Vaccine bioproduction: An industry in the spotlight

The global crisis related to SARS-CoV-2 infections that began in late 2019 placed the bioprocessing industry in the spotlight due to the key role it plays in the development and manufacture of safe and effective vaccines. The industry has historically contributed to (and continues to contribute to) the improvement of global health: innovating new technologies, optimizing workflows, strengthening vaccine platforms, and moving to late-stage clinical trials at record speed. Upon vaccine approval, the pressure falls on manufacturers to quickly produce the vaccine in unprecedented volumes, creating the challenge of sourcing critical process materials from reliable suppliers.

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Choose your vaccine platform

Industrial-scale manufacturing of viruses or virus-like particles is critical for multiple applications. This includes vaccines and recent therapies such as gene therapy and oncolytic virus immunotherapy. Gene therapy involves delivering a functional copy of a gene into a patient via a viral vector. Oncolytic immunotherapy involves using viral vectors—which have intrinsic or engineered tumor selectivity—to directly lyse the tumor or express genes with an anticancer effect.

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"Classical" vaccine platforms—such as those used for measles vaccinations—involve introducing the patient to either a weakened (attenuated) or killed (inactivated) version of the virus of interest. If the patient is later exposed to the viable whole virus, the immune system can readily recognize the virus and is primed to fight it. This significantly reduces or eliminates the dangerous symptoms and side-effects associated with infection.

Unlike these classical platforms, subunit vaccines require the identification of a viral component that best stimulates an immune response—the antigen—and the introduction of only this antigen to the patient, rather than the whole virus. Typically, subunit vaccines result in fewer side effects and are considered safer [1]. This platform has been successfully used for the HPV vaccine, which has the potential to eliminate or significantly reduce cervical cancer in the future. The subunit vaccine approach has been popular in the development of SARS-CoV-2 vaccines, with the spike protein of SARS-CoV-2 identified as a key target antigen for vaccine development. In 2020, the majority of SARS-CoV-2 vaccines in development were subunit vaccines [2].

A more recently developed vaccine platform—viral vectors—involves using the patient's body to produce the antigen. A genetically engineered virus (viral vector) carries the genetic material that codes for the antigen into the patient. Once it is introduced, the virus causes the patient's own cells to express the antigen. This platform eliminates the need to produce and purify viral peptides and is employed in gene therapy to deliver functional genes to patients.

Similarly, mRNA- and DNA-based vaccines involve using the patient's own cells to produce the antigen; however, genetic material is injected directly into the body rather than being introduced via a viral vector. The first mRNA vaccine authorized by the FDA for emergency use was the Pfizer-BioNTech SARS-CoV-2 vaccine. This was the first of its kind to successfully complete Phase III clinical trials and it, along with other SARS-CoV-2 vaccines, will likely pave the way for the introduction of future mRNA-based therapeutics to market [3].

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Media considerations

Different vaccine production methods have distinct cell line and media requirements, each method requiring a robust formulation to maintain productivity.

Traditionally, vaccine production media were supplemented with serum or other animal-derived components to promote cell growth and productivity [4]. However, in vaccine production processes, there has been a recent move away from using animal-derived components, in order to improve safety, increase consistency, and streamline the regulatory process [5]. A drawback to using media with serum or animal-derived substances is the potential to introduce contaminants, specifically adventitious agents, that may remain in the final product.

The importance of a strong supply of raw materials

Media manufacturers play an important role in ensuring and maintaining safety by retaining a strong and reliable supply of raw materials. Consistency is critical. Subtle changes in the vaccine production process have the potential to affect the purity, safety, and efficacy of the final product [6]. By offering serum-free and animal origin–free manufacturing options, cell culture media suppliers can produce clearly defined media that can precisely and accurately meet defined specifications, helping to ensure the safety and efficacy of the end product.

Maximizing the lifetime of a viral therapy or vaccine requires a consistent supply of raw materials. Sourcing materials that fail to meet required specifications and quality, or show high lot-to-lot variability, can lead to costly product recalls—eventually disrupting supply and impacting public health through the disruption of immunization programs.

Ensuring safety

Before vaccines or viral therapies transition to industrial manufacturing for market release, they undergo meticulous testing to ensure safety and effectiveness. Clinical evaluation of vaccine candidates can be divided into 4 stages: Preclinical, Phase I, Phase II, and Phase III. Each stage tests the safety and efficacy of the vaccine in larger and more diverse populations than the last, with the aim of reducing the likelihood of any serious adverse effects in the general population. Many vaccines will also undergo Phase IV, which are ongoing studies after the vaccine has been approved and licensed.

This process would typically take between 8 and 14 years [7]. So how have strategies like Operation Warp Speed—the U.S. government's plan to deliver 300 million doses of a safe, effective SARS-CoV-2 vaccine [8]—achieved this in a fraction of the time?

Although the clinical trials process for SARS-CoV-2 vaccines is accelerated, this does not mean that the rigorous safety testing is being rushed or left incomplete. Rather, stages are being allowed to run concurrently and evaluation of SARS-CoV-2 vaccines is being prioritized, which is dramatically reducing the time from development to approval. Further, governments around the world are investing millions of dollars in manufacturing and distribution capacity for approved vaccines [8].

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A global solution for a global challenge

Speed-to-market is a priority once vaccines and viral therapies have been approved, especially during a global crisis. Conventional vaccine production could take between 6 and 9 years [7], though during times of crisis this timeline is dramatically condensed. This leaves vaccine manufacturers in a precarious position. They need to get things right the first time. The global emergency related to SARS-CoV-2 infections has highlighted the pressure on suppliers to meet unprecedented demand and reduce the risk to public health from delays and failures.

A global crisis requires a global solution and suppliers that can deliver on a global scale. For wide-scale vaccine production, a consistent supply of process products—particularly large volumes of cell culture media—is required. In order to meet the global demand, media manufacturers will need support from a global network of harmonized media manufacturing facilities, able to produce the same quality of product across all sites. Media manufacturers must be able to deliver this consistency globally, not only during process development but also long after the product has reached the market, to prevent disruption to the vaccine supply.

Manufacturers with redundancy in capabilities, including excess staff, manufacturing capacity, and raw materials, will find they can support a surge in demand brought on by global crises now and in the future. Further, with concerns over a diminishing raw materials supply [9], manufacturers with a safety stock of raw materials and strong supply agreements—primary, secondary, and tertiary—will be in a uniquely advantageous position. At all times—but particularly during times of crisis—manufacturers require a strong supply network to prevent holdups in an already expedited process.

Without a doubt, this is a defining moment for the vaccine production landscape, with consistency and collaboration required across the industry. With all eyes on manufacturers to produce approved vaccines, they will be looking for a strong partner to provide a reliable and consistent supply of bioprocess materials. This pandemic has sent ripples through the industry, and the rate of innovation and development in response to it is merely a hint of what could be possible in the future.

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