that technology transfer, process validation, manufacturing of qualification batches, amendments to the filing, and an inspection could all be completed, in time for us to get the product onto the market with the second source within 18 months.

Our technical people already knew that the CMO did not run processes the same way that we did and that technology transfer is not that easy (we had already done it from clinical to the commercial facility). The internal estimate was closer to 36 months. Management's response was that we needed to be "Can do" people. We met them half way and became "Can try" people. Eventually, everything was completed in 35 months. In this case, not selecting the right people for the CMO visit and accepting an unrealistic timeline really thwarted our chances of bringing on a second source in the time we needed. As the saying goes, "if it sounds too good to be true, it probably is". But first you have to have the right knowledge to recognize a pipedream.

## Beware of change

In my next example, both due diligence and contracts worked well. Many people believe that if due diligence is done well and that

contracts and quality agreements are well executed, then nothing can go wrong. But I work with clients who can testify first hand that this is not true.

Sometimes something changes. Perhaps a company is bought out and the staff realize that they have a new owner whose strategy is not aligned. Or the parent company could fall on hard financial times followed by belt tightening. Sometimes, the parent company changes its business model and the CMO is suddenly not the main thrust of the company. What happens then? Firstly, funding decreases, so the company refocuses how they operate. Staff are laid off. And, it is often the "wrong" people that are let go. In many cases "institutional knowledge" disappears overnight and the quality systems and compliance suffer – and the downward spiral ensues. This does not necessarily manifest immediately. It may take several inspections or incidents to surface. But once they are in the regulatory bad books, it takes a lot of effort to extricate themselves.

Earlier in my career, we had outsourced a component of one of our kits and were dependent on a well-known supplier. As a quality professional, I tracked the performance of the CMO routinely. Everything was going well until I called my counterpart at the plant only to find that the phone had been disconnected. I tried the plant manager and found the same thing. I was immediately concerned. Such reorganization is often symptomatic of a major issue in the company. And I was right – the CMO had been subjected to a long inspection by the FDA and it had not gone well. Although our Quality Agreement called for notification in the case of an inspection, we were not notified. The inspection resulted in a severe warning letter that took a few years to lift. And we were thankful that we had a second supplier.

## Damage control

How can we prevent such problems from happening – or at least control the damage? In most cases, the deviation of a contractor is not, contrary to belief, something that happens overnight. It takes time to get into regulators' bad books. It can seem to happen abruptly but that usually because subtle warning signs have been missed.

The key to success in outsourcing is to be attentive to the status of your contractor. Your CMO may be a standalone company or a division of a bigger one. You need to keep tabs on the owner and look for signs of change throughout the company, such as not meeting financial quarterly targets, failure to get approval of a new drug, excessive recalls (even from other divisions) and bad inspections at other sites. In other words, look for the stability and health of the parent and all the siblings. You should also look for changes in business direction that may signal a change in focus or divestiture of assets.

At the more local level, your ongoing communication with the CMO can tell you a lot. A change in attention to detail or an unusually slow response to a question is a red flag. And changes in heads of quality or manufacturing may signal some issues at the plant – these people are usually the first to go when a significant issue occurs.

Of course, the obvious place to look for signs of potential problems in your contractor is the results of the routine annual GMP audit. Most people know to look at the audit – and it can certainly bring previously unnoticed issues to light, such as a rash of repeat deviations, or a higher than normal lot rejection rate. However, many problems are easily recognized and can be picked up much sooner than waiting for the annual audit by tracking company performance using key performance indicators.

## Plan B

When outsourcing does go awry, you'll be pleased that you've already carefully considered Plan B, such as a second source to fall back on. If you don't have a second source then it's worth qualifying one fast, just in case. One of my main tasks with clients is to line up a second source. To this end, networking and sharing experience is very important, while of course respecting confidentiality. When one of my clients has a problem with a CMO, I routinely ask colleagues in my LinkedIn network for their recommendations for replacement CMOs. And I also ask who we should stay away from. In most cases, my client is not the only person working with that particular CMO and I do sometimes find our CMO on a "not recommended" list. Mostly, I choose safely by going for the regular players on the "recommended" list, but sometimes a new player emerges. But you should remember that these lists can be rapidly changeable and what is recommended today may not be recommended tomorrow.

