A NEED FOR SPEED: HOW THE NEW PHARMA IS ACCELERATING THE BENCH TO BEDSIDE TIMELINE

The COVID-19 pandemic has brought death, suffering, and hardship to millions of people around the world.[1] Some positives have emerged, however. Together, the pharmaceutical industry's researchers, manufacturers, regulators, chemical suppliers, and other stakeholders brought novel tests, vaccines, and therapeutics to market with unprecedented speed, saving countless lives.

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"We had diagnostic tests within a week, effective therapeutics (in the form of dexamethasone) in 138 days and safe and effective vaccines in just over 300 days after the [World Health Organization] declared a public health emergency of international concern," writes Sir Patrick Vallance, the chief scientific adviser to the UK government, in the report *100 Days Mission to Respond to Future Pandemic Threats*.[2]

The question for pharma experts now: What will the pharmaceutical industry do with what it has learned, and what impact will this have on drug researchers and developers, manufacturers, and raw material suppliers?

The authors of *100 Days Mission*—prepared by the Pandemic Preparedness Partnership and presented to a group of G7 world leaders in June 2021—have outlined a road map to an even-faster response for future pandemics: to make diagnostics, therapeutics, and vaccines available within 100 days.

The report's recommendations for better pandemic preparedness call first for effective global surveillance and pathogen analysis to spot pandemic threats earlier. They then mark out vital steps that

governments, industry, and international organizations must take to improve readiness. These include building prototype vaccine and diagnostic libraries, modernizing vaccine technology, developing a common regulatory framework, and transforming the approach to clinical trial regulation.

Lessons learned from the COVID-19 pandemic will not only support readiness for future health crises but could revolutionize the development and manufacturing of pharmaceuticals designed to treat and prevent other diseases and illnesses.[3]

Global experts are now figuring out how to turn these lessons into actions that will ensure the future of pharma is fast.

CHALLENGING AND SHRINKING TIMELINES

Public health is upended when an outbreak becomes a global pandemic, and systems are often not in place to meet urgent requirements. Those include identifying the contagion and determining how to contain it; diagnostics to accurately confirm infection; therapeutics to treat symptoms; and effective vaccines to eventually help slow spread.

On average, it takes 10.5 years for a Phase I therapy to progress to regulatory approval.[4] The COVID-19 pandemic disrupted this model as timelines for drug development, regulatory approval, and manufacturing were challenged and ultimately reduced.

In the early part of the pandemic, as COVID-19 death rates rose rapidly, it was obvious that rigorously sticking to traditional pharmaceutical development strategies would have dire consequences. Vivek Kumar, biopharma market development manager at Spectrum Chemical, says the pandemic forced the pharmaceutical industry to radically rethink conventional processes from drug development to launch.

“COVID-19 has shown the industry that we can indeed shrink those timelines,” Kumar says. “Now we can bring diagnostic tests and therapeutics faster to the market rather than waiting for years.”

Julia Schaletzky, executive director of the Henry Wheeler Center for Emerging and Neglected Diseases at the University of California, Berkeley, acknowledges the rapid development of vaccines and therapeutics during this pandemic but cautions against believing that speed will immediately be a new normal.

“I don’t think we should lean back automatically into saying, ‘It was superfast; there’s nothing we need to change,’ because there was still friction in the system,” Schaletzky says. Diagnostic testing was “painfully slow” early in the pandemic, when red tape delayed the supply of test components and the delivery of results, she adds.

Now that the world has seen what is possible, however, the lessons learned

could drive radical changes in pharmaceutical research, development, approvals, and production, which will in turn affect how raw material suppliers meet these needs.

BOLD NEW APPROACHES

Pharmaceutical companies and researchers responded quickly to COVID-19 by simultaneously reevaluating past discoveries and embracing new technologies. Repurposing existing drugs and fast-tracking the development of new ones were critical moves.

The story of the antiviral remdesivir during this pandemic has shown how drug repurposing can be an effective component of a rapid response. The pharmaceutical company Gilead Sciences originally developed remdesivir to target Ebola. By the time the COVID-19 pandemic began, the company had already demonstrated that the medicine had antiviral activity against other viruses, including coronaviruses.[5] This advance testing showed "real foresight," Schaletzky says. She recommends testing existing compounds on all viruses of concern to accelerate pandemic preparedness.

