Response and Resilience:

Lessons Learned from Global Life Sciences Ecosystems in the COVID-19 Pandemic

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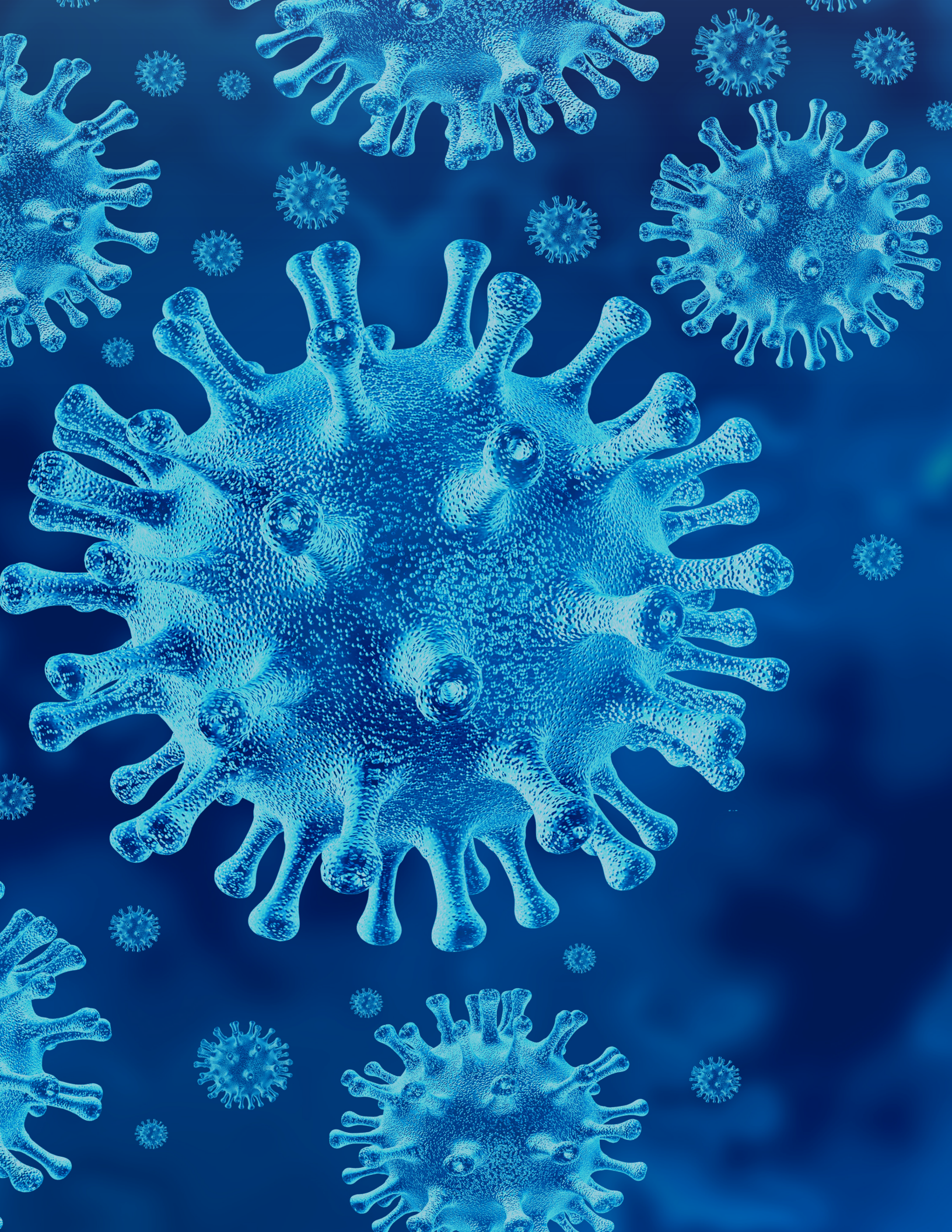


Executive Summary

The central goal of this study is to generate enhanced understanding of the favorable characteristics of global life sciences ecosystems that were able to energize their intellectual and infrastructural resources to respond to the COVID-19 challenge. It seeks to communicate the characteristics of best-practice ecosystems, so that the world and individual nations can be better prepared in the future.

"2020 Vision" has been the title of many plans, strategies, and projections over the past decade. It is doubtful that any of these forward-looking documents accurately foresaw the reality of 2020. While the year started out much like any other, the emergence of the coronavirus disease 2019 (COVID-19) quickly re-shaped daily life for much of the world's population and drove the global economy into recession.

What is now clear is that, without a vaccine or a group of effective treatments, COVID-19 will likely continue to impact humanity and commerce for a considerable amount of time. A race is on to find therapeutics and vaccines, and everyone has a stake in the race. Because of this, **COVID-19 has shone an extremely bright spotlight on the critical importance of life sciences research, and the commercialization of life sciences innovations, as mechanisms for effective pandemic response.** The ability of industrial life sciences ecosystems to develop diagnostic tests, vaccine candidates, and antiviral agents (and to rapidly scale-up their clinical trials, manufacturing, and distribution) will ultimately make the difference in resolving the pandemic.

There is, however, observable geographic variability in "capacity to respond," and there has been inconsistency in speed and effectiveness of actual national responses, suggesting that there are valuable lessons to be learned. From those locations that have responded effectively, we may learn "what to do" in terms of best practices in life sciences ecosystem development and the deployment of ecosystem assets in responding to a fast-moving pandemic event. Equally, those places that have struggled in their response may offer lessons regarding the gaps or barriers that constrained these ecosystems as they endeavored to mount a response.

This study identifies key lessons learned in national responses to COVID-19 and seeks to help policymakers across the globe focus on advancing favorable characteristics and emerging best practices that contribute to success. It does this through examining the approaches of 13 nations drawn from across the globe that have active biomedical life sciences ecosystems, producing a series of summary vignettes of approaches taken and lessons learned (see Figure ES-1).

A Viral "Perfect Storm"

Severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2, is a particularly challenging virus to control. Its incubation period is quite variable, at between 1 and 14 days, and symptoms may present between 2 and 14 days after infection. These symptoms range from being so mild that they go unnoticed through to quite rapid onset of acute life-threatening respiratory challenges and organ failure. The virus is transmitted human-to-human via respiratory droplets or via contact with contaminated surfaces, but there is also evidence of aerosolization of virus particles at a level that might be resulting in transmissions. Patients recovering from COVID-19 demonstrate far from a uniform immune serology, and it is unclear the level of protection accorded through prior infection. In some respects, it is a "perfect storm" of a virus—slow enough in causing symptoms to allow asymptomatic individuals to continue daily interactions that unknowingly spread the virus, just deadly enough to overwhelm healthcare systems in major hot spots, but apparently not deadly enough for some people to change their behaviors and take it seriously (thus perpetuating transmission).

Key Findings and Recommendations for Policymakers

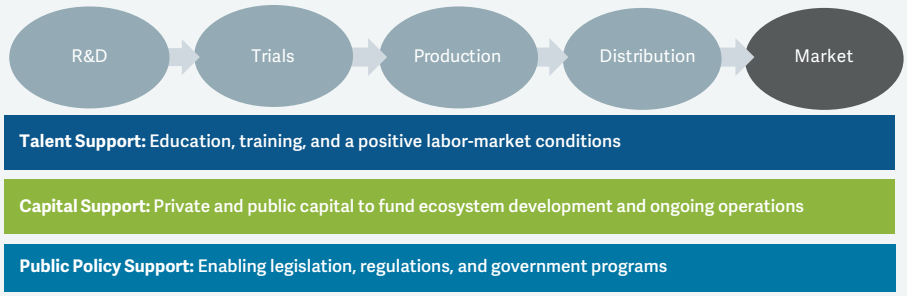
Life sciences advancements result from the presence and operations of a complex ecosystem, comprising intellectual assets, specialized infrastructure, a skilled workforce, complex production technologies, and sophisticated supply chains. These ecosystems comprise private-industry, academic, nonprofit, and government actors and are supported by a range of public- and private-sector capital resources. The life sciences ecosystem is presented in a simplified structure on Figure ES-2, comprising the key value chain from research and development (R&D) to market, and the cross-cutting support domains of talent, capital, and public policy that facilitate ecosystem operations.

Examination herein of pandemic-related activities, experiences, and challenges across global life sciences ecosystems has provided multiple lessons learned regarding the conditions that enabled life sciences ecosystems to effectively respond to the pandemic. It has also highlighted gaps and weaknesses in pandemic response for multiple nations.

Figure ES-1: Nations Reviewed for COVID-19 Life Sciences Ecosystem Lessons

Source: TEConomy Partners, LLC.

Figure ES-2: Simplified Life Sciences Ecosystem



Source: TEConomy Partners, LLC.

The report details 34 lessons learned (see Table ES-1 for a summary of many) across all key elements of the value chain from R&D to market and supporting domains of talent, capital, and public policy. Ultimately, the individual lessons can be summarized under five key themes with associated recommendations for consideration by policymakers:

1. **Prior investments and advancements toward a robust life sciences ecosystem matter greatly in responding to a pandemic.** The fact that, in the face of the COVID-19 pandemic, so many vaccine candidates and drugs have been brought forward into testing, trials, and emergency use is a heartening achievement and is a testimony to the foresight of those who have developed, work in, and support the complex life sciences R&D and industry ecosystems around the world. The complexity of the ecosystems that must be in-place to advance R&D, product development, and production and distribution of biopharmaceuticals, vaccines, and diagnostics is such that they cannot be stood up from scratch in a real-time situation. They must already be in place, fully operational, well proven, and well funded in advance of an emergent need.

   ***Recommendation** – Policymakers must prioritize and sustain investments in life sciences research infrastructure, workforce development, and advanced production systems. Enacted policies and regulations must support life sciences ecosystem development at scale and sustain favorable ecosystem operating conditions.*

2. **Promotion of collaborations is key to quickly mobilizing and pursuing new medical innovations.** Public- and private-sector collaborations, and inter-industry collaborations, have played a key role in rapidly advancing innovations for pandemic response. These collaborations often build upon the complementary and robust roles of public-supported academic basic research together with industry expertise in applied discovery, development, and clinical testing that routinely take place in high-functioning life sciences ecosystems. What the response to the COVID-19 pandemic has vividly demonstrated is the benefit of collaboration, even between peer companies, whereby different, but complementary, R&D and industrial strengths and capacities can be brought together for advancing medical innovations.