If you do run into trouble, you should try to work with your CMO to resolve the issue, but you also need to be realistic. How much can you pressure a CMO to change their ways? If you command 50 percent or more of their work or revenue, then you might be able to influence the outcome. But if you are a small player with 10 percent then your chances are small. Remember that the contractor is caught between a rock and a hard place since they will have many clients. But all is not lost. If you know some of the other clients, you might be able to work together to leverage your combined influence. And ultimately this should benefit the CMO too by keeping them out of regulators' bad books. But don't forget to plan for a plan B.

*Peter Calcott is President of Calcott Consulting LLC, CA, USA.*

REFERENCES AVAILABLE ONLINE

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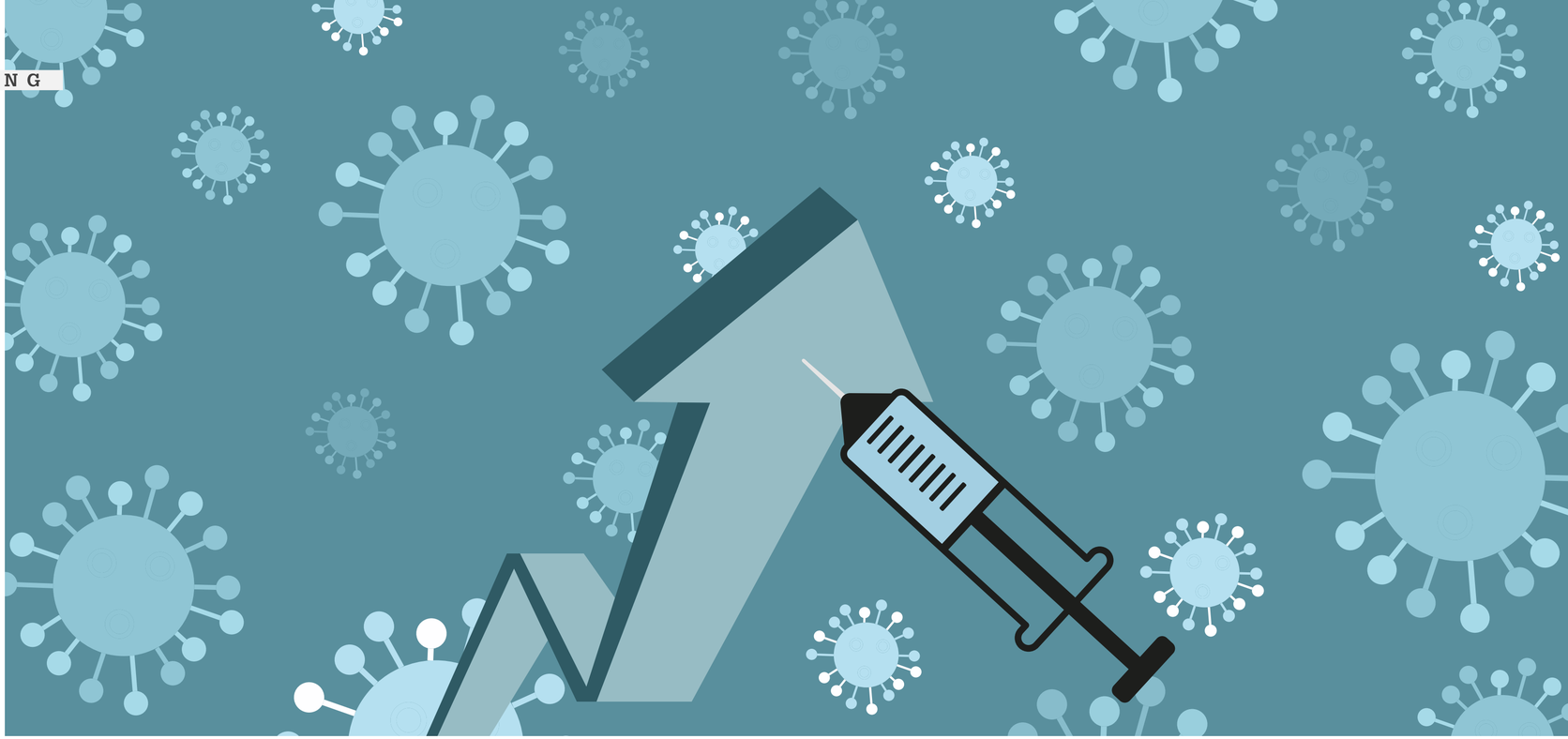
DEPARTMENT

# Trend Forecasting

As we enter a new year, pharmaceutical companies will undoubtedly be looking ahead. But how will the events of the past two years influence future aspirations? We asked three companies for their views.



