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LETTERS

Building trust in the quality of vaccines

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ABSTRACT

To date, several COVID-19 vaccines have been authorized for the voluntary immunization of adults. The quick availability of multiple vaccines is a good strategy to achieve herd immunity during a pandemic. However, the fast-track development of vaccines during this pandemic has raised concerns regarding the quality, safety, and effectiveness of vaccines. In response, USP organized a roundtable to discuss challenges and to solicit input on ways to build trust in vaccines. Key discussion points included manufacturing capacity, availability of a skilled workforce, and investment in new technologies that would enable the safety and quality of vaccine products. There was also a consensus that a rigorous and transparent clinical trial design is essential for understanding the safety and effectiveness of vaccines.

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Letter

Vaccines remain the most successful and effective mechanism for the prevention of infectious diseases. Timely development, manufacturing, and distribution of vaccines are critical to mitigate the spread, morbidity, and mortality of a pathogen. The COVID-19 pandemic has prompted researchers and manufacturers to take huge business and financial risks to develop the vaccines in fast-track mode, while meeting current good manufacturing practices (CGMP) to ensure that every batch is consistently and safely made and meets the expected quality requirements. Regulators have also taken a risk to release the products under emergency use authorization (EUA) to make vaccines available sooner based on a risk-benefit analysis of the data.[1] This joint effort to increase the speed of vaccine development, manufacturing, and approval is nothing less than impressive, but challenges still exist.

Unlike therapeutics, vaccines are given to healthy people. Hence, the bar for demonstrating safety and efficacy is much higher, as demonstrated by the recent pause of the Johnson & Johnson and AstraZeneca vaccines in few countries because of possible rare clotting side effects in a few vaccinated people out of millions who have received the vaccine. There is also no shortage of vaccines that have been recalled due to possible adverse events.[2] The fast-paced development of vaccines for COVID-19 has raised concerns about quality, safety, and effectiveness that affect trust among end-users. These concerns are a serious issue because herd immunity can only be achieved if a lot of people get vaccinated. The doubt surrounding vaccines is not new, as even vaccines with much longer development times and decades of real-world use are encountering a growing hesitancy.[3–5] The unusually swift response to COVID-19 has only exacerbated existing fears among the public.

To address this problem, the United States Pharmacopoeia (USP) organized a roundtable discussion "Building Trust in the Quality of Vaccines" on November 19, 2020. The meeting included an overview of modern vaccine manufacturing and the unique challenges and risks involved in vaccine development in a pandemic, presented by Sunil Gairola, Director of Quality Control at Serum Institute of India (SII); insights into the challenges to the supply chain during a pandemic, including cold chain shipment, storage, and distribution for the current leading COVID 19 vaccines in India presented by Harish Iyer, Senior Advisor to the Bill & Melinda Gates Foundation (BMGF); and a discussion of the use of new mRNA and DNA based technologies for the development of vaccines presented by Sanjay Singh, CEO of Gennova Biopharmaceuticals, and Kapil Maithal, President & Head of Vaccines and Diagnostics at Zydus. Fouad Atouf of USP addressed the role of public standards in maintaining public trust in vaccines. Atouf reiterated USP's commitment and initiatives related to new standards, training, and advocacy programs to support quality vaccines.

The roundtable discussion reflected on how the COVID-19 pandemic revealed many problems in the global effort to manufacture and distribute vaccines quickly. An approach worth examining is the one taken by India where manufacturers have managed to scale up the production of vaccines against SARS-CoV-2 very quickly due to existing vaccine manufacturing capabilities. One manufacturer, the Serum Institute of India (SII) has already provided ~60 million doses for the India Immunization program and has exported 70 million doses of the Oxford AstraZeneca vaccine to dozens of countries in the COVAX vaccine-sharing program, co-led by the Coalition for Epidemic Preparedness Innovations (CEPI), Gavi, and the World Health Organization (WHO). By the end of the year, SII will add 1.5 billion COVID-19 shots to the billions of doses it already produces against measles, polio, and many other infectious diseases.