   ***Recommendation** – Policymakers should develop and align incentives to encourage collaborations that will advance and speed the development and commercialization of medical innovations and take advantage of the full capacities found across life sciences research institutions and industry.*

A Powerful Collective Scientific Response

The complete SARS-CoV-2 genome was decoded by Chinese scientists extremely quickly in the early stage of the emergence of the disease. The sharing of the coronavirus genome worldwide activated existing international life sciences ecosystems that investigated the pharmacopoeia of drugs for potential candidate therapies against the virus, accelerated investigation of new molecules for potential effectiveness against the disease, and supported rapid R&D in existing and novel vaccine development and delivery platforms. Researchers from academia, government, and industry have shared data and rapidly stood-up domestic and international collaborations to access and share supercomputing resources, chemical libraries, analytical instrumentation, and other research tools. Governments, nonprofits, and private industry funders have stepped-up to provide large-scale capital resources; and private industry has taken substantial financial risk in accelerating product development and even building additional manufacturing capacity "at risk," in the humanitarian quest (both for human health and the economy) to get therapeutics and vaccines into clinical application against the virus as soon as physically possible. It has represented an unprecedented globally collaborative mobilization of research, production, and capital (both financial and intellectual).

3. **The convergence of digital technology with life sciences helps accelerate innovations and supports ecosystem resiliency.** One broad benefit of the COVID-19 pandemic has been the acceleration in the use of digital technologies across all stages of life sciences development and the industrial value-chain. Digital technologies are proving effective in speeding up research insight and innovation, sustaining trials and regulatory oversight, building supply chain transparency, facilitating trade, and supporting safer (remote) clinical healthcare interactions.

   Recommendation *– For the future, policymakers should continue to promote the use of digital technologies in R&D, clinical testing, supply chain management, and healthcare delivery and seek ways to further the integration across distinct activities to improve the effectiveness of life sciences ecosystems.*

4. **Flexibility in government regulatory approaches is making a difference.** Given the typical drug and vaccine development timelines of a decade or more, the speed of the overall response mounted by the global life sciences community to COVID-19 is nothing short of astonishing. This has been accomplished, in part, because of flexibility shown in regulatory processes by government. Perhaps the most-publicized area of flexibility is in the clinical testing of potential vaccines and therapies through mechanisms such as emergency use authorizations, compassionate use, conditional market authorizations, and short timeframe approvals, while still allowing for thorough scientific evaluation of a medicine's benefits and risks. Other less publicized forms of flexibility have also been advanced in the use of digital technologies in clinical trials

   The rapid acceleration of research, innovation, product development, commercialization, and production scale-up (all performed in the midst of an ongoing global pandemic affecting those doing the work) represents a collective effort deserving worldwide appreciation.

monitoring, remote manufacturing inspections, ability to make changes in suppliers, and allowance for joint ventures and other collaborations.[1]

Recommendation *– Policymakers should consider how increased flexibility with accountability can be achieved on a more regular basis as a means for ensuring that unmet medical needs are addressed to improve patient lives.*

5. **The existing business environment for innovation in life sciences ecosystems has proven to be highly agile and able to be effectively leveraged through the COVID-19 pandemic.** In challenging times there is a strong impetus for government to be seen to be "doing something." COVID-19 has certainly required critical government interventions and actions, but it is important to recognize that care must always be taken to avoid actions that may undermine the favorable ecosystem characteristics needed to maintain life sciences advancements and innovation. There are multiple "fundamentals" that are influenced by governments that must be sustained in order for life sciences ecosystems to flourish, requiring for example:

    - Substantial commitment of government funds to supporting R&D through well-funded research grant funding agencies, together with favorable tax treatment of private sector R&D investments.
    - Sustaining effective rules against trade barriers, and facilitating international trade, to enable resilient and flexible supply chains to operate that reliably meet demand for medical products.
    - Maintaining predictable and sustainable payer pricing systems that balance the need to manage health care payer costs with the need for return-on-investment for innovative life sciences companies.
    - Operation of a flexible, science-based regulatory system.
    - Robust intellectual property protections and enforcement.

1 Jerry Stewart, et al. "COVID-19: A Catalyst to Accelerate Global Regulatory Transformation." Clinical Pharmacology & Therapeutics. 29 September, 2020. https://ascpt.onlinelibrary.wiley.com/doi/10.1002/cpt.2046

The last bulleted fundamental is particularly critical. One of the core elements for life sciences innovation is having in place robust protection and enforcement of intellectual property rights, which provide the necessary incentives to advance novel medicines — especially when it may cost billions of dollars in private investment to bring a novel medicine to market. Beyond ensuring private investment funding, IP protections are proving to be effective in enabling collaborations to take place between organizations with solutions to different pieces of the puzzle (even among traditionally competing firms). With robust IP protections, innovators can collaborate and work together to advance such solutions, knowing that their R&D efforts, inventions, and creativity are secure. The first bulleted fundamental on government funding support for research is similarly important, and the life sciences ecosystem has responded well to government incentives aimed at furthering R&D into novel antivirals and vaccines and increasing production capacities within their nation.

***Recommendation** – Policymakers need to ensure that the core elements of high-functioning life sciences business environments are in place to facilitate innovation advancement. Some of the key elements to be advanced include strong IP protections and provision of secure market access for innovative medicines.*

The above recommendations are rooted in multiple lessons learned during the COVID-19 pandemic. Table ES-1 summarizes many of the lessons covered in the full report.

Table ES-1: Summary of Main Themes and Related Lessons Learned

Prior investments and advancements towards a robust life sciences ecosystem matter greatly in responding to a pandemic.

- Innovations derive from a diversity of university, government labs, non-profit research institutions and industry research settings with no single group of actors dominating.
- Research grants and development support set a key foundation for rapid innovation.
- Large-scale signature R&D and scientific infrastructure (e.g. supercomputers, synchrotrons, etc.) pay dividends.
- Scaling a life sciences workforce requires foresight and a long-time horizon.
- Venture capital and angel investment activity helps to prime the pump of innovation.
- Multiple sources of critical supplies are beneficial.

Promotion of collaborations is key to quickly mobilizing and pursuing new medical innovations.

- Collaborations appear to have accelerated the research and development of candidate vaccines and therapeutics.
- Inter-industry partnerships and collaborations make a difference.
- Big and small players will be contributing solutions and collaborating.

The convergence of digital technology with life sciences helps accelerate innovations and supports ecosystem resiliency.

- Advancement of life sciences, digital and advanced analytics convergence skills is required.
- Adoption of virtual and contactless solutions sustains clinical trials.
- Regulatory oversight of GMP production can be accomplished remotely.
- Digital supply chain monitoring is desirable and feasible.
- Virtualization or digitalization of healthcare has accelerated.

Flexibility in government regulatory approaches is making a difference.

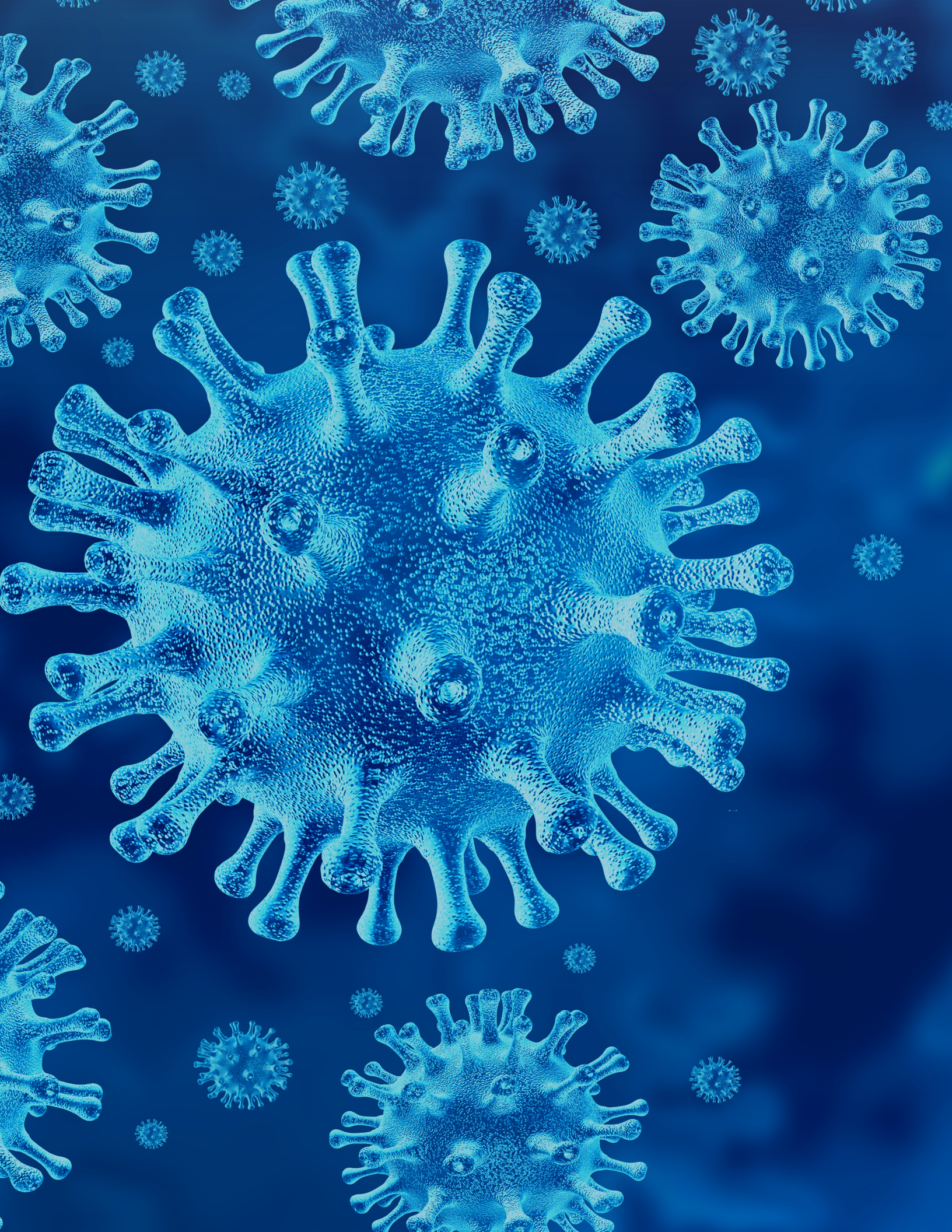
- Emergency regulatory flexibility in use of new medicines is required.
- Regulatory oversight of GMP production can be flexible in its approach.
- Universal, patient centric, access to care, diagnostics, therapeutics, and vaccines must be facilitated.

Existing business environment for innovation has proven to be agile and able to be effectively leveraged through incentives and co-investment.

- Public co-investment can be significant as a catalyst for commercial innovation advancement.
- Commitment to building strategic stockpiles and government purchasing is required.
- Government can facilitate the implementation of new biopharma production technologies.

The COVID-19 crisis has vividly illustrated the critical importance of life sciences research and innovation systems and the ecosystems that support the advancement of innovations through commercial deployment to address health needs. The pandemic has equally provided multiple lessons learned regarding what worked well in addressing the crisis and has highlighted gaps and weaknesses in pandemic response for multiple nations. These have been hard-earned lessons learned, with less-than-optimal responses to COVID-19 contributing to large-scale morbidity and mortality loads globally and extracting a heavy economic and social cost for humanity.