## Digitizing Supply

*Karan Singh, Managing Director at ACG, and John Carey, ACG Engineering*

Exposing considerable weaknesses in supply chains across the globe, the pandemic has compelled the pharma and healthcare sectors to move from a "just-in-time" approach to a "just-in-case" approach. In 2022 and beyond, we will see a rise in new delivery models built on a resilient value chain by leveraging the benefits of digitalization. But how can this be achieved? Smart, connected, and intelligent systems based on Industry 4.0 technologies will play a key role in these efforts.

Manufacturers will likely look to automation, data analytics, machine learning, and the Internet of Things (IoT) to address existing challenges. Smart factories that can use real-time data analytics and machine learning to reduce costs, improve quality, and reduce capacity constraints will be essential. Developments in predictive analytics will also make it possible for manufacturers to draw on vast pools of data, including information on resource consumption, machine performance, and storage conditions on factory floors to troubleshoot problems, optimize processes, and boost productivity.

Another prominent trend for 2022 is the move towards creating larger batch sizes. Larger batches mean companies can be more efficient by reducing costs associated with quality control and validation.

As we look to the future, the value of digital technologies is increasingly hard to ignore – especially for companies that are keen to stay ahead of (or even keep up with) the rest of the market.

## Outsourcing on the Rise

*Jim Hall, President at Lifecore Biomedical*

Over the last two years, 75 percent of new drug development in small-to-midsize pharma has been outsourced. There is also a particular demand for vial and syringe manufacturing capacity to meet the appetite for injectable products, which make up around 55 percent of the drug development pipeline and 44 percent of all NDA approvals.

The CDMO industry is arguably designed to be nimble with a model that allows for adaptation. We can invest holistically and plan capacity against the growth of companies' diverse development pipelines. But that means CDMOs must take a proactive approach to trend assessment – and then be willing to commit to investing in the necessary capabilities to meet the market's emerging needs. Investments must do more than cover process capabilities; it's also crucial to support the growth of expertise to build on existing systems to enable more long-term strategic partnerships with customers rather than focusing on transactional service provision.

These are complex times. Being able to adapt ahead of the curve will be the difference between the winners and losers. Creating flexible work schedules, identifying second and third sources of supply for critical components, and investing in multiple facilities will all be key if CDMO's want to please their customers and help the industry navigate today's tricky landscape.

## New Opportunities on the Horizon?

*Paul Smaltz, Head of Pharma, Roquette Pharma Solutions*

The COVID-19 crisis has challenged global pharma supply chains, with many companies forced to take remedial action to meet fluctuating consumer demand. At the very beginning of the crisis, for example, consumers began stockpiling supplies, which led to a huge rise in demand for over-the-counter (OTC) products, before quickly declining again. And then, when healthcare experts started experimenting with possible cures, we saw increased demand for specific drugs, until they were deemed ineffective. Meanwhile, we witnessed an increase in demand for new vaccines as manufacturers raced to find an effective solution against COVID-19.

Companies must be aware of how they can overcome supply-related challenges moving forward. We managed to overcome such issues mainly through alternative logistical measures and building stockpiles. For instance, in cases where we experienced problems with sea freight, we switched to air freight. This had wider cost implications of course, but it was necessary. Now, many global organizations are re-assessing drug manufacturing supply chains to reduce the risk of supply interruptions in the future.

What lies ahead now as some normality returns? The pandemic has reinforced healthcare as a major governmental priority across the world and we are seeing pick-up of new drug projects. In particular, pharmaceutical companies are capitalizing on the demand for specialized dosage forms, including pediatric/geriatric-friendly formats that melt in your mouth, and controlled-release formulations to help patients adhere to their medication regiment.

The expiration of blockbuster drug patents in 2022 could also be interesting for the development of the excipients market too – ushering in a new wave of product innovation amongst generic drug manufacturers looking to produce their own versions of once groundbreaking medicines and treatments.

