facilitating collaboration

Strategies for Ensuring Biomanufacturing Resilience for Biologics

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There is consensus among the global health community that long-term investment in resilient biomanufacturing capacity and supply chains is needed to ensure the reliable delivery of health technologies such as vaccines, even during crisis conditions.[1]

This article is the first in a series that highlights strategies that are essential to achieving this outcome, drawn from the experience of MilliporeSigma[2] during the global pandemic response and looking forward to how governments and the private sector, including profit and not-for-profit private health actors, can most effectively work together to deliver healthcare post-pandemic. The strategies focus on vaccines, monoclonal antibodies, and new modalities manufactured by biotechnology companies and institutes.

Challenges Presented by the Pandemic

During the COVID-19 pandemic, a sudden surge in demand for equipment and material to make biologics overwhelmed biopharmaceutical supply chains.

Once vaccines were developed and financing was available for their manufacture, companies faced high demand and, in many cases, were unable to rapidly ramp up production for various reasons that included timelines to build additional manufacturing facilities, difficulty increasing staffing and training during a global crisis, and constraints on supplies of raw materials.

The lessons learned during the pandemic are now applied by companies and other stakeholders to reinforce biopharmaceutical value chains, extend manufacturing capacity across regions, improve health regulatory systems, and create the right conditions for ongoing biopharmaceutical innovation and technology diffusion. These actions aim to create sustainable development and delivery of products like vaccines, therapeutics, and diagnostics even during crises, and their effectiveness depends on ongoing investments to provide universal access to healthcare in all countries.

Pandemic preparedness is but one motivation for these efforts. Focusing on resilience is an imperative for the global health community to successfully respond to the growing demand for and production of biologics over time, which in turn increases demand all along the biopharmaceutical value chain. At the same time, geopolitical developments, market volatility, uncertainty, and the evolution of manufacturing, all must be addressed as they will place further pressure on supply chains in the coming years. The need for crisis preparedness and response adds further complexity to this landscape.