Recent cost estimates for developing one new drug range from $314 million to $2.8 billion.[6] Kumar agrees that repurposing could boost future drug development by saving time and money in early-stage R&D. Because repurposed drugs have toxicology data available from previous clinical trials, these studies do not have to be repeated, he says.

Remdesivir has shown that successful repurposing is possible, and the market has taken note, Kumar says. The financial benefits have also been demonstrated. Gilead reported that overall product sales rose 26% in the fourth quarter of 2020, to $7.3 billion, "primarily due to Veklury® (remdesivir)."[7]

Most notably, the COVID-19 pandemic also heralded the arrival, rapid development, and global distribution of a new category of biotherapeutics: messenger RNA (mRNA)–based vaccines.

Conventional vaccines trigger an immune response by introducing small amounts of inactivated virus into the body; mRNA vaccines take a different approach. These vaccines carry a strand of genetic material containing instructions to produce a specific viral antigen, such as a protein from the SARS-CoV-2 coronavirus that causes COVID-19. Once an mRNA vaccine is in our cells, our bodies produce the protein it codes for, which prompts our immune systems to generate antibodies.

The process for making mRNA vaccines is much different than that for conventional ones. Conventional manufacturing requires dedicated facilities for multiple steps of cellular biotechnology, including fermentation, inactivation, harvesting, and purification. mRNA vaccines, on the other hand, are synthetically manufactured in a cell-free process that can be performed

in a laboratory. This is also a sophisticated process that involves several biotechnology steps, but because cell culture is eliminated it is far more quickly reproduced across facilities.

The speed of growth in mRNA technologies has been staggering. As Ryan Cross writes in Chemical & Engineering News, "Before 2020, the number of people to get an experimental injection of an mRNA therapy or vaccine numbered only in the low thousands. This year [2021], BioNTech, Pfizer, and Moderna distributed billions of their mRNA-based vaccines around the world. By late November, medical professionals had administered more than 437 million shots of an mRNA vaccine in the US alone."[8]

The pandemic has shown that mRNA is a fast, scalable therapeutic with the potential to revolutionize the pharmaceutical industry. The technology is still in its infancy, and adverse reactions to the COVID-19 mRNA vaccine have been reported.[9] But with 137 mRNA-based vaccine candidates in the pipeline[10] and an array of other therapeutics being developed globally,[11] the technology will continue to emerge, and safety profiles will be refined.

RETHINKING MANUFACTURING AND SUPPLY CHAINS

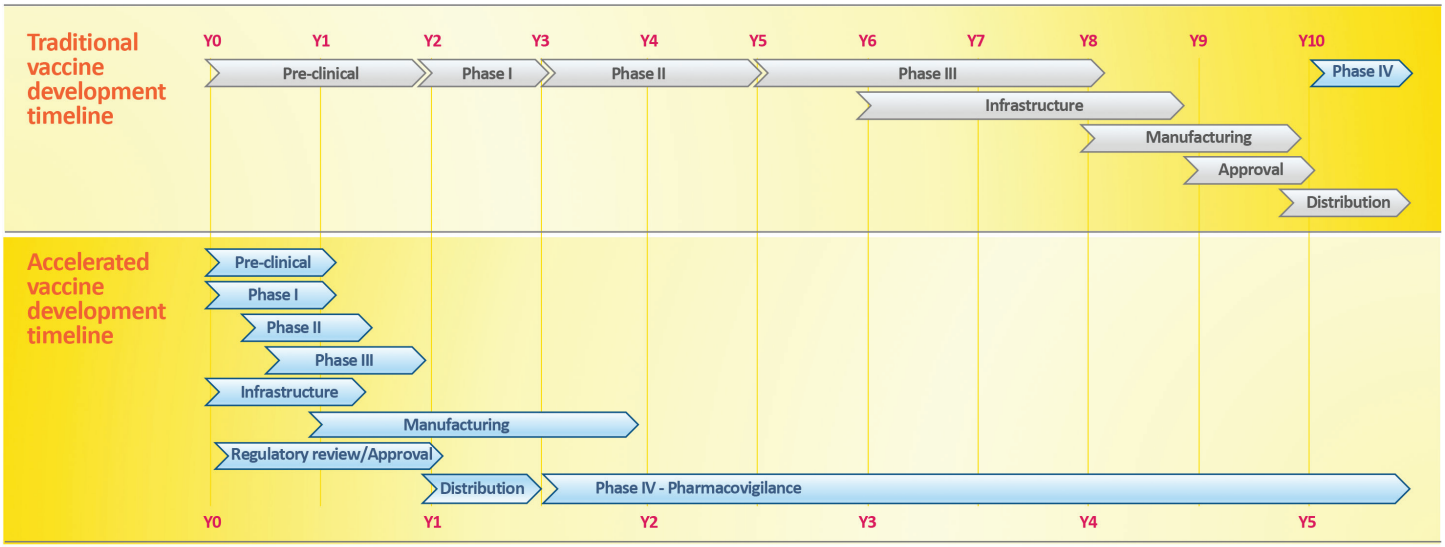
For some aspects of routine business, challenges that emerged during the COVID-19 pandemic revealed where there was room for a dramatic reconsideration of industry ideologies. The same principles behind the shortage of goods that left grocery shelves empty also influenced how fast pharma could move.

