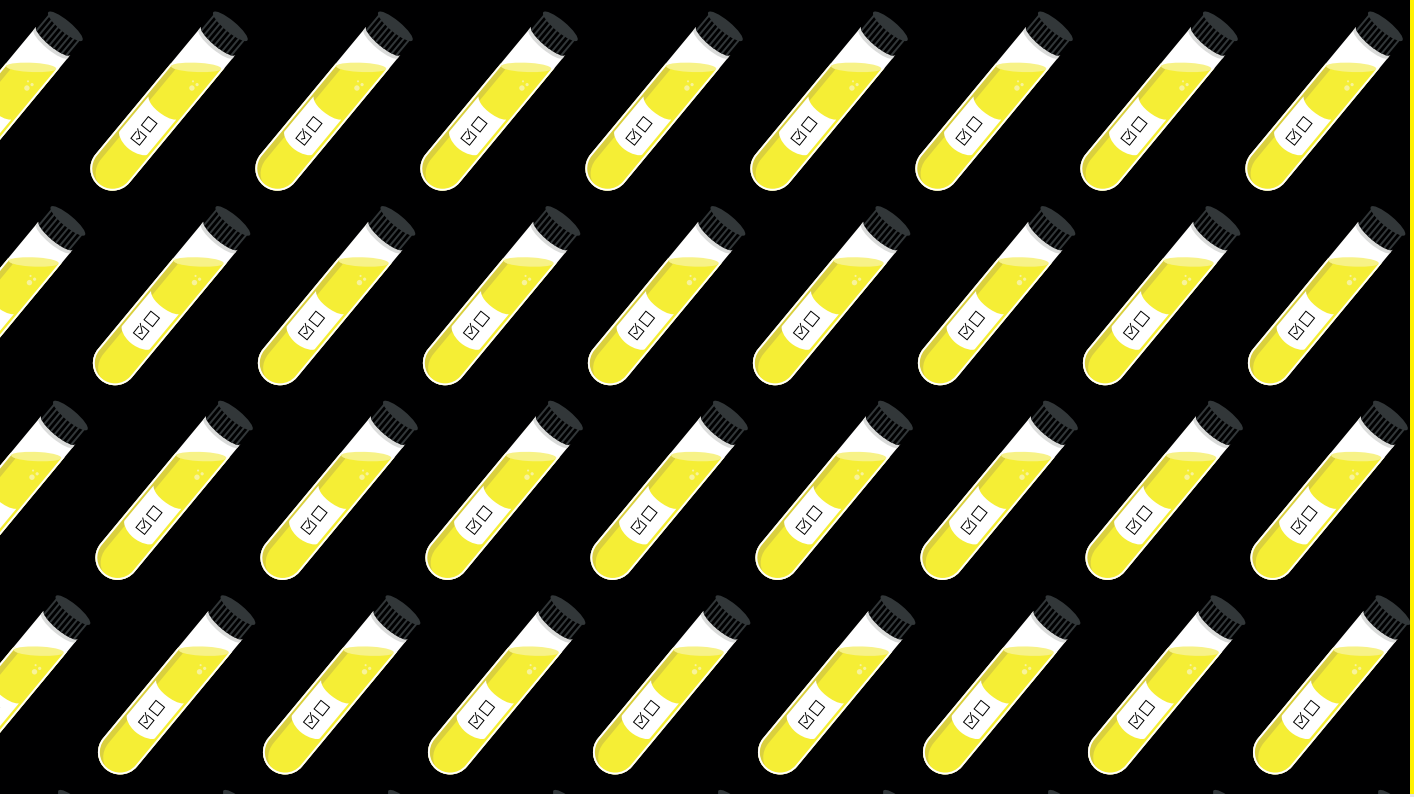

SARTORIUS

Success at Speed: Digging into Accelerated Vaccine Development

Part 1 – The Need for Speed and Safety

As the world grasps the severity of the ongoing pandemic, we must ask how we can accelerate vaccine development safely – for COVID-19 and other therapeutic areas.