The coronavirus caught humanity's leadership off guard in many places across the globe. When the next high-threat infectious disease emerges (and such an emergence is likely), all need to be better prepared. Funding, building, reinforcing, and sustaining robust life sciences ecosystems is a key component of that preparation. The lessons learned and recommendations herein are proffered as core elements for consideration in building resiliency and responsiveness into critically important life sciences ecosystems worldwide.



Introduction

The coronavirus disease 2019 (COVID-19) pandemic has shone a spotlight on the importance of national and international research and development (R&D), innovation, and manufacturing ecosystems in life sciences. As a novel virus, severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2, has illustrated the critical importance of having robust life sciences innovation ecosystems in place that can pivot to address a new and urgent challenge.

Were it not for the intellectual and scientific horsepower of industrial, academic, and governmental R&D communities, and their ability to characterize the virus and develop diagnostic tests, the pandemic would be orders of magnitude worse. The capacity of nations and the global life sciences community to develop and produce diagnostic tests, vaccine candidates, and therapeutic agents (and to then scale up their clinical trials, manufacturing, and distribution) is the direct result of prior investments in developing the science, technologies, and skilled people that power R&D, innovation commercialization, and advanced biopharmaceutical and medical product manufacturing.

The geographic variability in "capacity to respond," and the inconsistency in speed and effectiveness of actual national responses, suggests that there are valuable lessons to be learned. From those locations that have responded effectively, "what to do" may be learned in terms of best practices

A Highly Complex Sector

Even before the COVID-19 pandemic, it was well understood that the bar to advance life sciences development is higher than many other advanced industries and is rising with the fast pace and complexity of scientific advances.

The life sciences industry is more connected to, and dependent upon, basic science discoveries and their translation for driving innovations than other advanced industries. The industry not only has to advance product discovery, but also has to innovate and advance cutting-edge manufacturing processes to bring forward novel products (in complex areas, e.g., such as genomic-based medicines, immunotherapies, cell therapies, diagnostics, and vaccines). Advancing products from discovery through clinical trials and onward into production and distribution is complex, costly, time consuming, and highly regulated.

It is no easy feat to rapidly accelerate innovation in a pandemic—yet it seems some nations have done just that.

in life sciences ecosystem development and the deployment of ecosystem assets in responding to a fast-moving pandemic event. Equally, those places that have struggled in their response no doubt offer lessons regarding the gaps or barriers that constrained these ecosystems as they endeavored to mount a response. This study examined 13 nations from across the globe that have active biomedical life sciences ecosystems (see Figure 1). This report seeks to identify and summarize many of the main lessons learned.

Study Approach

The work herein recognizes that life sciences advancements result from the presence and operations of a complex ecosystem, comprising intellectual assets, specialized infrastructure, a skilled workforce, complex production technologies, and sophisticated supply chains. These ecosystems comprise private industrial, academic, nonprofit, and governmental actors and are supported by a range of public- and private-sector capital resources. Those ecosystems that innovate and produce products for human clinical application operate, by necessity, under strict regulations regarding efficacy and safety, and public policy plays a significant role in governing the operation of the ecosystems and their markets.

Understanding the structure of these ecosystems, or their operational "framework," is a foundational requirement for considering the context of lessons to be learned. To that end, the first step taken in the study approach was to develop an overview structure of a biomedical life sciences ecosystem framework. The framework (Figure 2) serves as the contextual canvas upon which lessons learned may be placed and understood.

As shown in Figure 2, the framework comprises a central "value chain," which contains the continuum of core activity from basic scientific inquiry, through applied research, preclinical and clinical testing, on-

Figure 1: Nations Reviewed for COVID-19 Life Sciences Ecosystem Lessons

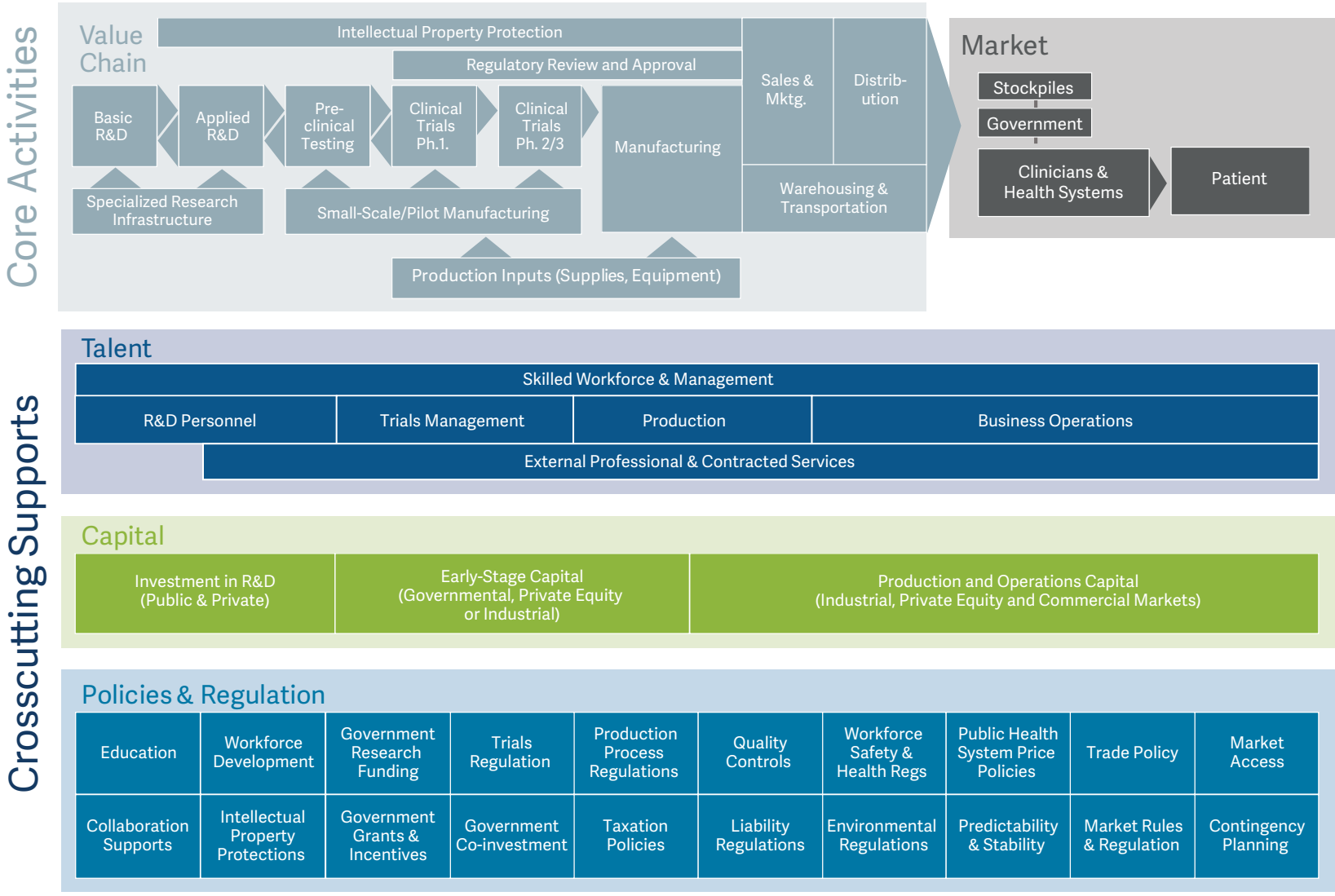
Source: TEConomy Partners, LLC.

ward into commercial development, manufacturing, distribution, and market application. In support of the operations of the value chain are three principal domains: talent (the human intellectual and skills resources required to operate the value chain), the capital required to build and fund activities across the value chain, and the public policies and regulations that support and impact the operation of the ecosystem. This framework is used as an organizing element in understanding and contextualizing the lessons learned from the varied life sciences ecosystems that deployed in response to COVID-19 across the globe.

The study has focused on identifying lessons learned from two perspectives. First, it considers the general lessons learned that may not be geographically specific and are observable across multiple life sciences ecosystems. Second, it reports on the research team's series of nation-specific examinations, producing summary vignettes of approaches taken and lessons learned in the countries shown in Figure 1. These nations were selected for examination because they have active biomedical life sciences ecosystems, yet the variation in response to COVID-19 and the effectiveness of their responses have differed quite widely (providing a basis for investigating what has worked and what has not worked in these locations).

The central goal of this study is to generate enhanced understanding of the favorable characteristics of national life sciences ecosystems able to energize their intellectual and infrastructural resources to respond to the challenge. It seeks to communicate the characteristics of best-practice ecosystems, so that the world and individual nations can be better prepared in the future.

Figure 2: Biomedical Life Sciences Ecosystem "Framework"



Source: TEConomy Partners, LLC.

Lessons Learned Across Life Sciences Ecosystems

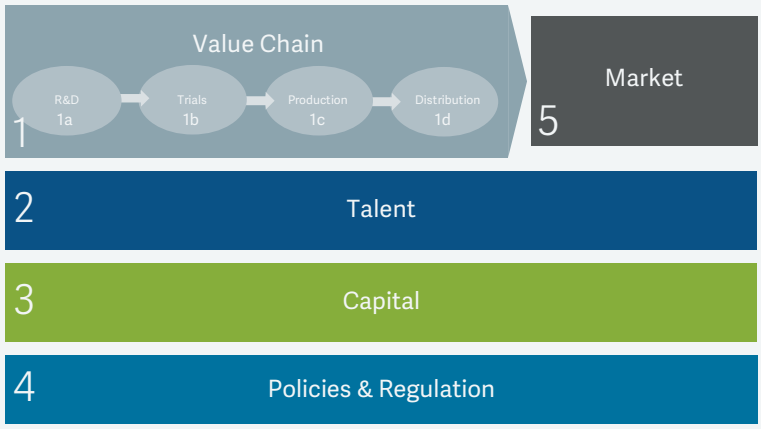
The complexity of the ecosystem required to advance R&D, product development, and production of biopharmaceuticals, vaccines, and diagnostics is such that it cannot be stood up from scratch in a real-time situation. It must already be in place, fully operational, and proven well in advance of an emergent need.

The research findings and lessons learned from this review are organized by macro framework element, as illustrated in Figure 3. The key focus is on life sciences ecosystems in relation to the development, production, and distribution of biopharmaceuticals and related products, including diagnostics, vaccines, and therapeutics (both small and large molecule). Much of what is found also holds relevance to the development and production of other critical products required in the pandemic response, including medical devices and supplies (such as personal protective equipment [PPE]).

Framework Element 1: The Central Value Chain

When a new biopharmaceutical product is deployed for clinical application, it will have followed a complex, time-consuming, and monetarily expensive path that originated in the initial scientific research insights upon which it is based and progressed through a rigorous process of preclinical testing, human trials, regulated Good Manufacturing Practice (GMP) development, packaging development, and supply-chain and distribution structuring. The

Figure 3: Simplified Framework



Source: TEConomy Partners, LLC.

degree of scientific, technical, and regulatory rigor deployed across this process is uncommon in other manufactured products.

