VACCINE INSIGHTS

COVID-19: HOW IS THE PANDEMIC CHANGING THE VACCINES SPACE?

SPOTLIGHT

Analytical development for rapid response vaccines: start early, think ahead

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VIEWPOINT

"As highlighted by the COVID-19 pandemic, early analytical development is key for the rapid scale-up of new vaccines. Careful consideration of assay development throughout the pipeline can expedite technology transfer, avoid costly missteps, and produce vaccines faster to fight future pandemics."

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The COVID-19 pandemic prompted laboratories around the globe to start developing vaccines against SARS-CoV-2. One important lesson from this unprecedented effort is that to achieve worldwide mass vaccination in record time, an early focus on assay development is key.

The analytical toolbox, comprising of all analytical methods needed to evaluate a vaccine candidate, is crucial for taking a vaccine from idea to commercialization – proving that it is safe and efficient by quantitatively testing critical quality attributes (CQA) such as potency, content, purity, etc, and characterizing the product according to regulations [1].

Most CQA assays are product- and/or platform-specific and need to be developed accordingly [2]. The time and effort required to develop appropriate methods – including reagents and reference standards – that can be qualified and validated, should not be underestimated. The earlier these assays can be utilized, the more relevant data can be generated to support a regulatory filing. This is vital if we are to meet the Coalition for Epidemic Preparedness Innovations (CEPI)'s goal of developing a vaccine in 100 days [3].

The first emergency use authorization for a COVID-19 vaccine was issued less than a year after the pathogen was identified. To make this possible, activities normally done sequentially have been performed in parallel (at financial risk to developers and other funders) without compromising safety; for example, scaling up manufacturing at the same time as conducting early-stage clinical studies. Developers conducted multiple tech transfers to scale up and scale out their manufacturing, usually to several countries, resulting in astonishing 13 billion COVID-19 vaccine doses produced in 2021 [4]. If rapid analytical methods were in place to support some of those time-consuming tech transfer steps, our response to the next pandemic could be even faster.

Products developed during a pandemic need to be as well characterized as those following a 'normal' timeline, so reliable analytics to ensure product quality and comparability, as well as proving lot-to-lot consistency, are essential. To match the manufacturing capacity and mitigate potential testing bottlenecks, tech transfer of analyses to multiple quality control laboratories, in addition to tech transfers to national release laboratories, were undertaken. This can be a laborious task and must be well managed to keep to tight timelines. The sooner new laboratories can initiate their work, the lower the risk of causing delays in getting vaccines to the world.

It is a regulatory requirement to show comparability between the materials used throughout clinical development of a product [5,6], thereby demonstrating comparability between the different manufacturing scales used for generating material – from small-scale preclinical toxicity studies to pilot-scale GMP clinical trial material, and ultimately to commercial scale. Any process modification or formulation change between these stages must also be covered by the CQA comparability exercise, to avoid costly and time-consuming clinical bridging.

Establishing stability indicating CQA assays is a particular priority. Allowing time for release testing by the manufacturer and national release laboratories, and global distribution, at least 6 months shelf life is required to make any vaccine viable. Robust assays to measure the physicochemical and biological stability of the drug substance and drug product over time when manufacturing material for Phase 1 clinical trials will generate real-time data in support of a longer shelf life when filing for licensure. Particularly in an outbreak situation, being able to initiate relevant stability studies, including transport simulations, as soon as possible enables a longer shelf life and increased usability of the vaccine.

CEPI has co-hosted several workshops with the Bill & Melinda Gates Foundation addressing various Chemistry Manufacturing and Controls (CMC) issues throughout the pandemic. The importance of addressing

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CQA at an early stage was covered at the 'Best practices for tech transfer workshop' [7].

In conclusion, robust analytical methods are needed early on in vaccine development. Assays showing that the products used in clinical studies are comparable to the product manufactured at different scales and sites are crucial. These assays are also key to demonstrating that the vaccine is safe and efficient when used – and a delay in assay development could delay product launch. To fight future pandemics and achieve CEPI's 100 days aspiration, the global health community must come together to ensure we have robust assays and other analytical tools at the ready.

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AUTHORSHIP & CONFLICT OF INTEREST

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