Vaccine platform technologies – Learnings from the COVID-19 pandemic


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In response to the global emergency caused by the SARS-CoV-2 virus, vaccine development was fast-tracked in 2020 from a decade or two, to less than a year. Can it be even faster? Could it be done in three months? The unusually rapid development and approval of several new vaccines was a result of separate achievements with one common goal – to stop the spread of a previously unknown virus. When the new coronavirus genome sequence was posted online in early January 2020, this enabled the expeditious development of diagnostics and vaccines worldwide.

Traditionally, the timeline for developing vaccines has been slow. Previously, the mumps vaccine was the quickest to have ever been developed, taking four years from development to deployment. Since vaccines are prophylactic, generally administered to large numbers of healthy individuals, the requirements for safety are very strict. Developers must prove that the vaccine is both effective and safe to use. The rigid regulatory process of pre-clinical activities is one of the rate-limiting factors in vaccine development. Based on the progression of vaccine platform technology, a better understanding of safe, efficacious vaccine design, and the leverage of accumulated knowledge, could result in extensively shortening development programmes.

In February 2021, NDA Group Advisory Board Members Dr Pieter Neels and Dr Steffen Thirstrup participated in a joint webinar organised by the International Alliance for Biological Standardisation (IABS) and the Coalition for Epidemic Preparedness Innovations (CEPI) on the use of platform technologies for vaccine development. The aim of the webinar was to share experience from the industry and the regulatory perspective to fully leverage the knowledge on platform technologies for the current as well as future pandemics[1].

A vaccine platform is a technology for production of different vaccine antigens; proteins or other biomolecules that stimulate the immune response. It is the backbone of a manufacturing process, which could be a mechanism, a delivery method, or a cell line that can be used for multiple targets. The methodology is consistent while the antigen, or the genetic code for the antigen, is tailored for the product. When a platform technology has been established it makes the process of altering the vaccine significantly faster as the vaccine does not have to be developed from scratch and the response to an outbreak or mutations of previously known viruses would, therefore, be faster.

There is a whole spectrum of vaccine platforms available, different technologies with both advantages and challenges. There are currently close to 300 vaccine candidates for COVID-19 and one third of these are in clinical development. The most frequently used platforms in the development of COVID-19 vaccines are RNA, protein subunits, inactivated virus, and non-replicating viral vectors[2]. Inactivated viruses have been used for decades and this method is a relatively straightforward way to produce safe and effective vaccines. Protein subunit vaccines contain isolated proteins from pathogens selected for their ability to stimulate immune cells. These two types of vaccines may require adjuvants and booster doses to achieve sufficient immunity. The viral vector vaccine is using a modified virus (the vector) to deliver genetic code for the antigen into human cells. For COVID-19, the most common strategy is to put coronavirus spike proteins on a virus backbone, e.g., adenoviruses. This vaccine mimics what happens during natural infection and triggers a strong cellular immune response.

Plug and play

A nucleic acid (RNA or DNA) vaccine uses a section of genetic material that provides the instructions for specific viral proteins essential for immunogenicity. It does not need a viral vector and can be delivered in nano lipid particles or as so-called virus-like particles. It can be designed more rapidly and deployed as soon as the genetic sequence has been identified.

The mRNA vaccine is a new class of drug product, which had never been licensed prior to the COVID-19 pandemic, therefore the knowledge level is still limited. However, this new platform has been used in the last decade for a number of cancer patients and recent data implies that mRNA vaccines induce a robust and prolonged immune response to SARS-CoV-2[3,4,5,6].

What makes mRNA vaccines so appealing is the potential to establish platform solutions that allow the rapid development of a range of vaccines against emerging infectious diseases or mutations based on an easily scalable technology platform.

Going for approval

Regulatory authorities approve products, not platforms or processes. Vaccine development is a sequential process, sometimes with overlap in phases. The data and proposed labelling are reviewed by the regulatory agency and, if it can be established that the benefits of the drug outweigh the risks, the drug can be approved. For COVID-19, early scientific advice from regulators helped speed up development. Companies may use various approaches to reduce development timelines, such as combining clinical trial phases or conducting studies in parallel where safe to do so.

In an FDA guidance document from 2020, opportunities to leverage knowledge accumulated with platform technology should be considered to accelerate the development of a SARS-CoV-2 vaccine manufactured using the same platform[7]. If a platform technology used to manufacture vaccines is well characterised, it is possible to use toxicology and clinical data accrued with other products using the same platform to support first-in-human clinical trials for a SARS-CoV-2 vaccine candidate.

In the EU, the concept of a vaccine platform master file (PfMF), was accepted for veterinary medicinal products. These guidelines are currently being drafted by the EMA and aims to reduce the administrative burden while guaranteeing the highest level of safety for new medicinal products for animals[8]. The PfMF should include all platform data that remains the same regardless of the antigen or gene added. Such a master file allows a manufacturer to reference prior approvals to fulfil data requirements in subsequent applications based on the same platform and intended for the same target species. This saves valuable time and energy when starting the development of a vaccine against a new disease.

In the first guidance documents it was proposed to accept a PfMF once the 'first-in-class' vaccine from the new platform was licenced. However, during the COVID-19 crisis, data were accepted from unlicenced products and, therefore, this requirement needs to be challenged. In the human sector of regulatory affairs, the current discussion is how a PfMF can be implemented to speed up the development of new vaccines and how this can improve the situation in times of a pandemic.

The sum of all parts

Collectively, the multiple efforts of both developers and regulators cut the rollout time of the COVID-19 vaccine by decades. Besides massive funding and governmental resources, companies were able to leverage vaccine platforms developed for immunotherapy targeting cancer, and other infectious diseases, which allowed them to hit the ground running with their COVID-19 vaccine efforts.

In conclusion, the platform technology is available and on standby for a rapid vaccine development and scale-up but, as the IABS/CEPI webinar concluded, the development of the technologies needs to continue moving forward, while learning from the current experience. Platform technology and a tailored regulatory framework, the acceptance of an approval of a PfMF, could further speed up the rapid response to tackle emerging infectious diseases.

For more information on Vaccine platform technologies contact: **asktheexpert@ndareg.com**

References

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