By Amélie Boulais, Vaccine Platform Marketing Manager, and Piergiuseppe Nestola, Global Vaccine Technology Consultant, both at Sartorius.

In collaboration with

the Medicine Maker

The Need for Speed and Safety

Immunology is not an exact science. There are still many aspects of the immune system that are not properly understood, meaning that vaccine success requires a number of attempts. On average, it takes 10 – 15 years to develop a successful vaccine. Challenges include identifying the right antigen to generate an immune response, developing the right manufacturing strategy to produce it at scale, and testing the vaccine in a large enough number of people to ensure efficacy and safety. As vaccines are used in large numbers of healthy people, extensive clinical testing is required, which is time (and money) consuming. Developers must measure vaccine response over time to see if long-term protection is offered, and side effects may only be seen when the vaccine is injected into large numbers of people. Consider dengue: when a vaccine was developed and began to see use in large numbers of patients, it was found that vaccination could lead to more severe cases of dengue in some patients. Such an example reiterates the need for extensive studies – and highlights the challenges of developing a successful vaccine. Although this example is not the norm in vaccine development, extensive studies are always required to ensure safety.

The first authorization for an Ebola vaccine was for emergency use only, prior to finalizing its clinical evaluation – a move that is typically used when the risk-benefit ratio of using an unapproved drug appears to be in favor of benefit, such as during a pandemic. With regards to COVID-19, there are ongoing discussions taking place in regulatory agencies, and so perhaps we will see a new framework created to cover pandemic vaccines.

The Need for Speed

It is essential to take the time to evaluate efficacy and safety during vaccine development, but it is possible to accelerate the timeline. At present, the industry is looking to develop a vaccine for COVID-19 in 12 – 18 months. Is this possible? Perhaps. Will it be a challenge? Absolutely.

First of all, the funding for pandemic vaccine development will be a considerable challenge. It takes about $1 billion to make a vaccine. But right now, we don't know which candidate and which approach is best, so resources must feed them all. →

When it comes to manufacturing, there are a range of ways in which developers can safely accelerate processes.

The Key Word Is Technology. Our Top Tips Are:

01. Rely on partnerships – including those with service providers.
We will not find a solution by working in silos and the industry must connect quickly. Start-ups and universities have expertise and promising vaccine candidates; established vaccine manufacturers have experience in running clinical trials and regulatory filings; contract manufacturing organizations have production capacities; critical suppliers have the capacity to ensure quality supply.
For example, Sartorius can offer services, such as cell banking and testing, cell line development assay developments, to ensure the development of a safe process right from the beginning.

→ Small start-ups and universities do not have the funding to develop candidates – and even the established players of the vaccine industry are taking a big risk before the outcome of clinical trials. Funding organizations, including not for profits, governments, and private corporations, will be critical to support this global health initiative.

We also need to consider the fact that our understanding of SARS-CoV-2 is still growing – and important questions do not have definite answers. Are patients immune from reinfection after contracting COVID-19? Is the virus mutating substantially? What percentage of the population has been infected? Why do some people develop cytokine storms? Who is most at risk? Who should be vaccinated first?

Despite incomplete or missing answers, there are well over one hundred vaccine candidates in development all over the world and this number is expected to grow in the coming months. Some candidates are already moving into phase 3 clinical trials. The race to a vaccine is like a marathon; the runners are all very close to one another at first, but as the race goes on certain groups will start to pull ahead – and hopefully at least one of them will make it to the finish line! Companies can accelerate development in many ways, while still respecting safety and efficacy. In traditional vaccine development, the different steps are usually sequential, but now they are happening in parallel – with production of a vaccine commencing even before the outcome of a clinical trial is known, to ensure readiness for distribution once approval is given. Clinical phases are also happening in parallel, with some beginning before the previous one ends. Patient recruitment for trials needs to be rapid, and the results must be communicated to all stakeholders quickly. →

02. Focus on single-use technologies.
They are much faster and cheaper to implement at large scale than stainless steel technologies (delivery and installation is faster, validation is faster, capex is lower) and offer flexibility to adjust production to demand. For example, you can invest first in a 2000 L bioreactor, and add another one later if required – or scale down to 500 L. You can also repurpose existing single-use equipment. Established suppliers of single use equipment, like Sartorius, have a strong supply chain and a reputation for quality – and this is important when speed is of the essence; you need to be able to trust your suppliers.