SITTING DOWN WITH

# Changing People's Perspectives

Sitting Down With… Akhil Ravi, CEO of Aurigene Pharmaceutical Services, a Dr. Reddy's Laboratories company, India

**How did you join Dr. Reddy's?**

I studied business before joining McKinsey and Company, where I worked across numerous sectors, including healthcare and other allied sectors. Dr. Reddy's is considered one of the most respected companies in Hyderabad – the city I grew up and lived in. After a few years as a consultant, I had the opportunity to go to Dr. Reddy's, but I had to think about it for a few years!

Eventually, I took the plunge. I knew a few colleagues at Dr. Reddy's, so I spoke with them about the culture, which is very important to me. I worked with a lot of promoter-driven companies in my time at McKinsey and I didn't enjoy that culture. But Dr. Reddy's has a very professional management team as well as a good reputation in India and globally. Since joining, I've worked in many different roles, including manufacturing, strategy for the active ingredients' division, and leading sales in Europe for that division.

**Why do you think working in the pharma industry is so rewarding?**

Everyone in the pharma industry has always found the work rewarding, but I think the reason for that has really hit home in the last three years – thanks to the impact we've collectively had across the entire chain of tackling the pandemic – from prevention to cure. We've gained control of the pandemic and we can now prevent severe COVID-19 disease.

When I first joined pharma, I found it a little frustrating because the pace was slow and conservative. You need to talk to many people to even move an inch! I think the pandemic has taught us that we can move faster while still making high-quality, safe medicines.

Many things came together during the pandemic; the industry was leveraging data sets and computational power; governments were prepared to play their part, and supply chains were adjusted to suit the vaccine roll out. Overall, it's really changed the way people and biotechs think about R&D and how we bring medicines to market.

**How have you settled into the role of Aurigene's CEO?**

It's been a very interesting journey so far with a lot of new opportunities and exposure to diverse areas. To be honest, I was a little surprised when I got the job! I was on vacation last year when I got a call along the lines of: "Hey, you know how this person left? Do you want the role?" There were then many conversations, but gradually I became more comfortable with the idea of leading Aurigene services, which is a contract research, development, and manufacturing subsidiary of Dr. Reddy's.

My division is focused on using cutting-edge science to partner with other companies and bring new medicines to patients. I've had to learn quickly. I've been looking at what works well, and what we need to change. And I've been focused on getting the whole team to see the same vision. We have a great opportunity to bring new medicines to the world through our partners and it's important to ensure that friction in our way is removed.

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# Digital Transformation and the Biopharma Supply Chains

How platform-agnostic eData enables manufacturers to see more, understand more, and drive more reliable logistical and analytical outcomes from their supplier network.

*By Stephen Wing, Head of Analytical & Logistical Services, Process Solutions, Merck*

The biopharma industry's traditional approach to managing supply chain complexity is not adequately meeting the current and future needs of this growing industry.

Receiving, identifying, testing, and validating raw materials and other manufacturing components taxes logistical teams, who are often faced with collecting supplier data from PDFs, emails, and paper records – labor-intensive work that can add weeks to the lot-release process.

Meanwhile, analytics and process engineering teams face their own challenges. With infrastructure built on the shifting sands of traditional, manual data collection, monitoring critical process steps to prevent out-of-spec situations or looking back to trace the root cause of a quality issue is not always easy or possible.

Exacerbating these internal drivers of supply and production headaches is the external environment: geopolitical conflicts, natural disasters, and unprecedented pandemics have thrown global supplier networks into turbulence.

Now more than ever, this situation must change – not only because existing approaches are failing manufacturers, but because the future of medicine depends on our industry's ability to evolve. Personalized therapies, for example, offer hope to those facing previously incurable disease, but they introduce novel manufacturing challenges related to traceability, scalability, and speed. To transform hope into reality and embrace a new era of therapeutic potential, our industry must adopt equally novel solutions for these challenges. It must transform.

## Digital solutions for supply chain insecurity

Behind its reputation as an industry buzzword, the concept of "digital transformation" carries a very real and vital promise. Our industry saw this promise in action during the COVID-19 pandemic, when manufacturers relied on digital solutions to run decentralized trials, accelerate regulatory approvals, and rapidly deliver lifesaving vaccines to a global population. This experience accelerated a shift away from time-intensive processes and toward automated, data-driven manufacturing. Amidst this rapid transformation, though, there's one crucial component still lagging behind: the biopharma supply chain. Chronic bottlenecks caused by raw data collection, manual data entry, and the multiple challenges of antiquated systems are preventing today's manufacturers from unlocking the full potential of digital transformation.

