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A practical guide to **scaling up in pharma and biopharma**

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Executive Summary

It's becoming difficult to remember a time when COVID-19 wasn't the dominant theme in our personal and professional lives, and its impact will be felt for years to come. Like nothing any of us have ever experienced in our lifetimes, this pandemic has shaken healthcare systems, international relations and economies to the core – and shone a light on the pharmaceutical supply chain.

As questions about the availability of PPE and common generic drugs used to treat COVID raged, the race to develop a safe and effective vaccine began in earnest. With government backing, teams have been working to timescales never seen before and the stakes couldn't be higher.

One of the biggest questions has been around capacity, specifically, how a company can scale up production to deliver the required number of doses without impacting other areas of production.

Anyone who has scaled up previously will be well-aware of the commercial risks involved – and those who are developing a vaccine right now cannot depend on government funding and advance orders to mitigate them all. Their reputation and contracts with existing customers and governments are on the line too, not to mention how they are perceived by the public.

Expansion is now on the cards for US pharma companies, regardless of whether they are developing the vaccine, and the debate about planning and capacity has come to the fore.

Lessons will be learned from this pandemic and it will no doubt prompt production planners to review and bolster their planning and scheduling processes, if they weren't doing so already. In particular, they'll be thinking about how best to use digital technologies to optimize resources, collaborate with colleagues around the world and have confidence in their decision-making.

Whatever your company's reasons for expansion, our practical guide will show you how to scale up production and future-proof your manufacturing operations.

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Drug manufacturing today

US pharmaceuticals and biopharmaceuticals companies lead the way on drug development and pioneer the complex manufacturing processes required to get these new treatments to market.

Quality employees, infrastructure, favorable tax environments and access to capital are among the reasons why the country ranks so highly – but it is also important to note the market's maturity is no barrier to future growth.[1]

One of the most important growth areas is biopharma manufacturing, which according to one article, delivers the 'cutting-edge medicines developed hand-in-glove within the R&D ecosystem, providing high-wage STEM jobs, a growing source of exports and sustained investment and productivity gains.'[2]

The author goes on to say that 'process innovations are as important as product innovations', and manufacturers 'constantly research, develop and adopt new technologies and processes, such as continuous manufacturing, high-volume cell processing, and advanced purification, preservation and distribution modes.[3] But while continuous manufacturing has been adopted in some solid dose facilities, experts stress there are still a number of challenges to overcome if it is to be applied to biopharma.[4]

We're finding that growing numbers of industry professionals recognize that poor scheduling methods are a barrier to growth. Planners know this but so too do the senior management teams also pushing for change. When working at the same capacity, it is possible (albeit difficult) to schedule hundreds of tasks in a specific sequence using spreadsheets. But as soon as you start to increase capacity, or introduce new products, traditional planning and scheduling methods are no longer fit-for-purpose.

This is important given the shifts taking place in the industry at the moment. As companies move away from 'blockbuster drugs for large numbers of patients to more focused products targeting smaller populations' facilities will have to be capable of producing more than one treatment.[5]

Demand for new therapies is only going to accelerate over the coming years – driven by an ageing population and associated comorbidities in the US and other developed nations.

Beyond their immediate efforts to tackle COVID-19, drug companies must continue to invest in new therapies for cancer, diabetes, heart disease and other conditions and the risks for some are high. While the median cost of developing a new drug between 2009 and 2018 stood at $985million, the median for oncology and immuno-modulatory drugs was $2.8billion.[6]

Drug companies know they must deliver innovative new treatments that will gain FDA approval, improve outcomes for patients and deliver returns for their investors.

Furthermore, with the debate over drug pricing shows no sign of abating, manufacturers have to protect their margins. Smart technology, including machine learning, could improve the effectiveness and lower the cost of clinical trials – but they'll have to invest in lean and data-driven production processes too. When it comes to pioneering new treatments, no company can afford delays in getting them to market, caused by inefficient labor and equipment utilization.

[1] Source: www.news-medical.net/news/20191206/US-pharmaceutical-industry-continues-to-shine-according-to-CPhI-2019-Annual-Report.aspx

[2] Source: catalyst.phrma.org/new-report-advanced-manufacturing-powering-innovative-biopharmaceuticals

[3] Source: Ibid

[4] Source: https://ispe.org/pharmaceutical-engineering/ispeak/facility-challenges-developing-continuous-process-based-biopharma-products

[5] Source: www.scienceboard.net/index.aspx?sec=sup&sub=can&pag=dis&ItemID=536

[6] Source: JAMA, cited in www.biopharmadive.com/news/new-drug-cost-research-development-market-jama-study

Lessons from COVID-19

COVID-19 brought to light many of the issues that have been simmering away in the industry for a long time. It's raised questions about the resilience of pharmaceutical supply chains, the location of manufacturing facilities and their capacity to deliver vaccines and treatments for the population.