03. Ensure your analytical assays are properly validated.
Analytical development is the most critical piece of the puzzle because you need to ensure the quality of your drug product.

→ To accelerate development safely, manufacturers will need to have regular meetings with regulatory authorities to discuss the next steps based on clinical outcomes, and the potential risk-benefit evaluations that must be considered. It may also be necessary to redesign clinical trials and perhaps consider challenge studies, but this latter point raises ethical concerns.

COVID-19 – and Beyond

A pandemic of this scale is a first for our modern world but, in reality, the scientific community has seen this coming for a long time. We live in a globalized world, with pockets of high population density. There is an enormous amount of global travel and the climate is changing. All twhe conditions are there for a pandemic. Influenza has been a potential pandemic threat for some time, spurring the vaccine industry to modernize its manufacturing processes by moving away from egg-based to cell culture-based production. However, the World Health Organization already identified the threat of a pandemic from another source – calling it "Disease X" – and the Coalition for Epidemic Preparedness Innovations (CEPI) was created specifically for this eventuality: to prepare for a pandemic and to support the industry.

Coronaviruses have also been previously identified as a pandemic threat. A paper from 2007 concluded: "Coronaviruses are well known to undergo genetic recombination (375), which may lead to new genotypes and outbreaks. The presence of a large reservoir of SARS-CoV-like viruses in horseshoe bats, together with the culture of eating exotic mammals in southern China, is a time bomb. The possibility of the reemergence of SARS and other novel viruses from animals or laboratories and therefore the need for preparedness should not be ignored." [1]

Although COVID-19 has become a clear focus for vaccine manufacturers, there are also many other therapeutic areas that should not be forgotten during the pandemic. For example, cancer vaccines and vaccines against unmet indications such as HIV, malaria, and RSV. There are also many existing vaccines that can certainly be improved upon, such as influenza (moving from egg-based to cell culture-based vaccines, developing a universal flu vaccine, and assessing pandemic readiness) and tuberculosis (improving the BCG vaccine). And all vaccines can benefit from faster development – because patients are waiting all over the world.

04. Make use of the increasingly digital world.
Tools such as design of experiment and multivariate data analysis (MVDA) software will help to accelerate scale-up and de-risk tech transfer, while ensuring process robustness. In addition, multivariate real-time monitoring can deliver continuous insight of your process and allow you to predict and correct deviation before it occurs. It helps to keep quality consistent, maximize efficiency and reduce cost – this is particularly important for COVID-19 because, when trying to accelerate development, companies will not have the number of batches required during normal development (for engineering runs, PPQ run, and so on). Therefore, it is essential for data generated during manufacturing to be used in a clever way to ensure that the manufacturing process is under control. Don't forget: the process is the product.

05. Discuss your strategy early on with regulatory authorities to get clear guidance.
Regulators are prioritizing COVID-19 programs and are very willing to engage with manufacturers.

Reference

[1] V CC Cheng at al., “Severe Acute Respiratory Syndrome Coronavirus as an Agent of Emerging and Reemerging Infection,” Clin. Microbiol. Rev., 20, 660-694 (2007)

Germany
Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen
Phone +49 551 308 0

USA
Sartorius Stedim North America Inc.
565 Johnson Avenue
Bohemia, NY 11716
Toll-Free +1 800 368 7178

For further information, visit
www.sartorius.com/covid19

Specifications subject to change without notice.
Copyright Sartorius Stedim Biotech GmbH.
Status: 07 | 2020