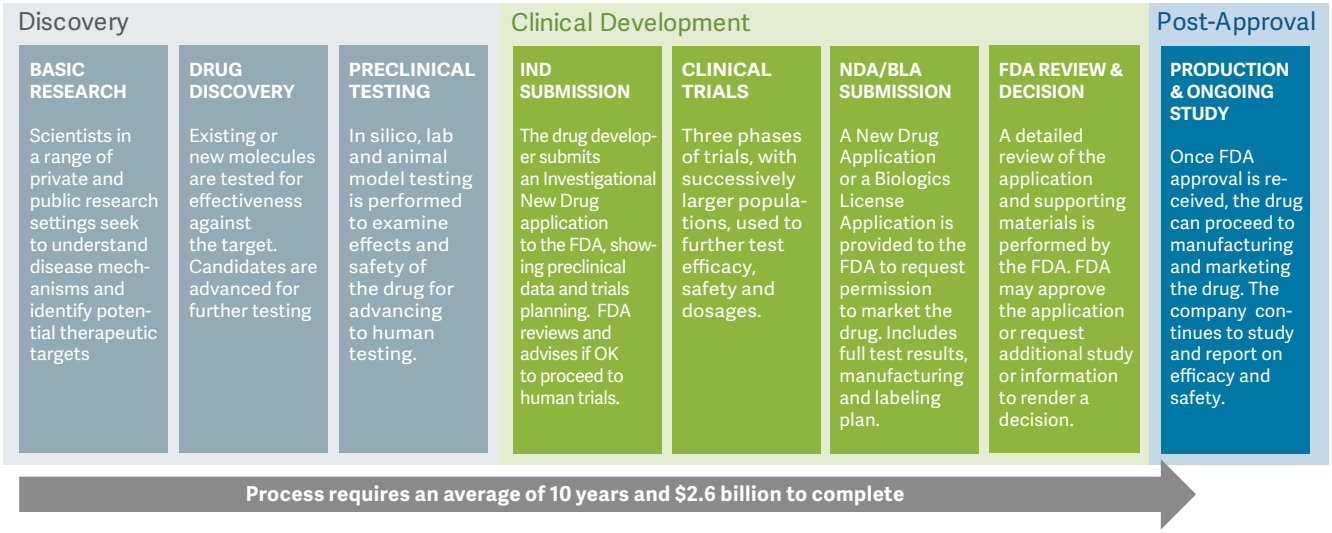
PhRMA notes that:

> *On average, it takes at least ten years for a new medicine to complete the journey from initial discovery to the marketplace, with clinical trials alone taking six to seven years on average. The average cost to research and develop each successful drug is estimated to be $2.6 billion. This number incorporates the cost of failures – of the thousands and sometimes millions of compounds that may be screened and assessed early in the R&D process, only a few of which will ultimately receive approval. The overall probability of clinical success (the likelihood that a drug entering clinical testing will eventually be approved) is estimated to be less than 12%.*[1]

The process to advance from first scientific insight just through the full R&D process comprises the steps shown in Figure 4. This is the process for biopharmaceuticals regulated by the U.S. Food and Drug Administration (FDA), and it is typical of that required in other nations. The development pathway for **vaccines** is similarly complex and regulated—understandably so given that vaccines are preventative agents provided to healthy patients. Vaccines carry their own unique challenges that complicate development, including for example, the ability of targeted pathogens to mutate and develop subtypes, challenges in activating a robust immune response in diverse patient populations, and the fact that vaccines often target infant populations who are still developing. As noted by the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA):

> *The intention of a vaccine is to prevent an infection and/or a disease in a healthy population. Since vaccines are given to healthy people throughout life, from childhood to older age, it is necessary to establish a very large safety database, by carrying out many studies involving thousands of participants, before a vaccine can be licensed. Ultimately, the benefit of the vaccine must significantly outweigh any risks. Before a vaccine is licensed and brought to the market, it undergoes a long and rigorous process of research, followed by many years of clinical testing. The overall development*

Figure 4: Primary Steps in the Biopharmaceutical R&D Process



1 PhRMA. Biopharmaceutical Research & Development: The Process Behind New Medicines. Accessed online at: http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf.

of a vaccine consists generally of a discovery phase, a pre-clinical phase, the clinical development phase (phases I to III) and the post licensure phase (phase IV), and it takes on an average about 10 to 15 years.

Key Finding

Given typical drug and vaccine development timelines, the speed of the overall response mounted by the global life sciences community to COVID-19 is nothing short of astonishing. The rapid acceleration of research, innovation, product development, commercialization, and production scale-up (all performed in the midst of an ongoing global pandemic affecting those doing the work) represents a collective effort deserving worldwide appreciation.

Diagnostic tests are an order of magnitude less costly and time consuming to develop. They are able to be developed, tested, and reviewed more rapidly than therapeutics and vaccines because they do not themselves represent a product administered into a patient. Certainly, a diagnostic has to be proven to have efficacy in clinical use, because false positives or false negatives can have serious implications for patient health and the ongoing transmission of a disease. A false positive may result in a patient being prescribed unnecessary treatments or therapeutics that may have a risk of adverse side effects, while a false negative leads to a misdiagnosis of a patient, missed opportunity for timely and effective treatment of the patient, and (in the case of an infectious disease) enhanced

A Multidisciplinary International Response

The fact that, in the face of the COVID-19 pandemic, so many vaccine candidates and drugs have been brought forward into testing, trials, and emergency use is on the one side an astonishing achievement; but, it is also a testimony to the foresight of those who developed, work in, and support complex life sciences ecosystems around the world.

The full SARS-CoV-2 genome was decoded extremely quickly by Chinese scientists in the early stage of the emergence of the disease—an achievement possible only because of previous investment in genomics technologies built upon original U.S. and UK investment in the Human Genome Project and subsequent rapid advancement of genomics tools and techniques. The sharing of the coronavirus genome worldwide activated international life sciences ecosystems that investigated the existing pharmacopoeia of drugs for potential candidate therapies against the virus, accelerated investigation of new molecules for potential effectiveness, and supported rapid R&D in existing and novel vaccine development and delivery platforms. Researchers from academia, government, and industry have shared data and rapidly stood up domestic and international collaborations to access and share supercomputing resources, chemical libraries, analytical instrumentation, and other research tools.

Government, nonprofit, and private industry funders have stepped-up to provide unprecedented capital resources, and private industry has taken substantial financial risk in accelerating product development and even building additional manufacturing capacity "at risk," in the humanitarian quest (both for human health and the economy) to get therapeutics and vaccines into clinical application against the virus as soon as physically possible. It has been a mobilization of research, production, and capital (both financial and intellectual) akin to that deployed in previous world wars, only this time the war is against a microscopic insentient entity and the whole world is fighting the threat together.

The Importance of Fundamental Research

Basic (fundamental) life sciences research is typically conducted in academic or government labs and seeks understanding of the processes that govern life. Basic research advances the stock of knowledge upon which later applied discoveries may build. Applied research focuses on developing technologies, solutions, or processes with practical application to observed life sciences opportunities, challenges, and needs. It is important to note that a healthy basic research environment is the platform upon which later applied research advancements are built.

Applied R&D in medicine is built upon a vast library of fundamental research advancements—advancements that elucidated the role of microbes in disease, immune system function, processes of evolution and mutation, the structure of DNA, and discovery of chemical elements, to name just a handful. The advanced tools used in drug discovery similarly are built upon fundamental advancements in chemistry and physics. Advancements in mathematics and computational theory are similarly fundamental in enabling the advanced data analysis, artificial intelligence, visualization, and modeling algorithms used by life sciences companies and research teams.

The advancement of basic science is very much dependent on public funding. Basic research is inherently nonmarket in nature (focused on phenomena or subject matter without an immediate line-of-sight to a market application). Because of the speculative nature of early fundamental research, because of the long time horizons involved in the performance of much basic inquiry, because of the risk of experiment failures, but most importantly, because of the lack of immediate line-of-sight to a market, private-sector investment in basic science is relatively scarce.

potential for the patient to infect others (e.g., through not being quarantined or encouraged to social distance). The development of novel diagnostic platforms can be a lengthier process (more akin to medical device or biopharmaceutical development); but, for the most part, diagnostics are developed to use existing platform technologies at clinical diagnostic laboratories or point of care (POC) locations.

The complexity of the ecosystem that must be in-place to advance R&D, product development, production, and distribution of biopharmaceuticals, vaccines, and diagnostics is such that it cannot be stood up from scratch in a real-time situation. It has to be already in-place, fully operational, and well proven in advance of an emergent need. Similarly, the complexity of the process to advance a novel drug, vaccine candidate, or diagnostic platform to market, and the timeline for doing so, places further urgency on ensuring life sciences ecosystems are constantly innovating, advancing, and equipped to respond to urgent needs.

Framework Element 1a: Life Sciences R&D

The story of the global life sciences ecosystem response begins with R&D. R&D forms the basis of discovery that then underpins innovation. There are certainly locations that serve only to host routine manufacturing or a distribution center without being engaged in innovation. Such locations would not be characterized as having a complete life sciences ecosystem, because they are limited in innovation and advancement of novel solutions to challenges—rather, they primarily work with the innovations that were generated elsewhere. Such non-innovative locations are generally at risk of losing their sectoral position if other locations are able to offer more inexpensive labor, taxation advantages, or other incentives for relocation. **R&D, on the other hand, which is rooted in scientific infrastructure and, most notably, the tacit knowledge of skilled and highly educated people, is a key anchoring force in a life sciences ecosystem.** Advanced manufacturing locations can

also be innovation hubs if they perform proactive work to innovate more efficient systems, advance continuous manufacturing processes, etc.

The COVID-19 pandemic has illustrated the central contribution that R&D and associated innovation plays within the life sciences framework and an ability to mount a scientific and technological-based response. Several global ecosystems have proven particularly effective, and there are significant **lessons to be learned** from them.

Summary of Lessons Learned for Life Sciences R&D:

- *Innovations derive from a diversity of research settings in universities, government labs, nonprofit research institutions, and industry, no single typology dominates.*
- *Collaborations appear to have accelerated candidate vaccines and therapeutics.*
- *R&D-performing entities themselves will be negatively impacted in a pandemic.*
- *Prior investment in large-scale signature R&D and scientific infrastructure (e.g., supercomputers, synchrotrons, etc.) pays dividends.*
- *The economic cost of a pandemic dwarfs the investment in the R&D resources needed to address it.*

Lesson 1a.1: Innovations derive from a diversity of research settings in universities, government labs, nonprofit research institutions, and industry, no single typology dominates.