Just before the global health crisis erupted, FDA was told that while the US leads the way on drug discovery and development (thanks to advances in biomedical research), manufacturing has declined. Around 30% of API (active pharmaceutical ingredient) manufacturing facilities are now located in India and China, compared with 28% in the US – something that can be attributed to lower labor and utilities costs, fewer regulations and proximity to raw materials and intermediary suppliers.[7]

At the height of the pandemic, there were fears that tensions between the US and China would escalate, leading to essential drug supplies being cut off. This reignited the debate on whether manufacturing should be insourced.[8] Geopolitics notwithstanding, the threat of shortages also loomed when India reduced its exports due to factory shutdowns.

Yet it is testament to the strength of the pharmaceuticals industry that it responded so quickly to the crisis. In recent months, we've seen 'industry operations leaders [rally] to enable the supply of key medicines across borders, manage workforce safety, and handle evolving government restrictions all while beginning to prepare for new vaccines and therapeutics.'[9]

Those who demonstrated agility and innovative thinking during the crisis are now well-placed to make the most of opportunities that lie ahead – particularly in new drug development and meeting the healthcare needs of an ageing population.

Whether they are scaling up to deliver a COVID-19 vaccine or treatment, or moving into new markets, firms will need to focus their efforts across five key areas, discussed in more detail below.

Speed

Whereas it might take a decade or more to get a vaccine to market normally, the timescale for a COVID-19 vaccine is expected to be around 18 months. It would be impossible to work like this all the time. For a start, the government's Operation Warp Speed initiative is enabling firms to accelerate the development and production process in order to deliver 300million doses of the vaccine, but this kind of support would not normally be available.

This does not mean bypassing steps in the traditional timeline (and risking safety and effectiveness) but undertaking them simultaneously, for example, manufacturing at an industrial scale 'well before the demonstration of vaccine efficacy and safety.'[10]

Recently, Pfizer and BioNTech were awarded $1.95 billion[11] to develop a vaccine, while Regeneron received a $450million[12] to deliver an antibody cocktail to treat and prevent COVID-19. Government backing may reduce the financial risk – but companies are under immense pressure to get products out quickly and cannot afford any inefficiencies to hold them back. After all, politicians, the public and healthcare professionals are all watching intently.

The circumstances firms now find themselves working in are exceptional, though it will likely push some to adopt new ways of working.

Last year, FDA Commissioner Scott Gottlieb said efforts to streamline product development 'can be frustrated by legacy business models that discourage collaboration and data sharing, and the adoption of disruptive technologies that make clinical research more effective.'13 This, he suggests, results in missed opportunities to lower costs and validate new drugs.

Any investment made in speeding up clinical trials should be mirrored in the manufacturing process too. Given the costs involved in development, there is a clear incentive to maximize every resource.

[7] Source: www.fda.gov/news-events/congressional-testimony/safeguarding-pharmaceutical-supply-chains-global-economy-10302019

[8] Source: www.independent.co.uk/news/world/americas/us-politics/coronavirus-china-us-drugs-trump-rubio-china-virus-xinhua-hell-epidemic-a9400811.html

[9] Source: www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/pharma-operations-the-path-to-recovery-and-the-next-normal

[10] Source: www.hhs.gov/about/news/2020/06/16/fact-sheet-explaining-operation-warp-speed.html

[11] Source: www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-agreement-us-government-600

[12] Source: investor.regeneron.com/news-releases/news-release-details/regeneron-announces-manufacturing-and-supply-agreement-barda-and

Capacity

Increasing capacity is non-negotiable for anyone working on a vaccine project. There are plenty of barriers to overcome but governments, healthcare providers and the wider public will take a dim view of any company that does not tackle them successfully.

As a result, manufacturers have been increasing their capacity and production. They are stepping into the unknown, with no clear idea when these products will be ready, nor how long they will take to manufacture, but they are driven by the tremendous sense of urgency.

Moreover, the US government has signalled its determination to ensure drug stocks do not run low during this pandemic, or another in the future. It recently commissioned Virginia-based Phlow Corporation to increase production of both APIs and generic drugs as part of a $354million deal.[14]

There are going to be few, if any, occasions when capacity has to increase so dramatically, and it's not yet clear whether insourcing will continue beyond the pandemic. But investments are being made in new manufacturing facilities all the time, like the $470million site Eli Lilly is planning at North Carolina's Research Triangle Park.[15]

As well as building new facilities, firms are also increasing capacity at their existing sites, both in the US and in nations where they operate, and making process improvements that drive up productivity.