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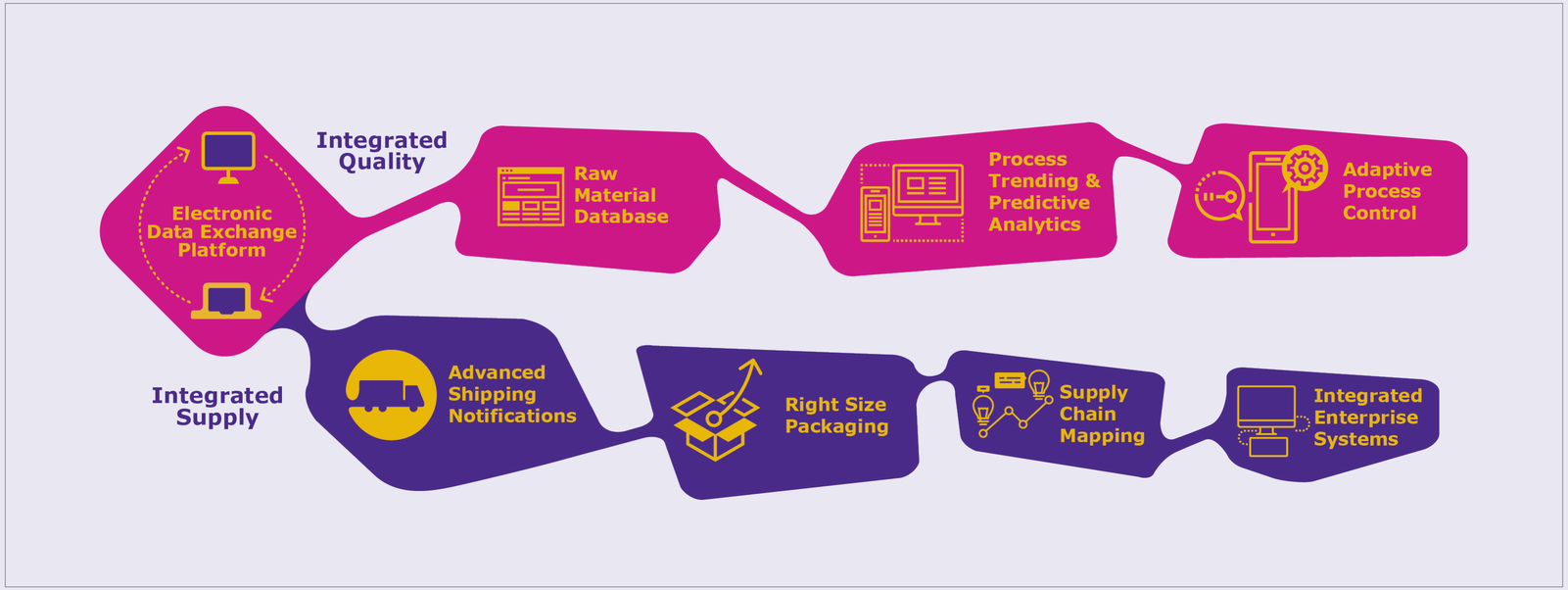
*"The goal is to bring the vision of bioprocessing 4.0 to supply chain logistics and analysis, giving manufacturers the transparency they expect from suppliers in this age of rapid digital transformation."*




Even before the pandemic, we initiated development of a standardized platform designed to modernize the supplier-customer relationship. The goal is to bring the vision of bioprocessing 4.0 to supply chain logistics and analysis, giving manufacturers the transparency they expect from suppliers in this age of rapid digital transformation. That level of transparency is the key to a flexible, fast-moving, and future-ready manufacturing operation, capable of sustained resilience against the behavior of an unpredictable global supply chain.

What does this future of digitally enabled supply chain transparency actually look like in practice?

- Manufacturers control a single, harmonized data lake.
- Through a secure cloud interface, suppliers push platform-agnostic electronic data (eData) to the manufacturer's data lake. This signals the end of juggling multiple logins for supplier-side portals, playing phone tag with supplier sales teams, or searching email attachments for paper-based records.
- User groups across the manufacturing lifecycle—from production planners to data scientists—have secure, persona-based access to this wealth of integrated and contextualized supplier eData, including certifications, genealogy information, and in-process insights.
- This eData flows up to an ecosystem of logistical, operational, and enterprise-level data, eventually enabling advanced predictive analytics and AI-driven self-correcting process control.