As ecosystems have responded to the R&D challenges of the pandemic, it is evident that innovations addressing the challenges of COVID-19 are being derived from a broad range of organizational types and sizes. Diagnostics, vaccine candidates, and therapeutics have been rapidly researched and advanced into trials by many organizations including private industry (ranging from small entrepreneurial firms through major multinational biopharmaceutical companies), research universities and academic medical centers, independent nonprofit research institutes, and government labs.

No single organizational type dominates the innovation sphere, and **it is notable that many of the faster-advancing approaches have been driven forward by collaborations between organizational types.** Private industry is the most cross-cutting of all organizational types, demonstrating a contributory presence in the case of almost all innovations advancing toward commercialization to address the pandemic.

Lesson 1a.2: Collaborations appear to have accelerated candidate vaccines and therapeutics.

In normal situations, it is logical for an inventing entity to keep its invention closely held and seek to singularly advance its innovation with a clear goal of maximizing return on investment. Certainly, clinical trials will engage multiple parties, but usually a single entity is in control and structured to receive the core returns. The urgency of need for products to address COVID-19 has evidently opened up a more dynamic marketplace for joint ventures in commercialization and intensive collaboration. Collaborations have occurred between previous competitors, between nonprofit and for-profit entities, and internationally. Figure 5 summarizes information reported by the Regulatory Affairs Professional Society on many advancing COVID-19 vaccine candidates, and it is apparent that the vaccines more rapidly advancing into trials have a propensity to demonstrate significant collaborations in their development and advancement.

Collaborations include partnerships between companies and close collaboration between universities and other R&D organizations and companies. In several cases, the collaborations are international, crossing national boundaries. Some examples of collaborations include the following:

- The University of Oxford (UK) and AstraZeneca (HQ: UK) collaboration to advance development and production of the ChAdOx1 nCoV-19 vaccine innovated by the Jenner

National Findings: Nonprofit Research Institutes Contribute as Ecosystem Actors

Independent nonprofit research institutions have played an important innovator role during the pandemic.

Brazil—Initiatives to develop a domestic vaccine candidate are being coordinated on the government's behalf by the Oswaldo Cruz Foundation, a long-standing public-health research institution.

France—One of the strongest directed efforts at vaccine development is coming from the Pasteur Institute, a nongovernment, private nonprofit laboratory with a long history in microbiology and, more recently, molecular biology.

South Africa—Recognizing that the fight against COVID-19 leverages some of the same contact-tracing and public-education skills needed to fight the HIV and tuberculosis epidemics in-country, the nation mobilized entities including (but not limited to) the Aurum Institute that have long experience in these other infectious diseases.

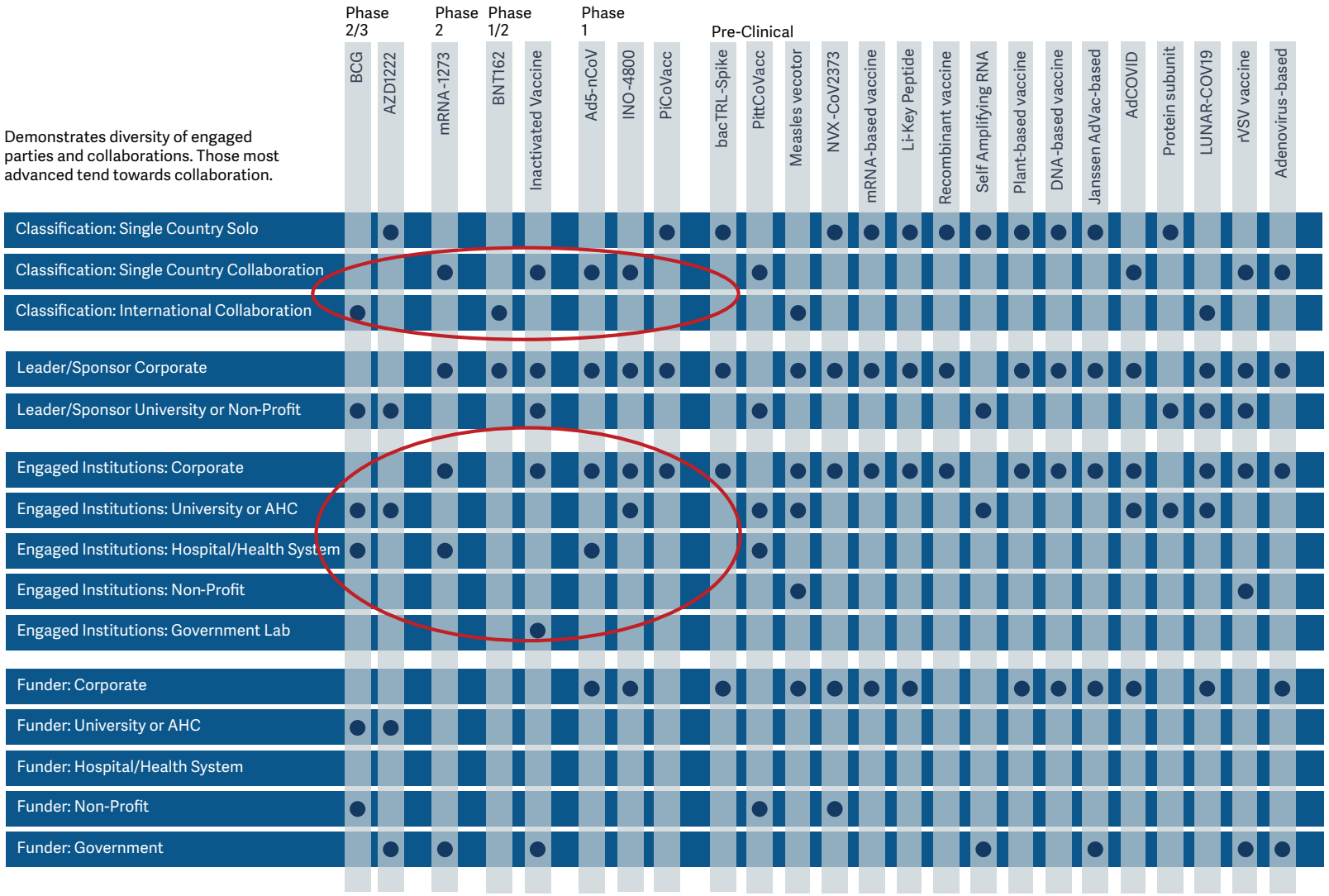
UK—The Oxford vaccine candidate reflects a collaboration with the Jenner Institute, now loosely affiliated with the university, but with a long history as an institute for farm animal health supported by both government and private contributions.

USA—The nonprofit Battelle Memorial Institute rapidly innovated and produced a novel container-based system using vaporized hydrogen peroxide for on-site decontamination and sanitation of PPE.

Institute and Oxford Vaccine Group, at the University of Oxford.

- Roche Holding AG (HQ: Switzerland) and Gilead Sciences (HQ: USA) teaming-up for trials for a drug combination to treat COVID-19.
- BioNTech SE (HQ: Germany) and Pfizer Inc. (HQ: USA) collaborating to advance candidates from BioNTech's messenger ribonucleic acid (mRNA) vaccine program.
- Merck (HQ: USA) and the nonprofit scientific research organization IAVI (HQ: USA) collaborating to develop a vaccine candidate using the recombinant vesicular stomatitis virus (rVSV) technology that is the basis for Merck's Ebola Zaire virus vaccine.
- Sanofi (HQ: France) and GSK (HQ: UK) co-developing an adjuvanted vaccine for COVID-19, using innovative technology from both companies. Sanofi has contributed its S-protein COVID-19 antigen, which is based on recombinant DNA technology, while GSK contributed its proven pandemic adjuvant technology.
- Heat Biologics, Inc. (HQ: USA) collaborating with Waisman Biomanufacturing, a subsidiary of the University of Wisconsin (USA), to manufacture Heat's experimental COVID-19 vaccine.

Figure 5: Engagement of Various Organizational Types in Advancing COVID-19 Vaccines into Clinical Trials. Evidence of Positive Effect of Collaborations in Information Reported by the Regulatory Affairs Professionals Society[1]



1 TEConomy analysis of data reported by the Regulatory Affairs Professionals Society (RAPS). https://www.raps.org/news-and-articles/news-articles/2020/3/Covid-19-vaccine-tracker. It should be noted that this is not a complete listing of vaccine candidates.

A Diversity of Collaborations

In **Brazil**, the Ministry of Science, Technology, Innovation and Communication (MCTIC) and the University of Sao Paulo formed and funded a new Virus Network bringing together specialists, government representatives, funding agencies, researchers, and universities to integrate initiatives. Also, the Instituto Butantan is collaborating on vaccine development with the Bill & Melinda Gates Foundation and pharmaceutical companies.

In **China**, the Global Health Drug Discovery Institute—a nonprofit comprising a partnership among the School of Pharmaceutical Sciences at Tsinghua University, the Bill & Melinda Gates Foundation, and Beijing municipal government—was an early mover in sharing its compound libraries and opening its high-throughput screening capacity to researchers. Much of the institute's capability and findings are shared through a portal hosted via an open GitHub repository.

In **Singapore**, the cPass rapid test was developed through a collaboration between the Duke-National University of Singapore Medical School, the A*STAR Diagnostics Development Hub, and GenScript (a Chinese-headquartered biotech firm). Singapore's Immunology Network is also collaborating with Chugai Pharmabody of Japan on antibody optimization, and Duke-NUS received a national grant to work with US-based company Arcturus on mRNA vaccine development.

The largest-scale international collaboration is being coordinated by the **World Health Organization (WHO)**. "Solidarity" is an international clinical trial for COVID-19 solutions. The Solidarity Trial compares options against standard of care, to assess relative effectiveness. As of July 1, 2020, nearly 5,500 patients had been recruited in 21 countries (among 39 countries that have approvals to begin recruiting). WHO reports that more than 100 countries in all 6 WHO regions have joined or expressed an interest in joining the trial.

Lesson 1a.3: R&D-performing entities themselves will be negatively impacted in a pandemic.
Insights and innovations stemming from the life sciences R&D community represent a key tool in addressing the challenge of COVID-19, yet at the same time, the R&D environment itself has been negatively impacted by the pandemic. R&D is an essentially human activity, advanced by a highly skilled scientific and technical workforce—typically working in relatively close confines in research laboratories.