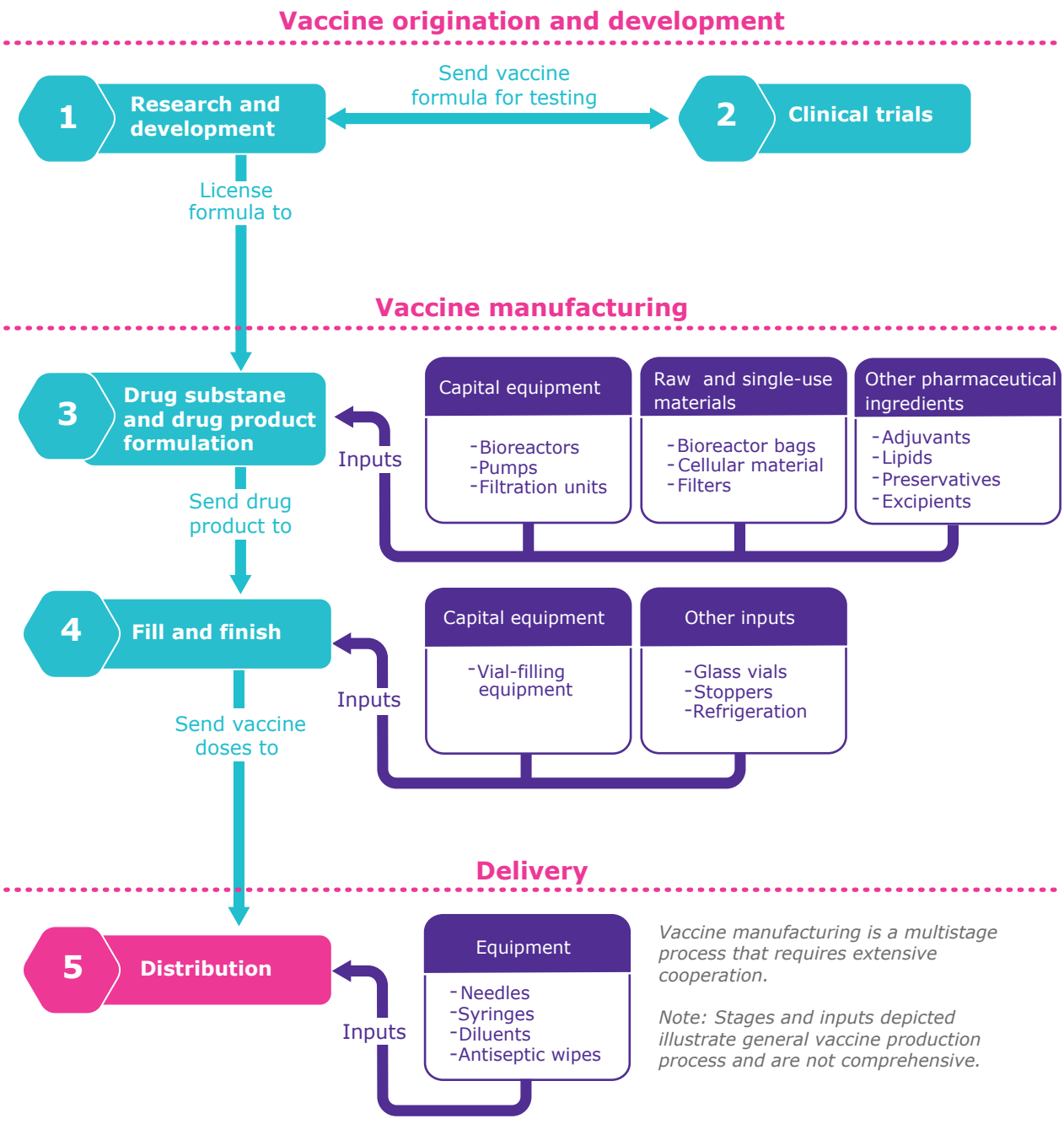
The Growing Demand for Biologics in Global Healthcare – and the Use of Backwards Integation

Biologics are increasingly central to healthcare as incomes increase and populations age. They are also more likely to be prescribed as health systems improve and the diagnosis and incidences of noncommunicable diseases rise. **The global biologics market accounted for nearly USD 294 billion in 2021 with an estimated CAGR 9.24 per cent growth between 2022-2027**.[3] Biosimilars are also experiencing explosive growth, particularly since they are relatively less expensive than originator products and thus may be more cost effective.

The global market for biosimilars is expected to grow from USD 13 billion to USD 60.8 billion from 2021 to 2027 with emerging countries, notably India and China, accounting for an increasing percentage of manufacturing.[4]

Manufacturing biologics – whether originator products, biosimilars, or vaccines – is complex and requires a high level of expertise, a multistage process, and extensive collaboration (Figure 1).

Figure 1. Stages of vaccine manufacturing[5]