We call this solution the eMERGE™ Program. It's optimized to proactively exchange eData with our customers and enhance their knowledge management approach without ever requiring them to leave their established data ecosystem – and it's poised to digitally transform logistical and analytical processes.

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# Celebrate the Best and Fix the Rest

An exchange of perspectives on supply chain challenges between Sebastian Moritz (supply chain expert and principal at the economic consultancy TWS Partners of London) and Darren Verlenden (Head of Process Solutions at Merck).

**COVID-19 tested biopharma. There were successes and challenges. As an industry, what did we learn? What did we do right? What must change?**

*Moritz:* We saw a phenomenal response to COVID-19. It was the biggest vaccination campaign in history. The industry supported a massive ramp up. COVID-19 was great proof of the industry's capabilities and dedication, but it also exposed a need to reshape the future of biopharma.

*Verlenden:* We saw incredible collaboration and increased transparency across the industry. Companies that might not typically work together banded together for the greater good; for example, large biopharma originators working with CDMOs, integrators and technology partners to increase capacity. We worked closely with government agencies and saw a greater level of transparency from our customers. This collaborative approach broke down barriers and enabled us to drive critical prioritization to serve our customers, and ultimately, patients across the world.

*Moritz:* The public sector helped remove impediments to a holistic end-to-end initiative – spanning R&D, clinical trials, production, cold-chain distribution and mass administration. Ample, almost unlimited, funding was helpful. There were, of course, disruptions to supply chain resources, capacity, infrastructure and offtake. We must handle these better in future emergencies.

*Verlenden:* COVID-19 challenged our industry in unprecedented ways. But with great challenge comes great opportunity. I witnessed incredible tenacity from colleagues who showed commitment to our customers in the face of unimaginable adversities. There are many examples – from our frontline workers in our China manufacturing facilities who volunteered to sleep at our plant to keep our operations up and running, to our technical and quality teams equipping our global sites with smart glasses to enable virtual customer audits, technical support and training. Throughout the pandemic, we redeployed R&D efforts to assist in our manufacturing output and made R&D an essential workforce.

**Are there lessons we can learn about a supply chain under such extreme stress?**

*Moritz:* The most critical lesson is the importance of aligned interests and incentives for all players. It doesn't matter which industry, responsiveness is severely hampered if each player at every stage of the supply chain only acts when the next contract with their customer is signed, or an accurate volume forecast is available.

*Sebastian Moritz*

*Verlenden:* COVID-19 exposed the vulnerability of supply chain and distribution networks, whether it be due to tariffs, lockdowns, or a lack of capacity in major shipping ports. To mitigate these supply disruptions, it is critical to have a robust and geographically diverse supply chain. COVID-19 also taught us the importance of having a strong prioritization plan to serve critical needs. Transparency (both good and bad) between customers and suppliers is also key. While there will be challenges, it's critical to have open communication so that actions can be put in place to mitigate them, and realistic outcomes can be established.

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*Moritz:* The good question to ask today, in the aftermath, is how a single entrepreneur in charge of the entire supply chain might view the challenge of expanding biopharma's capacity and capabilities globally. Such a person would look at the bottlenecks at different levels of the supply chain and roadblocks to collaboration and how to address them.

**What can biopharma consider by looking into the experiences of other industries?**

*Moritz:* It's very case specific. Automotive and aerospace can provide examples of where it is necessary, for example, to provide longer-term commitments and visibility in the supply chain. Aerospace has extremely long lead times and its supply relationships reflect this. The automotive industry found it necessary to step in to support its component suppliers by entering into direct negotiations with the semiconductor industry.

*Verlenden:* Use of digitalization to speed up processes and gain better transparency was a transformation in many industries. Biopharma has begun to make these adjustments, as well. For example, there are services available for supply chain mapping across raw materials to help monitor and predict potential disruptions.

*Moritz:* While this trend is not specific to biopharma, new technologies make it possible to better monitor complex supply chains – even in real time. You know at any point in time which feedstocks have been produced, where they are, and whether a problem has occurred somewhere in the chain. This allows for faster and more targeted interventions. But only if you have accurate, relevant data, which requires incentives for all to share what they know.