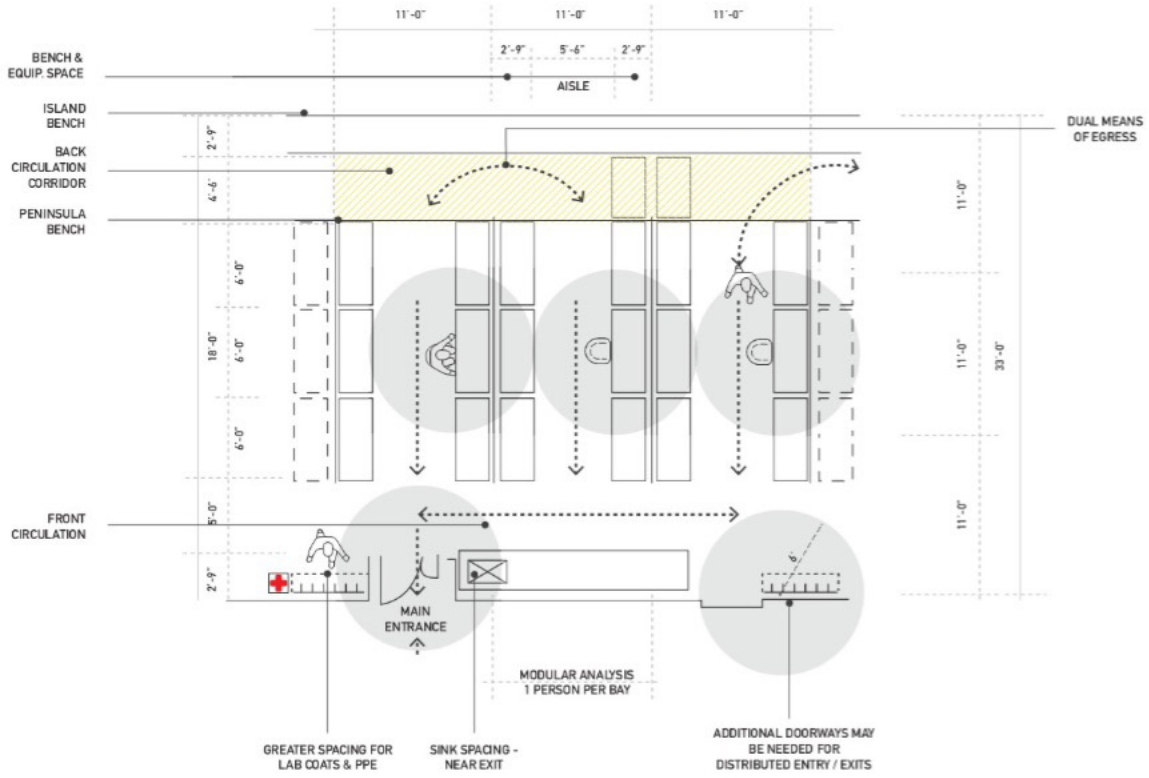
Universities closed or deeply restricted campus activities, and for those labs remaining open, the requirements of social distancing substantially reduced operational capacity, and thus productivity, in labs and specialized research spaces.

Similar space and occupancy restrictions led to a decline in corporate research productivity also. McKinsey & Company (McKinsey) reports, based on a survey of life sciences R&D leaders, that at life sciences companies "R&D labs are operating at below 50 percent of normal capacity" and "across all R&D related groups, companies estimate productivity has fallen by between 25 and 75 percent due to remote working."[2]

Architects and space planners specializing in life sciences research environments at Flad Architects note that: "the recent and ongoing COVID-19 Pandemic is requiring new paradigms and a fundamental shift in how we think about research design and space use at all levels of interaction. With the goal of lessening density and creating

2 McKinsey & Company. "The Next Normal." https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/Covid-19-implications-for-life-sciences-r-and-d-recovery-and-the-next-normal.

Figure 6: Researcher Density Greatly Reduced Through Lab Social-Distancing Requirements.



Source: Flad Architects

safer environments, many perspectives will be needed to plan for safe and effective solutions"[3] (see Figure 6).

It is anticipated that there will be long-term implications for life sciences R&D space planning as a result of lessons learned from the pandemic. **Most notable is likely to be a need for more lab space as the density of personnel allocated to existing lab space will need to reduce in the "new normal."** The bottom line is likely to be that the capital cost of space for performing research will increase.

Lesson 1a.4: Prior investment in large-scale signature R&D and scientific infrastructure pays dividends.

SARS-CoV-2, as a novel coronavirus, has markedly **illustrated the importance of prior investment in major shared scientific assets.** As the threat of COVID-19 became evident, signature national scientific assets—the "big iron" of science—were brought to bear on immediate study and characterization of the virus. Ranging from supercomputers to synchrotron X-ray light sources (particle accelerators), national research assets have been made available for use in coronavirus research on a prioritized basis.

3 Flad Architects. Scientific Workplace Strategy. Expert planning to reoccupy safely and economically. https://www.flad.com/stories/scientific-workplace-strategy.php.

Many of these world-class international scientific facilities were established and funded by governments because of the very high level of capital expenditure involved; and they typically operate as "user facilities" available for use by academic, industry, and other scientists based on submission of research proposals. These powerful research assets have been pivoted to prioritize COVID-19 research, and scientists at the facilities are proactively networking to share results. For example, the international network of X-ray Science Facilities, composed of X-ray Synchrotron Radiation and X-ray Free Electron Laser Facilities, came together in April 2020 to share experiences and lessons-learned and to develop a cooperative strategy to maximize the usefulness of their resources in the fight against the pandemic. The collaboration is facilitating sharing of results and data and facili-

Examples of Signature Research Assets Leveraged for SARS-CoV-2 and COVID-19 R&D

The **U.S.** National Synchrotron Light Source II at Brookhaven National Laboratory (which cost US$912 million and opened in 2014) has provided expedited rapid access for groups requiring beam time for projects directly related to COVID-19.

Diamond Light Source, the **UK's** national synchrotron (a UK£383 million facility), is being used on a wide range of Covid-19 projects ranging from examining fundamental interactions of the virus to drug repurposing.

European high-performance computing (HPC) centers are coordinating access to supercomputers and other HPC assets across Europe through the EU PRACE COVID-19 Initiative. Supercomputing centers in Germany, France, Finland, Italy, Ireland, Czech Republic, Slovakia, and Switzerland, for example, are providing prioritized access to computer resources and specialized support services for computationally intensive studies.

Japan operates a national network of seven non-university research institutes with specialized scientific infrastructure. Several key assets were made available to COVID-19 researchers, including the Fugaku supercomputer, the SPring-8 synchrotron, and the Mendeley Data Repository.

In **South Africa**, the science and technology agency's Centre for High Performance Computing has made computing time available for COVID-related work including using huge amounts of telephone network data for contact tracing.

In **Australia**, the National Biologics Facility of the Commonwealth Scientific and Industrial Research Organisation (CSIRO) is being leveraged to produce vaccine candidates at pilot scale, while preclinical work has leveraged investment in biosecurity facilities at the Australian Centre for Disease Preparedness.

In **Canada**, Genome Canada's national resource base for high-throughput sequencing and analysis (with nodes in Montreal, Toronto, and Vancouver) received C$20 million to apply to leveraging its resources to address COVID-19.

In **Sweden**, the RISE institutes (a network of industry-facing applied research institutes) were mobilized to provide testing certification of protective devices.

Four of **China's** National Supercomputer Centers provided free usage of resources to COVID-19 researchers.

tating access to light-source beamlines around the world when local beamlines are at capacity.

Processing and analyzing the massive amounts of data being generated worldwide through research tools applied to COVID-19 could have been a bottleneck for advancing solutions to the pandemic. However, the international COVID-19 High Performance Computing (HPC) Consortium was quickly established to manage and provide access to a "range of computing capabilities that span from small clusters to some of the largest supercomputers in the world."[4] Comprising HPC centers of industry, academia, and government, the consortium leverages the expertise of global leaders like Microsoft, Intel, and Amazon Web Services, together with university-based supercomputing centers in the U.S., UK, and Switzerland, and the scientific computing resources of U.S. National Laboratories and federal agencies. The U.S.-based consortium is collaborating with other similar initiatives, such as the EU PRACE COVID-19 Initiative. The EU has highlighted "on-demand, large-scale virtual screening" of potential drugs and antibodies at the HPC Centre of Excellence for Computational Biomolecular Research, as well as "prioritized and immediate access" to supercomputers operated by the EuroHPC Joint Undertaking.[5]

It is important to note that such specialized, capital-intensive scientific infrastructure projects (such as synchrotron light sources and supercomputing facilities) would not have been available to address the virus were it not for billions of dollars in prior investment and the foresight of multiple governments and supporting organizations in committing to the development and ongoing operations of infrastructure focused on advancing fundamental and applied scientific discovery.

Lesson 1a.5: The economic cost of a pandemic dwarfs the investment in the R&D resources needed to address it.

It is certainly the case that the development and ongoing operation of a comprehensive life sciences research ecosystem runs into the tens of billions, if not hundreds of billions, of dollars (depending on the geographic scale of the ecosystem considered). Scientific research staff and specialist supporting personnel, life sciences laboratories, and specialized research instrumentation do not come cheap. Research ecosystems will typically comprise Tier 1 research universities, clusters of R&D-oriented life sciences companies (including large and mid-size companies and emerging entrepreneurial ventures), and a host of specialized support services and infrastructure required to support the collective research effort. In some locations, major government laboratories are also part of the research ecosystem. It is a substantial investment.

What the COVID-19 pandemic makes clear, however, is that the economic cost of a major pandemic that causes business shutdowns and wide-ranging social-distancing requirements will be orders of magnitude higher than the cost of the research infrastructure required to address the crisis.

As noted by the U.S. Congressional Research Service in its updated September 4 report on impacts of the COVID-19 pandemic:

> *Since the COVID-19 outbreak was first diagnosed, it has spread to over 200 countries and all U.S. states. The pandemic is negatively affecting global economic growth beyond anything experienced in nearly a century.*[6]

The financial cost of the pandemic is of an unprecedented scale. The International Monetary Fund (IMF) estimates that:

4 https://covid19-hpc-consortium.org/who-we-are.

5 Oliver Peckham. "Global Supercomputing Is Mobilizing Against COVID-19." HPC Wire. March 12, 2020. https://www.hpcwire.com/2020/03/12/global-supercomputing-is-mobilizing-against-Covid-19/.

6 Congressional Research Service. Global Economic Effects of COVID-19. Updated September 4, 2020. Accessed online at: https://crsreports.congress.gov/product/pdf/R/R46270.

> ***Government spending and revenue measures to sustain economic activity adopted through mid-June 2020 amounted to $5.4 trillion and that loans, equity injections and guarantees totaled an additional $5.4 trillion, or a total of $11 trillion.***[7]

To fund investment in pandemic response and associated economic supports, governments are increasingly borrowing funds. The IMF estimates that increase in global borrowing by governments will rise dramatically from a pre-pandemic estimate of 3.9% of global gross domestic product (GDP) in 2019 to 13.9% in 2020.[8]

The World Bank notes the following:

> *Over the longer horizon, the deep recessions triggered by the pandemic are expected to leave lasting scars through lower investment, an erosion of human capital through lost work and schooling, and fragmentation of global trade and supply linkages.*[9]

Against this background of severe economic damage wrought by COVID-19, it is clear that the investment of funds in the life sciences ecosystems combatting the crisis pales in comparison. Put another way, the return on government investment in life sciences research is high when considering the alternative (an inability to bring forth diagnostics, vaccines, and therapeutics to combat it).