Collaboration

COVID-19 projects are closely-guarded but we are seeing strategic partnerships – oftentimes between small-scale companies developing treatments and larger players with more manufacturing capacity. Not long ago, the government sanctioned information sharing with drug-makers outside the US in order to scale up capacity of antibody treatments.[16]

Collaboration is vital in pharma manufacturing today, whether teams are working in different companies, territories or sites within the US. It makes sense to share resources and expertise with like-minded organizations as well as internal teams, especially when working on novel drugs.

Location and costs

We've seen how supply chain disruption could quickly threaten the availability of life-saving drugs. This is why, according to one report, the focus is moving away from landed costs towards the costs associated with location risk. As a result of the pandemic, we may see manufacturing move to lower-risk countries or closer to end markets.[17]

However, one of the strengths of the pharma industry is that it is truly global. Joint agreements will enable companies to collaborate and scale up production capacity quickly, wherever they are located.

Digital technology

The way medicines are developed, manufactured and delivered is also changing thanks to advances in technology. Wearables, for instance, could improve the speed and accuracy of clinical trials by monitoring participants remotely using 'real-time, real-world' data.

One of the biggest differences between the COVID-19 trials and any other is that there are legions of volunteers willing to test a potential vaccine. This should create a valuable data set that speeds up the approvals process.

Digital technology is also transforming production processes, enabling planners and senior managers to perform detailed what-if analysis before manufacturing begins – whether it be the impact of taking on new orders, or even building a new facility. While the task can be performed using spreadsheets, advanced planning and scheduling software allows you to model different scenarios quickly and accurately. Later, we'll see how one biopharmaceutical manufacturer is on track to save time, reduce costs and increase the number of batches produced using advanced planning and scheduling.

[13] Source: www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-new-strategies-modernize-clinical-trials-advance

[14] Source: www.hhs.gov/about/news/2020/05/19/hhs-industry-partners-expand-us-based-pharmaceutical-manufacturing-COVID-19-response.html

[15] Source: www.thepharmaletter.com/article/lilly-to-invest-more-than-470-million-in-new-manufacturing-facility

[16] Source: www.reuters.com/article/us-health-coronavirus-pharmaceuticals/u-s-clears-way-for-drugmakers-to-share-COVID-antibody-capacity-idUSKCN24O30E

[17] Source: www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/pharma-operations-the-path-to-recovery-and-the-next-normal

[18] Source: www.nsmedicaldevices.com/news/wearable-tech-industry-healthcare-pharma

Build confidence in your planning and scheduling processes

As companies expand their range of new and innovative therapies, planners need to have a clear understanding of the complex processes involved in large-scale production and working to a compressed timescale they are not used to.

Whereas the focus might previously have been on yield and quality, COVID-19 is now pushing manufacturers to significantly increase capacity without compromising quality. The world has changed, almost overnight, and the push to deliver a COVID-19 vaccine means companies are faced with rapidly reorganizing their schedules and processes.

The big challenge is to schedule the hundreds of tasks involved in producing a vaccine – or any biopharma product – to make the most of capacity, without causing bottlenecks. Production teams who already use Six Sigma or lean methodologies are well-placed to make the kind of process improvements necessary for growth.

In response to COVID-19, small-scale 'boutique' pharma firms that invest heavily in R&D are working with bigger ones with more manufacturing capacity. Strategic partnerships, like the one between Oxford Biomedica and the Vaccines Manufacturing and Innovation Centre, require collaboration and continued innovation on both sides.

Once a COVID-19 vaccine and treatments are licenced for production, manufacturers will need to move quickly to produce a blockbuster while still honoring the agreements they have with governments around the world.

Their first step is to understand what capacity is available at sites in the US, Europe and elsewhere. Although drug recipes are always tightly-guarded, few would have the capacity to produce the required dose of vaccine on a global scale. Indeed, AstraZeneca is working with the Serum Institute of India (SII) to deliver one billion doses of the Oxford vaccine to low and middle income countries.[19]

Again, collaboration and innovation are key, as we don't yet know how long it will take to produce a single batch – it might be six weeks, it might be thirty-six.

An advanced planning and scheduling (APS) system assists with both day-to-day planning and capacity planning on a large-scale. It also supports what-if? analysis, so planners can see how taking on new contracts would impact their existing commitments at each site.