The pandemic prompted Schaletzky to reexamine supply and manufacturing practices at a societal level. For decades, she says, supply and manufacturing have been driven by profits. In practice, this means designing manufacturing processes to maximize productivity and minimize waste. Schaletzky cites the widespread use of just-in-time (JIT) supply chains, in which suppliers send goods just before they are required in the manufacturing process. Since goods are not stored locally, this approach can collapse when subjected to disruption or a crisis, she adds.

Lean, JIT strategies rely on many elements coming together seamlessly to function.[12] Schaletzky believes that supply challenges during the pandemic exposed the drawbacks of doing more with less, having fewer employees, and eliminating warehousing. She suggests that the solution is to build production systems that are "a bit more resilient" even if they cost "a bit more money."

Innovations along the supply chain will also be vital if future pharma is to reap the benefits of shrinking clinical trial and manufacturing timelines. That innovation may be as simple as making different choices early in a process to speed steps later.

For example, pharmaceutical companies typically start incorporating current good manufacturing practices (cGMPs) into their workflow as new products



COVID-19 accelerated vaccine development by performing steps in parallel rather than in succession.

Source: World Health Organization

enter clinical trials with hundreds of patients, Kumar says. cGMP guidelines provide guidance for consistency in processes, ingredients, and manufacturing conditions to ensure that a product is safe for human consumption and use. "If [pharmaceutical manufacturing] timelines are shrinking to less than 1 year, why not start with the best at the very beginning?" he asks.

Kumar points to Spectrum Chemical's bioCERTIFIED™ products, which undergo rigorous testing in the company's cGMP-compliant facilities to ensure that all chemicals and ingredients meet stringent quality standards. "Start with a fully tested material and you don't have to make any changes down the line," he says.

RED TAPE AND REGULATION

Responding to the race to save lives during the COVID-19 pandemic, global regulatory authorities approved vaccines and therapeutics in record time. Nine months after the World Health Organization (WHO) declared COVID-19 a pandemic, the US Food and Drug Administration issued the first emergency use authorization of the Pfizer-BioNTech COVID-19 vaccine.[13] The UK's Medicines and Healthcare products Regulatory Agency had approved the same vaccine several days earlier, on Dec. 2, 2020.[14]

The speed of that regulatory approval has prompted many experts to ask how a similar method can support the future deployment of lifesaving medications. Kumar suggests that the key may be the way regulatory agencies and pharmaceutical companies work together. Schaletzky agrees, heralding the success of COVID-19 vaccines as a "big team effort" that demonstrated the critical role of public-private partnerships.

Successful collaboration also depends on establishing clear roles for all parties,

Schaletzky says. Regulators should let pharmaceutical companies lead in their areas of expertise, such as drug development. The role for regulators is then to "make sure [new products] can move forward and see that questions that need to be addressed are addressed," she adds.

ALL TOGETHER NOW

The COVID-19 pandemic has demonstrated that fast pharma is achievable. Drug discovery, clinical trials, and manufacturing timelines have been reduced in ways that would have been unimaginable prepandemic; supply chains have been reexamined and streamlined; red tape has been cut; lives have been saved. Lessons learned will have a direct impact on future pandemic preparedness. These lessons may even extend to the development and manufacture of new vaccines and therapeutics for some of the planet's most destructive diseases.

Schaletzky sums up her observations by noting that the pandemic has shown that when the right structures are in place and the right people are around the table, scientific progress can be stunning: "What I've seen is that if everyone works together, we can do amazing things— and also really fast things."

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