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To ramp up quickly, manufacturers such as SII had to take a chance on scaling up manufacturing before vaccines were approved. Manufacturers usually only make these kinds of investments after years of research and clinical trials, but the pandemic fostered a variety of public-private funding approaches to decrease risk. Philanthropic organizations such as the BMGF know how to work with governments and the pharmaceutical industry and have dedicated billions to get COVID-19 vaccines to more than 150 countries. BMGF, via Gavi, provided SII with 150 USD million to start scaling up production on the Oxford AstraZeneca vaccines early. Notably, the funds did not have to be repaid even if the vaccine failed, which means SII would not have to bear all the risks themselves. Since then, SII has received an additional 300 USD million at-risk funding from Gavi to develop and make other promising vaccines. The company will also start churning out 40–50 million doses of vaccines developed by Novavax, SpyBiotech, and Codagenix, in addition to AstraZeneca while seeking emergency authorization use or approval.

Besides SII, other vaccine manufacturers have been contracted to produce vaccines that they have not developed to increase the global capacity of doses. Gland Pharma, Hetero Biopharma and Stelis Biopharma have partnered with the Russian Direct Investment Fund (RDIF) for the development and launch of their recombinant adenovirus-based vaccine. Additionally, there has been a strategic partnership between US company COVAXX, the United Nations Children's Fund (UNICEF) and the Indian company Aurobindo Pharma to expand global development and commercialization of multitope peptide-based COVID-19 vaccine. Biological E Ltd, which has several WHO Prequalified vaccines, plans to contract manufacture for scaling up production for the J&J vaccine. Biological E has an agreement with US-based Baylor College of Medicine and Dynavax for the development of a subunit vaccine candidate. Indian manufacturers have a long history of producing vaccines in collaboration with innovators, and they could leverage these preexisting relationships to increase manufacturing capacity. For example, SII leveraged its previous work with Oxford and Novavax for malaria vaccines to become the manufacturing partner for both of their COVID-19 vaccines. Manufacturers who consistently produce large volumes of vaccines typically ensure a strong supply chain versus a new vaccine manufacturer trying to establish a new supplier relationship under pandemic conditions.

Additional takeaways from the discussion included:

- Developers should establish clear correlates of immunological protection provided by their vaccines. To accomplish this, they need to implement well-designed global clinical trials in collaboration with regional participants.
- Manufacturers should perform iterative process validation under CGMP compliance to ensure quality vaccine development in short development timelines. Innovator companies must collaborate with different regional players with proven capacity and capability to ensure the global availability of quality vaccines.
- Developers and regulators should adopt and evaluate the use of novel high-end technologies like single-use bioreactors, NMR, and mass spectrometry, which are not typically used for vaccine production and testing but help scale up efforts. Proper implementation of these technologies and training of the workforce is essential.
- Governments should invest more into workforce development to have a readily available labor force when greater capacity is required. There is a need to invest in translational programs that can help basic science researchers transition from academic programs to the use of technologies and quality management systems used by industry. Global regulatory bodies can work with both government agencies and manufacturers to provide such training.
- Governments and companies in the distribution network should provide better capacity for cold chain storage so that vaccines can be delivered to rural locations. Rigorous procedures must be in place, training provided and verified to ensure the integrity of the supply chain.
- Securing the availability of high-quality raw materials is critical, particularly since many of these components are used by multiple manufacturers to produce billions of doses of vaccines.
- Manufacturers and regulators should adopt a transparent, data-driven approach to build public trust in vaccine safety and efficacy.

Moreover, it is essential to educate the broader public about all aspects related to ensuring high quality vaccine programs, as well as the risks and benefits associated with vaccines. Increased transparency with the wider public will help fight vaccine hesitancy and increase the acceptance of vaccines as a solution to pandemics. Key elements that need to be brought to light include the fact that the vaccine industry has been investing for decades in state-of-the-art technologies which underpin the rapidly produced high-quality vaccines. Additionally, organizations with expertise in product development and operational quality are collaborating with government bodies during the rollout of the COVID-19 vaccine programs. It is also imperative to increase transparency in clinical trials of vaccines and make available safety and efficacy data. Lastly, advocacy programs for patients and healthcare professionals are needed to build awareness of the safety and efficacy of the vaccines as well as the importance of contributing to herd immunity to move out of the pandemic through behaviorally informed strategies.

Finally, relying only on vaccines to solve a pandemic will always be inefficient. No matter how fast we can make a vaccine, we will always be behind the surge of infections. Therefore, public health authorities must attempt to prevent or slow down disease spread while manufacturers work on scaling up the production of the needed doses. The best way to accomplish this goal is by educating people about how to decrease the spread of infection.

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No potential conflicts of interest were disclosed.

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