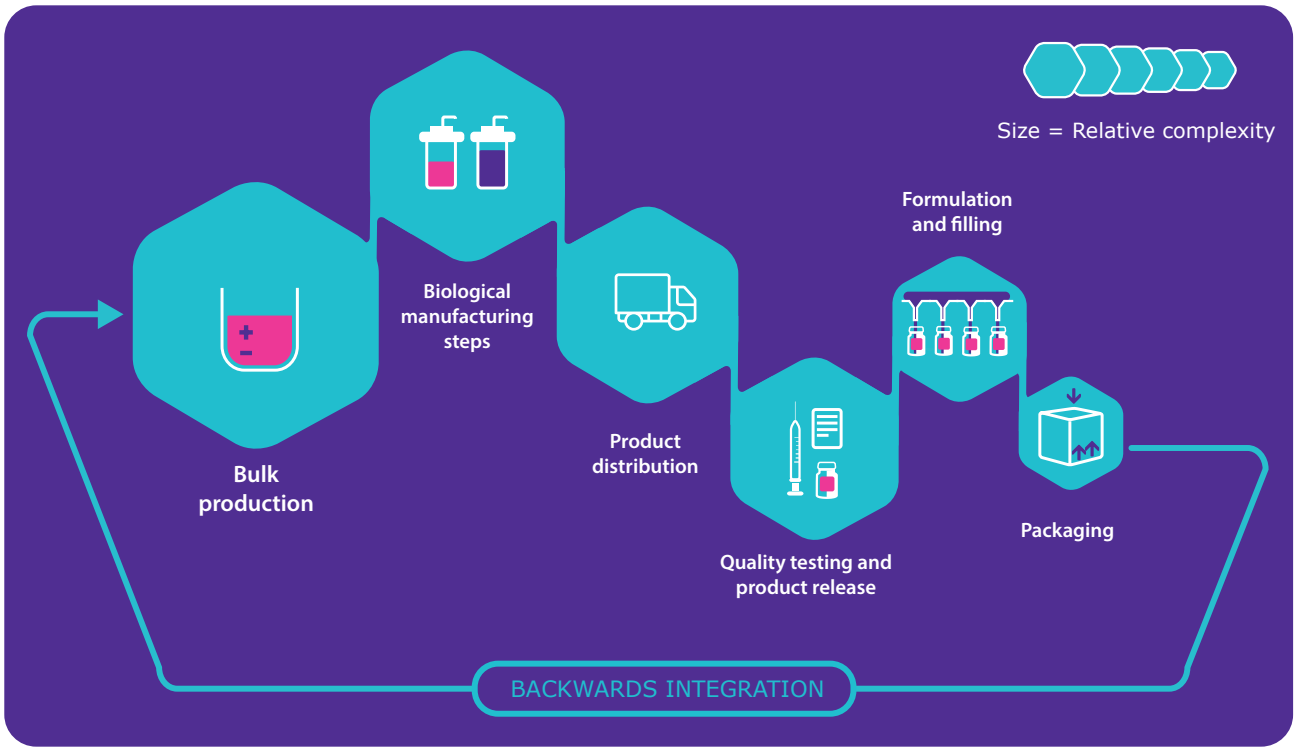


Vaccine manufacturing is a multistage process that requires extensive cooperation.

Note: Stages and inputs depicted illustrate general vaccine production process and are not comprehensive.

These products are subject to the most stringent regulatory and quality standards, in part because they are typically administered by injection. The manufacture of biologics requires several steps, and many producers enter these global value chains by completing the final stages of the process, such as packaging and distribution, or fill and finish, which is a highly technical endeavor. With the support of international technology transfer partners, many of these new entrants gain skills and expertise that enable them to move up the value chain to complete higher-value activities, in a process known as **"backwards integration"** (Figure 2). **Working side-by-side, the partners exchange know-how and build capacity over time.**

Figure 2. A schematic of the backwards integration process



The experience of Biovac, a public-private vaccine developer and manufacturer founded in 2003 in South Africa, gives a sense of how organizations move along this pathway. In 2021, Pfizer announced that Biovac would become a partner for manufacturing the Pfizer-BioNTech mRNA vaccine for distribution within the African Union.[6] Biovac had already worked with Pfizer and other international tech transfer partners, such as Sanofi Pasteur,[7] for many years, enabling them to improve their technical and scientific capacity. Biovac's collaborations included producing innovative, complex vaccines such as Pfizer's polyvalent pneumococcal vaccine, Prevenar 13. Continuing its progression via backwards integration towards the highest value activities in manufacturing, Biovac recently announced a tech transfer and licensing

deal with the non-profit International Vaccine Institute, headquartered in South Korea, to manufacture an oral cholera vaccine.[8] This project will enable the Biovac Institute to gain capacity to manufacture drug substance, a step in the vaccine manufacturing value chain that does not yet exist in Africa.

