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TECHNICAL NOTE

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Toward Standardization in Biotechnology Platforms to Support Smart Manufacturing

Reference

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ABSTRACT

The current race to develop and manufacture vaccines and therapeutics to prevent and treat coronavirus disease 2019 (COVID-19) has led to an increased recognition of and investment in various technology platforms, including manufacturing and measurement platforms, across many sectors of biotechnology. We are also witnessing the convergence of multidisciplinary technologies to enable rapid response and capacity building for diagnostics, treatments, and prevention, and in biosurveillance and monitoring. Addressing this global challenge requires smart and distributed manufacturing underpinned by robust standards that are necessary to ensure the quality and consistency of bioproducts.

Keywords

coronavirus disease 2019, biotechnology, vaccines, therapeutics, platforms, measurements, standards

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Introduction

Global response to the current coronavirus disease (COVID-19) pandemic crisis is leading to rapid advances in biotechnology, including an unprecedented transformation in the development and manufacturing of vaccines.[1] Significant investments have been made to simultaneously develop a number of vaccine platforms in an effort to rapidly deploy a safe and effective vaccine.[1,2] As a part of this effort, the community is working to advance several new vaccine platforms, including nucleic acid (i.e., deoxyribonucleic acid [DNA] and ribonucleic acid [RNA]) vaccines, viral vector vaccines, and protein (or subunit) vaccines in addition to the more traditional vaccine development strategy utilizing inactivated or highly attenuated viruses. A common theme among the newer vaccine platforms is that, conceptually, they can be rapidly redesigned to treat a wide range of infectious diseases.

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The concept of technology platforms started prior to the advent of COVID-19. Indeed, several industrial roadmaps had been developed to identify opportunities, including the use of technology platforms, for the development and manufacturing of vaccines, protein therapeutics, and cell and gene therapies as well as other therapeutic modalities.[3–7] In parallel, the concept of biotechnology platforms had gained industrial attention.[8] The urgency associated with COVID-19 has led to the recent surge in investments to simultaneously advance multiple platforms in the hope that one or more will result in a safe and efficacious vaccine. Recent advances in biotechnology, engineering biology, virology, immunology, and cell and gene therapy are critical to these efforts.

In this short technical note, we highlight the emerging prominence of biotechnology platforms, including platforms for vaccines and therapeutics as well as platforms needed to manufacture and test and release products. Fueled by recent bioscience and biotechnology innovations, such as genome sequencing (DNA read), genome synthesis (DNA write), and genome edit as well as cellular engineering and manufacturing, biotechnology platforms will continue to evolve and will be used increasingly in biomanufacturing of healthcare and nonhealthcare products. Realization of this vision will require a robust standards infrastructure, which will enable industry to architect and integrate product development and manufacturing processes, manage supply chains, and ensure quality and consistency of bioproducts.

Biotechnology Platforms

All vaccine platforms are designed to target or disrupt specific viral entry or replication pathways, or both, to elicit various innate and adaptive immune responses.[1,2] Traditional approaches to finding a safe and efficacious inactivated or attenuated virus vaccine can be time-consuming and labor-intensive. In addition, these vaccines typically take longer to manufacture. For these reasons, other vaccine platforms are under development to provide faster solutions[1,2,9]:

- Nucleic acid–based vaccines: DNA or RNA is injected into a person to instruct the production of a harmless piece of virus protein, which allows the immune system to learn to recognize and quickly respond to a real infection. This vaccine platform clearly leverages the DNA write platforms and delivery platforms, among others.
- Viral vector–based vaccines: Similar in principle to the nucleic acid vaccines, this platform uses a viral vector (engineering viruses containing a piece of harmless pathogen genome) as the delivery system. This vaccine platform uses engineered producer cells as the manufacturing platform as well as a viral vector as the delivery platform. Other platforms include those that produce the viral genomes.
- Protein/subunit vaccines: Here, a small piece of the viral protein is produced using producer cells as the manufacturing platform.