It should be noted that, while it takes considerable funding to build up a life sciences ecosystem over time, the net real economic returns to that investment will likely be high—with revenues generated via innovation commercialization, ongoing sales of life sciences products and services, and positive returns realized through improved health associated with life sciences innovations. The argument for investment in life sciences R&D holds strong even without a major public health crisis, but a global pandemic adds a whole new level of argument for the positive returns achieved.

Framework Element 1b: Clinical Trials

No matter how urgent the need, nor dire an infectious disease, promising biopharmaceuticals and vaccines cannot be introduced for use until they have been tested, with rigor, in clinical populations. The formal process of clinical trials, outlined in Figure 4, has evolved out of necessity, and comprises best practices to ensure that therapeutic products for human use have been tested for efficacy and, most important of all, for safety.

The clinical trials ecosystem has been heavily impacted by the COVID-19 pandemic. At the most macro level, three distinct pathways have occurred in terms of the performance of clinical trials:

- **Pathway 1**—Clinical trials for COVID-19 therapeutics and vaccines. Given expedited clearance and prioritized activity.
- **Pathway 2**—Clinical trials in high-priority disease areas and serving high-risk patients with life-threatening conditions (e.g., cancers or neurodegenerative diseases) that were important to continue during the pandemic.
- **Pathway 3**—Clinical trials in lesser-priority diseases or conditions that could be suspended during the pandemic, together with new trial starts delayed and enrollments stopped.

Overall, outside of specific COVID-19 trials, McKinsey notes that clinical trials have been "affected with disruptions in both new enrollment and in keeping existing patients on therapies."[10] Because clinical trials typically require trial participants to have physical interactions with clinicians at medical

7 Ibid.
8 International Monetary Fund. World Economic Outlook Update. June 24, 2020.
9 The World Bank. "The Global Economic Outlook During the COVID-19 Pandemic: A Changed World." June 8, 2020.
10 McKinsey & Company. "The Next Normal." https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/Covid-19-implications-for-life-sciences-r-and-d-recovery-and-the-next-normal.

Moving at the Speed of Crisis

At Genentech, and our parent company Roche, we've launched trials to study one of our medicines in COVID-19 pneumonia in a matter of weeks rather than the more typical months, expanded production capacity from hundreds of thousands to millions of doses to ensure sufficient supply, and developed two diagnostic tests, ramping up manufacturing exponentially in record time to help meet unprecedented demand. These actions have been made possible by the exceptional efforts of government and regulatory institutions, as well as partnerships across the health care ecosystem with distributors, insurers, patient organizations and providers.

Alexander Hardy, CEO Genentech. Guest post on the PhRMA website. "What will we learn from COVID-19?"

practices and at hospitals, any location experiencing significant COVID-19 caseloads became problematic for trial participation; and, even if still allowed to visit clinical sites, some participants have chosen to miss hospital visits as a result of concern over virus exposure (especially if they are immunocompromised or otherwise concerned with pre-existing conditions).

Trials specific to COVID-19 have experienced the reverse situation—accelerating at a dramatic pace. Chicago-based life sciences start-up accelerator, MATTER, has conducted discussion panels with life sciences companies in relation to pandemic response experiences and clinical trials. The chief executive officer (CEO) of MATTER notes the following:

> *According to participants, in the face of this pandemic, regulatory groups have become exceptionally collaborative, which has allowed projects to move through much more quickly. One participant shared that they've been able to stand up studies in two weeks versus a normal timeline of several months.*[11]

This finding is echoed in an article in Nature Review Drug Discovery which notes that "the response to the COVID-19 pandemic has shown that exceptional efforts can dramatically accelerate the clinical development of vaccines."[12] The authors find that "the overnight review of COVID-19 protocols, the waiver of the 30-day investigational new drug (IND) application waiting period and analogous clinical trial application (CTA) provisions, the delivery of scientific advice almost in real time and virtual meetings between sponsors and regulators have all enabled rapid decision-making in response to COVID-19."

It appears that for clinical trials, while COVID-19 has created challenges for trials in some non-pandemic related products, the crisis has revealed pathways towards streamlined and digitally enabled regulatory processes likely to prove beneficial for future biopharmaceutical and vaccine development.

Summary of Lessons Learned for Clinical Trials:

- ***Adoption of virtual and contactless solutions sustains trials.***
- ***Proactive and responsive regulatory guidance is highly important.***
- ***Speed in trials for vaccine and therapeutic advancement is critical.***

11 Steven Collens. "Four ways life sciences companies are adapting to a COVID-19 world." May 1, 2020.

12 Rod MacKenzie, Peter Honig, Judy Sewards, Robert Goodwin and Marie-Pierre Hellio. "COVID-19 must catalyze changes to clinical development." *Nature Reviews Drug Discovery*. September 3, 2020. https://www.nature.com/articles/d41573-020-00149-2

The U.S. Coronavirus Treatment Acceleration Program (CTAP). A novel process to rapidly advance innovations and trials for COVID-19.

The process is designed to bring the strongest proposals to the front of the line:

- As soon as received, proposals for new drug and biologic therapy development and evaluation are triaged, directed to the right FDA team members, and generally responded to within one day.
- Applicants are provided with rapid interactive input on most development plans. Interactions are prioritized based on a product's scientific merits, stage of development, and identification as a possible priority product in consensus documents.
- Ultra-rapid protocol review is performed. Some have been performed within 24 hours of submission.
- Close coordination is maintained with applicants and other regulatory agencies to expedite quality assessments for COVID-19 products.

Lesson 1b.1: Adoption of virtual and contactless solutions sustains trials.

Several emerging approaches to patient interactions and supply of drugs for trials—approaches that remove the need to physically visit a provider—have been expanded during the pandemic.

As alternatives to participants visiting a clinical site to receive their trial drugs, direct home shipment has been deployed and virtual/telemedicine consultations operationalized between clinical staff and participants. Trial sponsors and managers have found it increasingly feasible to transition to decentralized trials with remote monitoring and source document verification (SDV) to ensure that participants may continue to participate. Video consultations, access to telemedicine platforms, home/wearable monitoring devices, eConsent forms, etc., have come together to enable a "physically contactless" approach.

The shift that has occurred has been quite dramatic, with McKinsey noting that "among major pharma companies, 60 percent are already using telemedicine for trial visits in response to the COVID-19 crisis and more seem likely to follow."[13] It should be anticipated that, should this approach be found to have been effective and safe, policies and regulations will be permanently modified to allow this approach to be used long term.

Lesson 1b.2: Proactive and responsive regulatory guidance is highly important.

The penalties for stepping outside of national regulatory requirements can be severe for life sciences companies, and firms are understandably cautious in making modifications to trials performance norms. The unprecedented global challenges posed by COVID-19 have, however, necessitated change in order to keep trials running and rapidly advance new trials to address the disease.

The back-and-forth between companies seeking guidance, and regulatory agencies providing it, has been accomplished quite rapidly. A good example of this is the U.S. Coronavirus Treatment Acceleration Program (CTAP), at the FDA, representing a proactive response by the FDA to advance clinical

13 McKinsey & Company. "Winning against COVID-19: The implications for biopharma." https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/winning-against-Covid-19-the-implications-for-biopharma.

trials for COVID-19 as fast as possible while sustaining efficacy and safety protocols. Under CTAP, FDA medical and regulatory staff were repurposed to specific COVID-19 review teams, and emergency streamlined processes and operations enabled for responding to developers' and scientists' questions and requests. CTAP also enables clinicians and researchers to submit emergency requests for the use of investigational products for patients with COVID-19 infections. CTAP's implementation process (see sidebar) has been well received.

What is clear is that the trials world is shifting, and that companies will need to closely monitor regulatory decisions and be proactive in seeking guidance from relevant regulatory agencies. As nations move into the post-pandemic recovery phase, companies with active trials during the pandemic will need to seek advice regarding missing data procedures and the ongoing use of telemedicine, remote monitoring technologies, home nurse visits, and contactless drug delivery systems. McKinsey notes the following:

> *The gradual and staggered path to recovery could lead to a greater emphasis on creative ways to generate evidence. For example, supplementing controlled data with real-world evidence, using master protocols or adding arms to in-flight trials are all top of mind for R&D leaders and likely to figure prominently in discussions with regulators and in health-technology assessments. None of these approaches are unheard of but could gain further momentum in the next normal.*[14]

Lesson 1b.3: Speed in trials for vaccine and therapeutic advancement is critical.

As noted earlier in this report, vaccine development is a complex science; and it is typical for the research, development, and clinical trials process to require upward of a decade to complete. For diseases that are endemic and long-standing, for example, malaria or HIV-AIDS, the ever-present nature of the disease provides long-term access to impacted or potentially exposed patient populations to enable research and trials activity. In the case of COVID-19, however, the rapid transmissibility and spread of the disease, its incubation period, and other factors place an extraordinary urgency in advancing a vaccine (while ensuring safety and efficacy). In Europe, where COVID-19 appears to be currently quite well contained,[15] it is a challenge for vaccine developers to gain sufficient exposure of vaccine trial participants to the coronavirus in order to evaluate immune response and efficacy. It is generally considered unethical to deliberately expose a vaccine trial participant to the virus; instead, protocols require a significant population to be tested and impacted by natural exposure to the virus in daily activity—thus, if the development takes too long, and mitigation efforts are successful, the prevalence of the disease becomes too low for study.

The likelihood of a resurgence of COVID-19 in the fall and winter of 2020/21 will provide a further vaccine trial window, but the obvious preference is for a vaccine to have been developed and distributed to prevent this resurgence. It is a paradox not easily resolved, and a similar situation exists for the development of novel therapeutics for the coronavirus also.

The key lesson to be learned from this is that well-funded fundamental research programs in vaccine platform technologies must be encouraged, especially in regard to the development of flexible and fast development platforms, to ensure that when the next novel virus presents, candidate vaccines can be produced and advanced into trials as rapidly as possible.

It should be noted that moving fast in product development and the conduct of clinical research carries significant risk that will likely require government intervention to address. It presents issues in regard to legal liability, high risk of product development failures and lost capital resources,

14 McKinsey & Company. "The Next Normal." https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/Covid-19-implications-for-life-sciences-r-and-d-recovery-and-the-next-normal.

15 As of the date of writing this report section (June 25, 2020).

and potential for process errors to occur that may have negative regulatory implications for product developers. These issues are discussed further in the Policies and Regulations section of this report.

Framework Element 1c: Production

By necessity, diagnostic test kits, vaccines, and biopharmaceuticals are manufactured under especially high standards, with strict requirements and rigorous approvals to ensure the safety, quality, and reliability of production to protect patients and deliver the intended therapeutic benefits.