Our organization recently collaborated with the Texas Children's Hospital Center for Vaccine Development at the Baylor College of Medicine to optimize a platform for the manufacture vaccines for tropical diseases. In response to the pandemic, the optimized process was transferred to companies within the Developing Countries Vaccine Manufacturing Network (DCVMN) network located in India, Indonesia, Bangladesh, and Botswana, to adapt for SARS-CoV-2 vaccine production.

Collaboration Accelerated the Pandemic Response

By summer 2022, there were 381 recorded partnerships in the COVID-19 vaccine space, 88 per cent of which involved technology transfer.[9] These collaborations were necessary to develop vaccines and establish geographically dispersed manufacturing and distribution networks to connect biopharmaceutical value chains.

Given the complexity of vaccine development and manufacturing, it is more important than ever for vaccine manufacturers to collaborate with experienced technology providers. Such partners can provide critical support from development through manufacturing, helping to eliminate bottlenecks and accelerating production of urgently needed vaccines.[10]

The advancement of manufacturing technologies have helped accelerate and improve the global response to emerging biological threats.[11] For example, the vaccine industry has accelerated the use of single-use technologies in manufacturing to resolve biohazard and contamination risks, especially when handling live attenuated microorganisms or when aseptic processing is required. Partnerships between technology providers and vaccine developers are also setting the stage for establishment of new flexible manufacturing facilities which offer numerous benefits including decreased overall expenditure, time, and footprint, as well as accelerated production and increased flexibility. Facility construction time is also significantly reduced.

Production and distribution of vaccines can also be accelerated through public-private partnerships focused on process optimization. To provide **one example**, MilliporeSigma had been working with the Jenner Institute at Oxford University since 2018 to develop a robust, scalable manufacturing process for the adenoviral vector vaccine candidate.[12] This work intensified when the pandemic started, and the years of partnership, trial and error, and practice resulted resulted in swift development and rapid scale-up in response to the pandemic.[13]

Our organization also took part in a collaboration with Technovax and Innovative Biotech in which a scalable virus-like particles (VLP) vaccine platform was optimized for use in a production facility in Nigeria in response to the need for local production of SARS-CoV-2 vaccines. The flexibility and robustness of the platform enabled its rapid deployment to support the West African pandemic readiness program. Initial development of the VLP process began in late 2019 and by March 2020, was already adapted for production of a SARS-CoV-2 vaccine.[14]

Other forms of collaboration also accelerated the pandemic response; for instance, innovators worked closely with regulatory agencies to expedite review without sacrificing patient safety or drug product quality. Global health experts have pointed to an unprecedented level of cooperation between regulatory authorities, on the one hand, and clinical researchers, academics, large and small pharma companies, non-profit institutions, and other government agencies. They recall constant dialogue and expedited turnaround of clarification and data requests, on both sides.[15]

The Future is Collaborative

A clear takeaway from the COVID-19 pandemic is that no single company, research institute, global health organization, or other actor can do everything on its own. The pandemic stimulated a rapid innovation response from the biopharmaceutical industry. Alongside efforts from the private sector, government support in all regions was instrumental in supporting R&D for novel technologies, clinical trials, assessment of manufacturing infrastructure, de-risking investments to upgrade manufacturing capacity, and other activities that were needed for the pandemic response.

Looking to the future, engagement among government officials, industry, research institutes and universities, NGOs, and others will be needed to create resilient systems for developing and delivering biologics and other health technologies.

Be sure to watch for additional content coming soon in our series on Strategies for Securing the Supply Chain. In the next installment, we'll discuss how lessons learned during the pandemic are informing new approaches to improving supply chain resilience.

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2 MilliporeSigma Life Science is a biopharmaceutical manufacturing company providing state-of-the-art technology and services that support discovery of cutting-edge and life-saving products, process, and research. MilliporeSigma Life Science, known as MilliporeSigma in the United States, also supports companies with contract development and manufacturing, in addition to delivering products and services for mRNA development, vaccine development and manufacturing, and CRISPR-based gene editing.

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