**What are drivers of digitally transformative trends in biopharma supply resilience?**

*Verlenden:* Even before the pandemic, the biopharma market trends were evolving from new modalities to cost pressures and speed in new plant deployments. Some of the key business drivers of digital transformation trends are increased production speed, quality robustness, agility, and manufacturing cost reduction. These can result in more efficient, resilient, flexible, and intensified manufacturing to help enable the facility of the future.

*Moritz:* Most advanced analytics provide users with a rear-view mirror plus can generate predictive models. This is potentially powerful in supplying pharma. Again, the main issue for players in biopharma will be addressing incentives. Not every player has an incentive to share information in a way that would ultimately benefit everyone in the industry.

*Verlenden:* For the products that we supply to the market, we work with our partners to reshape standards for electronic data exchange between suppliers and customers to streamline processes, improve manufacturing forecasts, and improve the reliability of supply.

**Can individual companies solve these big challenges in the supply chain?**

*Moritz:* Not when acting alone. The resources a single player would expend to solve the problem are so enormous that the cost-benefit ratio would discourage the player from doing it at all. A challenge is creating benefits for each player in a holistic optimization of the supply chain. That is how the industry can be ready for the next pandemic and be able to support the next generation of treatments in clinical trials.

*Darren Verlenden*

*"From an economic perspective, it will be crucial that the contributions from each player are proportionate to the benefits they receive – otherwise they'll stay out of it."*

*Verlenden:* Due to the interdependencies that exist, it will take the entire ecosystem to drive change. But individual companies can start asking the right questions. The pandemic brought out the best in a lot of organizations at the same time it exposed deficiencies. Defining new standards and driving innovation together is the way ahead. During the pandemic, companies joined forces to develop, manufacture and distribute vaccines with great success. There is a lot of good to come from future collaboration.

**To what extent are players in the industry prepared to improve sharing of data?**

*Moritz:* Everyone recognizes the benefit of it, no doubt. But, in the worst case, everyone is just waiting for others to solve the problem. It therefore requires leadership, and a cross-industry initiative to rethink the collaboration framework. From an economic perspective, it will be crucial that the contributions from each player are proportionate to the benefits they receive – otherwise they'll stay out of it.

*Verlenden:* We are working with customers in piloting eData exchange. There are also established industry consortiums that are working collectively to help align and connect the right individuals toward driving some of these holistic outcomes. Leaders are stepping up. Consensus is emerging, but this is an undertaking we need to tackle together.

**Is the BioPharma manufacturing base expanding fast enough to meet needs in the coming decades?**

*Verlenden:* In order to meet future needs, geographic diversity of supply chain networks will be crucial. We have bolstered our supply by increasing our global capacity and capabilities through capital deployment and regionalization to support the growing demand for life-saving and life-enhancing therapies.

*Moritz:* A big trend is more local production of vaccines and drugs. The industry has painfully experienced how challenging it can be to secure local capacities and capabilities. If biopharma tries to solve this issue in each and every country individually, we require enormous efforts. Also, here other industries hint at potential solutions like global and scalable manufacturing solutions.

**What makes you excited about the future of biopharma?**

*Verlenden:* This industry continues to reach new milestones that were previously considered unachievable, and the latest COVID-19 dynamic is an excellent example. But as pioneers in the industry continue to reshape modern medicine and transform the path from treatments to cures to help serve patients around the globe – that's what makes me most excited.

*Moritz:* As a game theorist, I always say, "If you can't win the game, change the game." The pandemic has shown that the old way of working in the biopharma supply chain does not work anymore, and the COVID-induced "whatever it takes" approach is probably not sustainable. Therefore, we have the unique opportunity to rethink an entire industry – what could be more exciting than that?

FIND OUT MORE

## ABOUT OUR CONVERSATIONALISTS

*Darren Verlenden is the Head of Process Solutions Merck. He has 28 years of experience with multifunctional roles in pharma and biopharma. Darren joined Merck in 2010 and has served in roles of increasing diversity, complexity and responsibility in the process development and commercial areas. Verlenden is obsessed with creating customer value, and he is passionate about improving the way biopharma delivers value to its patients through product and digital technologies.*

*Sebastian Moritz is a supply chain expert and managing partner at the economic consultancy TWS Partners. After studying applied game theory, Moritz obtained his PhD in supply chain management on the topic of supplier selection in high-risk scenarios. With offices in Munich, Berlin, London and Utrecht, TWS Partners is the only global company focused on applying the Nobel Prize-winning field of game theory to improve business performance.*

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