Such platforms are more general and not specific to vaccines, but the current need has focused the attention of biomanufacturing platforms on vaccines and treatments for COVID-19.

As noted, one major advantage of the technology platform is that it can be rapidly redesigned to meet a specific need. For example, the development of a viral vector vaccine can be greatly accelerated by leveraging an existing viral vector platform demonstrated to be safe and known to induce robust and durable immune responses. This would help to clear the first few major hurdles of vaccine development. Furthermore, these vaccines can be manufactured using an existing producer cell platform with high titer viral vector using well-controlled media.

For the current pandemic, once a vaccine is shown to be safe and efficacious, a major challenge will be the need to rapidly manufacture a large number of doses.[10] This raises a host of other issues, such as manufacturing capacity, production scheduling, and distribution, all of which involve supply chains. The newer vaccine manufacturing processes generally require the use of various nucleic acids (plasmid DNA, RNA, etc.), proteins, and lipids as raw materials. Such raw materials need to be secured rapidly, and their quality must be ensured. Raw materials are then processed into drug substances that may have to be frozen and shipped to another facility to be

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developed into drug products and for finish and fill. Yet another site may conduct release and stability testing of critical raw materials, drug substance, and drug products. Such complex manufacturing and testing processes are not unique to vaccines but are applicable to many biopharmaceutical products.[3] Similar challenges may arise in nonhealthcare-related biotechnology sectors.

Challenges faced by the biomanufacturing industry are in fact quite similar to those addressed by the manufacturing community at large under the smart manufacturing umbrella. Smart manufacturing is a synthesis of digital transformation of manufacturing and advanced manufacturing technologies.[11] Key characteristics of smart manufacturing include interoperability of information systems, connected devices for real-time control, collaborative supply chains, integrated decision making, and advanced sensors and big data analytics.

Solutions to these manufacturing problems include a high level of quality assurance and quality control. This has given rise to the emergence of another category of platforms—measurement platforms—that are critically needed to accelerate product development (to demonstrate safety and efficacy during *in vitro*, animal, preclinical, and phased trials involving humans), manufacturing, and release. Validated assays are critical to test the quality of raw materials and intermediates as well as drug substance and drug products.[12] Assays are used throughout the manufacturing process to ensure that process variations are under control. All vaccines and therapeutics must be tested using a suite of release assays to ensure safety and efficacy. For vaccine development, assays are also critical for understanding patient responses to various vaccine platforms.

Standardization

The importance of biotechnology platforms can be traced to the fact that the platforms are more stable and last longer than the commercial lifecycle (time spent from conceptualization to discontinuation) of the products they produce. Because of this, various biotechnology companies are moving to platforms to gain better return on their investment. Some platforms, particularly manufacturing and measurement platforms, can serve as a common starting point that can be rapidly validated and adapted for the specific needs that arise in the industry.

Knowledge gained in each platform can be codified as the best practices in standards and protocols, and these can be continuously improved and updated. For the emerging and rapidly advancing biotechnology industry, standards can facilitate interoperability and communications and manage expectations. Standards reduce the cycle time, errors, and costs in the development and delivery of bioproducts. Multiple suppliers and medical professionals can be trained ahead of time and deployed quickly to respond to an emergency. Manufacturing processes can be replicated quickly around the world while maintaining quality. Standards also accelerate regulatory approval process. All these promote economic growth and industrial innovation while safeguarding public health. Hence, we anticipate a strong role for standards development organizations, such as ASTM and the International Organization for Standardization, in the post–COVID-19 era.

Conclusion

COVID-19 has put a spotlight on biotechnology platforms. These platforms include manufacturing platforms, measurement platforms, and, for COVID-19, vaccine platforms. Advances in these platforms allow rapid development and deployment of biotechnologies. Standards will play an important role to promote interoperability and rapid development of technology platforms and to ensure the quality and consistency of processes and products.

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