It is worth remembering that while few would have capacity to meet global demand, it is not uncommon for pharmaceuticals manufacturers to have unused capacity. As an analogy, a highway may only run at full capacity during rush-hour and holiday season – while it stays relatively empty at other times, planners must consider the maximum number of vehicles it needs to hold.

Planners need full visibility across their facility and other sites around the world, wherever they are working, in order to create the master schedule. There is no point loading all tasks into the schedule on a Monday morning putting a strain on resources and potentially causing bottlenecks. Similarly, there's no point machinery or people sitting around idle. Where necessary, advanced planning helps with social distancing, since you can schedule tasks so that staff do not come into close contact with each other.

[19] Source: www.astrazeneca.com/media-centre/articles/2020/astrazeneca-takes-next-steps-towards-broad-and-equitable-access-to-oxford-universitys-potential-covid-19-vaccine.html

What does good planning and scheduling look like?

Good planning means everyone is working together to deliver the desired outcome, wherever they are, following this four-step approach:

Co-ordinate:

Understand what resources and capacity you have and use automated scheduling to optimize every task.

Communicate:

A single live schedule, visible to all authorized personnel, ensures everyone knows what tasks need to be actioned and all updates are communicated. It also makes reporting to senior managers quicker, easier and more consistent.

Collaborate:

By spending less time on manual scheduling, experts are freed up to add more value to work and collaborate closely with colleagues in their production team and at other sites.

Co-operate:

All this promotes a spirit of co-operation, with everyone working together to achieve the same desired outcomes.

The way medicines are developed, manufactured and delivered is also changing thanks to advances in technology. Wearables, for instance, could improve the speed and accuracy of clinical trials by monitoring participants remotely using ‘real-time, real-world’ data.

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Engineering growth at one biopharmaceuticals plant

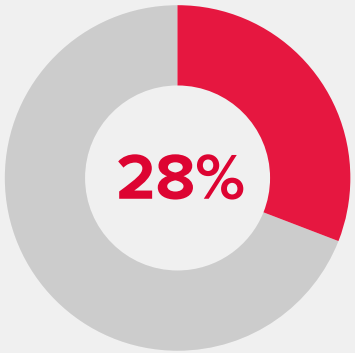
Capacity is a priority for any pharmaceutical company, regardless of whether they are working on COVID-19 contracts. Inefficiencies in planning and scheduling mean that companies will struggle to increase their output, and therefore revenue and profitability, unless they optimize their processes.

This was certainly the case for one of our customers, a major biopharmaceuticals manufacturer based in North Carolina. It had realized that a system of spreadsheets and flip boards meant it lost valuable time – for example, when staff had to decontaminate every time they left and re-entered a sterile area to check a chart. Moreover, tasks like machine maintenance were not included in the schedule, which could potentially disrupt production.

It is important to remember that even the smallest inefficiencies add up over time. At this particular company, shop floor employees were spending several hours on manual scheduling every week and it was difficult to adapt the schedule if changes occurred.

But an independent study showed that the planning team would see significant time savings and be able to make evidence-based decisions if they moved to an automated web-based schedule. A single schedule, visible to all authorized personnel, could reduce decontamination and scheduling times, while improving communication across the production team and with senior managers.

The study also found that, had the production team made process improvements via APS, they could have produced 4.65% more batches last year. Now, with an APS system in place, the site has capacity to produce almost **28% more batches** in a full year. As well as putting the company on track to significantly increase revenue, data from the APS system also showed they could make major cost-savings by rescheduling the cleaning crew to work only day shifts, not 24/7.



Conclusion

While few diseases threaten the world's population in the same way that COVID-19 has done, we never know what is around the corner. Recent years have brought deadly outbreaks of Ebola, MERS, SARS, Zika – and the industry has always moved quickly in response. Even without a global pandemic, we know demand for new therapies will only increase further in the coming years.

In preparing for future challenges, pharmaceuticals companies need to have the correct knowledge and infrastructure in place from the start. As we have seen co-ordination, communication, collaboration and co-operation are key to ensuring they can work effectively and scale up quickly if necessary.

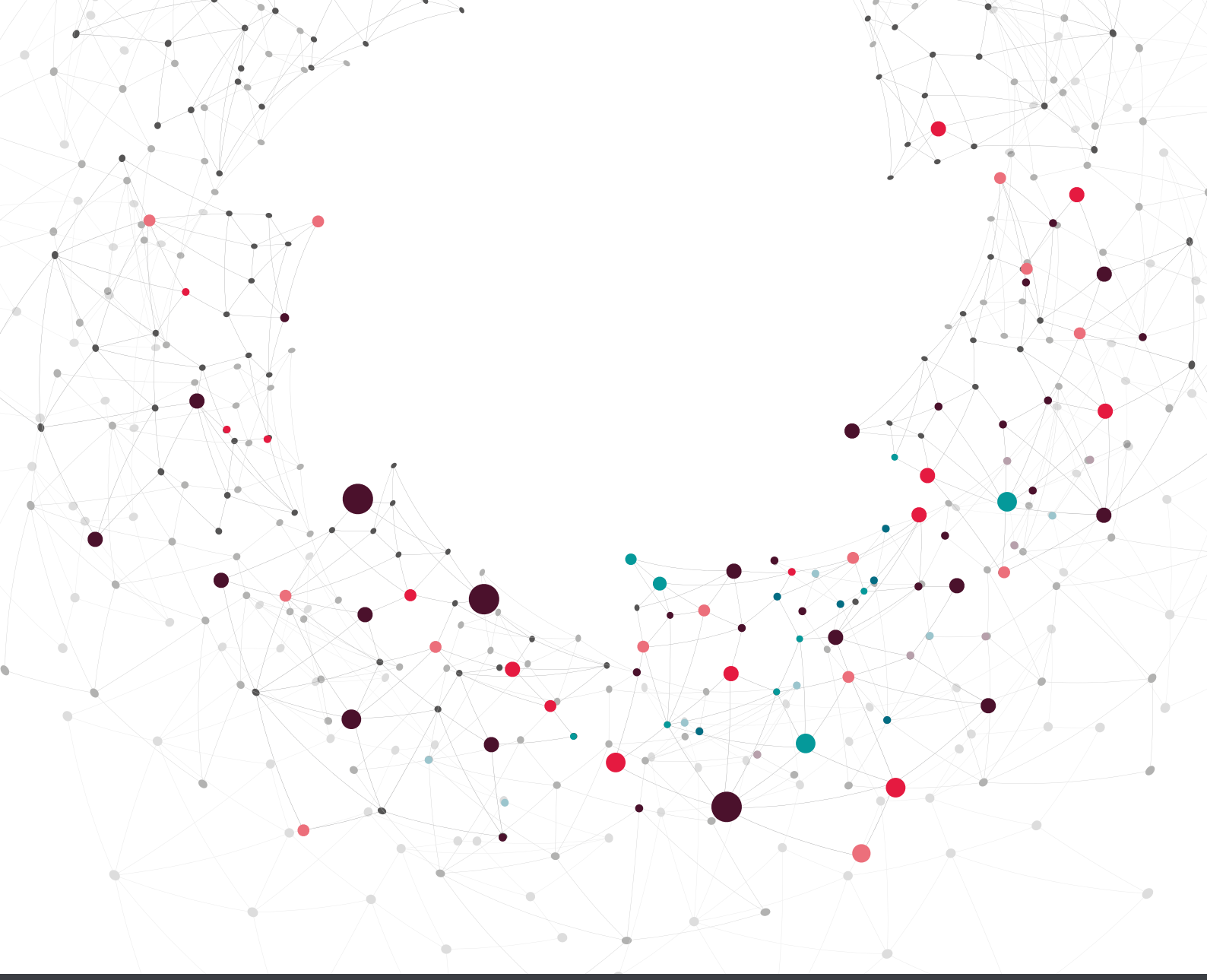
Whether you want to understand capacity at existing facilities, or one not yet built, advanced planning and scheduling methods allow you to make decisions with confidence. Technology is not designed to replace years of expertise but to remove the manual calculations, reporting and updating spreadsheets that currently take up valuable production time.

Scheduling is even more critical than before and greater efficiency not only benefits the production team. Increased savings and revenue both help to offset the high costs associated with R&D and manufacturing complex therapies, not to mention the cost of failed clinical trials and approvals.

The world is changing rapidly, and pharma companies must invest in both their manufacturing processes and drug development programs. Once a COVID vaccine is approved, the industry will be judged on how quickly it can manufacture the required doses and make them available at the right price point.

Finally, there has been heated debate about the safety of any vaccine or treatment that has been 'rushed through'. But while there may be more accelerated clinical pathways, it is important to remember that the laws do not change, and it still has to pass the same tests as any other drug. With so much investment, and so many volunteers taking part in trials, it is possible to move from development to production far more rapidly than usual and create a blueprint for scaling up manufacturing successfully in the future.

For more resources on pharma manufacturing today, click here.



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