To a significant degree, the manufacturing of biopharmaceuticals is an international undertaking. Companies specialize in the production of active pharmaceutical ingredients (APIs), excipients, organic and inorganic fine chemicals, encapsulation materials, etc., that are raw materials for the production process undertaken by biopharma original equipment manufacturers (OEMs) or contract manufacturers; and some of these raw material producers are clustered in a few nations around the globe. China is one of the largest suppliers of APIs into the global pharmaceutical manufacturing network (although in the U.S. the majority of APIs are produced domestically[16]), and much of the production of generic drugs and vaccines for global use occurs in India.[17]

The worldwide COVID-19 pandemic raised questions about the ability of these national clusters to meet existing and new demand at OEM and contract generic pharma production sites in Europe, North America, Asia, and other markets, due largely to restrictions on export from these countries. The pandemic has highlighted the importance of sustaining a resilient supply-chain framework that may have implications for biopharmaceutical and vaccine production in the future.

There is talk of new supply-chain networks needing to be designed that would balance total cost versus supply-chain interruption risk. But care needs to be taken not to overreact, since it appears that biopharmaceutical supply chains have proven quite resilient. If the balance swings more toward risk mitigation, then there may be shifts in the geography of the industry.

Some actions are already being observed in the market. The government of India, for example, has allocated an equivalent of US$1.3 billion for its pharmaceutical industry to adopt alternatives to Chinese-sourced APIs.[18] It is imperative, however, that any potential changes in the supply chain be carefully assessed in terms of their impact on markets, costs, and resiliency. The "commoditization" of products has led to global supply chains that have been structured to promote desirable cost efficiencies and standardized quality and care must

Resiliency may be enhanced through the development and adoption of harmonized international standards for diagnostics, biopharmaceutical, and vaccine manufacturing. Harmonized standards need to be pursued both for existing production platforms, and for emerging continuous manufacturing, single-use systems, and modular manufacturing facilities.

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use is developing standards and attempting to incorporate new manufacturing techniques into the existing regulatory structures. Reaching agreement and achieving universal international adoption of standards should be a priority.

16 Chris Sloan, Massey Whorley, Mitchell Cole, and Alessandra Fix. "Majority of API in US-consumed Medicines is Produced in the US." Avalere. July 15,2020. https://avalere.com/insights/majority-of-api-in-us-consumed-medicines-is-produced-in-the-us

17 Abhishek Dadhich. "The COVID-19 pandemic and the Indian pharmaceutical industry." European Pharmaceutical Review. April 22, 2020. https://www.europeanpharmaceuticalreview.com/article/117413/the-covid-19-pandemic-and-the-indian-pharmaceutical-industry/

18 Ivan Gandayuwana. The Science Advisory Board. "COVID-19: A double-edged sword for the pharma industry." https://www.scienceboard.net/index.aspx?sec=prtf&sub=def&pag=dis&itemId=700&printpage=true&fsec=sup&fsub=bioproc).

be taken to not offset these characteristics. Rules against trade barriers and agreements allowing fair competition between medical products regardless of origin also play a critical role in maintaining resilient supply chains.

The other factor evident in discussions related to COVID-19 relates to manufacturing processes themselves. Biopharmaceutical products are produced under two quite different production regimes—with small-molecule drugs being produced using chemical processes, and biologics produced using biological processes. In both cases, manufacturing operations are typically built to produce an individual product on a large or relatively large scale, and the production processes themselves are not very amenable to changes in process technologies or production scale. It may take many months to design, build, and commission a new biopharmaceutical facility; and large-scale production equipment comes from a select few global manufacturers. COVID-19 appears to be accelerating interest in alternative production systems, such as the use of continuous manufacturing systems and smaller batch processing and disposable systems in biologics manufacturing. Increased levels of automation may also be considered given challenges with the workforce and social-distancing and PPE requirements.

Summary of Lessons Learned for Production:

- ***Big and small players will be contributing solutions and collaborating.***
- ***Supply-chain resiliency must be built.***
- ***Advanced production methods need to be accelerated.***
- ***Regulatory oversight of GMP production can be accomplished remotely.***

Lesson 1c.1: Big and small players will be contributing solutions and collaborating.

Products moving through trials for application to COVID-19 are coming from large multinational biopharmaceutical firms such as Pfizer, GSK, Merck, Regeneron, and Sanofi, but are also being generated by smaller up-and-coming and midsize ventures such as Moderna, CanSino Biologics, and Translate Bio. A key takeaway is that innovation may emanate across the company size spectrum. However, when it comes to manufacturing, it is evident that the robust experience base of large multinational biopharmaceutical companies, and the expertise in major biopharma contract manufacturing firms, is likely to be leveraged by smaller innovators who do not have manufacturing expertise, or only limited manufacturing resources themselves. Collaborative partnerships focused around manufacturing and bringing a product quickly to market are evident in collaborations between:

- Pfizer and Gilead, with Pfizer providing contract manufacturing services for Gilead's Remdesivir.
- Moderna working with Lonza for manufacturing its mRNA vaccine
- Eli Lilly and Co. partnering with Vancouver-based biotech AbCellera on a COVID-19 antibody treatment
- BioNTech partnering with Pfizer (PFE)
- Ridgeback Bio working with Merck on a potential COVID-19 antiviral
- Vir Biotechnology teaming with Biogen
- Novavax and Vaxart both collaborating with Emergent BioSolutions for manufacturing.

As companies have come together to facilitate rapid advancement of products, they have had to work rapidly on developing agreements on patents, trade secrets, proprietary manufacturing systems, etc., while navigating potential challenges such as anti-trust regulations.

While some governments have expressed a goal of localizing biomanufacturing supply chains (especially for APIs whose lack might inhibit timely or full production of a vaccine or therapeutic), the reality is that even new manufacturing efforts have required international cooperation and interchange to work. Examples are as follows:

- **Brazil—**The Instituto Butantan, long a leader in antivenom serums and other aspects of tropical medicine, is collaborating with China's Sinovac Biotech on producing quantities of the company's vaccine candidate for clinical trials in Brazil, and with the Bill & Melinda Gates Foundation of the United States.
- **Germany—**Merck KGaA has become the manufacturing partner to the UK vaccine candidate being developed by the University of Oxford and the Jenner Institute, reducing the process development phase from 12 months to 2 months.
- **Singapore—**The Prime Minister has committed to building up biomanufacturing capacity to serve vaccine developers, not only to meet domestic needs which are relatively small but also to serve as a base for export. This will inevitably involve global connections. For example, Switzerland-based Lonza–the company selected as manufacturing partner by U.S.-based Moderna–has the option to use its existing Singapore plant.

Lesson 1c.2: Supply-chain resiliency must be built.

It is likely that intense attention will now be paid to ensuring that assets and supply chains are organized for risk mitigation and resiliency. Achieving this goal does not, however, automatically mean geographic redistribution of the production of manufacturing inputs or OEM production plants. Elements of resiliency can be built through requiring more information transparency up and down the supply chain, so that producers know in real-time the situation of their suppliers, and also those who supply their suppliers. Digital tracking tools for inventory management across the supply chain may be leveraged to accomplish this. Resiliency can also be enhanced in life sciences production systems through increasing inventory levels of critical supplies and medicines. While cost efficiencies have been built around efficient delivery of supplies in manufacturing, the post-pandemic production environment may require more "just-in-case" stockpiling of critical inputs and resources to enhance resiliency. Building relationships with multiple suppliers of the same inputs, particularly suppliers not located in the same region as each other, may also be pursued.

The pandemic interrupted some of the modes of transportation for products. One of the lessons learned is that shipment by dedicated air transportation service providers (such as FedEx) were comparatively less impacted than shippers that relied more on transportation in the cargo holds of passenger air carriers. In terms of international sea–based shipping (which carries 90 percent of global trade), interruptions were created by national measures and local restrictions in response to the pandemic. Challenges were further exacerbated by ports experiencing reduced workforce capacity and also by antiquated administrative processes, procedures, and systems (many of which are still paper based rather than digital). Logistics challenges not only impacted raw materials and finished product shipments, but also hampered the distribution of important R&D materials being moved between international research locations.

Another key lesson learned for all across the supply chain has been the critical importance of having on-hand, and sustaining, a significant inventory of PPE so that critical workers could be maintained on the job and protected from disease transmission.

Lesson 1c.3: Advanced production methods need to be accelerated.

Because of the opportunities related to an emerging personalized medicine market, multiple biopharmaceutical companies have been studying alternative and flexible production technologies. This has been an ongoing trend for several years, but COVID-19 and its need for rapidly installed, scalable, and distributed production systems has increased the potential urgency for development and deployment of alternative production systems. Some of the alternative production systems being considered also lend themselves to smaller production operations, providing a potential fit with a distributed local production ecosystem that some are raising as an option to build post-pandemic ecosystem resiliency. The technologies and production systems anticipated to see more widespread use include the following:

- Wider adoption of continuous manufacturing technologies, which requires less space and less upfront investment and generates flexibility.[19] According to the Director of the FDA's Center for Drug Evaluation and Research (CDER), the FDA has approved "several continuous manufacturing applications."[20]

- More single-use systems (SUS) process lines and facilities (as opposed to traditional large stainless-steel systems). Respondents to BioPlan's Survey of Biopharmaceutical Manufacturing expect that "pandemic-related new facilities will largely engage SUS due to its flexibility which will be needed, combined with SUS speed and much lower capital investment. Long-term, this flexibility will imprint on the responses to future pandemics and health crises. Due to the speed, cost and flexibility benefits of SUS, most pandemic-related new facilities and process lines are expected to be SUS-based."[21]

- Increased adoption of modular facilities, which facilitate rapid development and cloning of formats in multiple locations.[22]

It should be noted that the anticipated significant increase in the use of SUS systems will mean that attention will need to be paid to the supply-chain resiliency of the companies that make these systems and supply the materials used in them (such as polymer membranes and affinity media).

Daniel Blackwood at Pfizer notes the following:

> *Continuous manufacturing initiates a cascade of transformational advances in technology. It allows process intensification, which enables miniaturization of systems that have small footprints and reduced energy consumption. Miniaturization makes modularity and ultimately portability possible. … Focusing on portable, continuous, miniature, and modular technology will allow Pfizer to transform how it develops, manufactures, and distributes its drug products. Such technology might make it possible for pharmaceutical companies to share space and possibly some operations if precompetitive agreements are in place.*[23]

Lesson 1c.4: Regulatory oversight of GMP production can be accomplished remotely.

Restrictions on travel have impacted the usual regulatory practices of manufacturing plant inspections and have complicated access to experts and contractors for manufacturers seeking to change or improve their processes. It is anticipated that

19 McKinsey & Company. "The Next Normal." https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/pharma-operations-the-path-to-recovery-and-the-next-normal.

20 National Academies of Sciences, Engineering, and Medicine 2020. Innovations in Pharmaceutical Manufacturing: Proceedings of a Workshop—in Brief. Washington, DC: The National Academies Press. https://doi.org/10.17226/25814.

21 Ronald A. Rader and Eric S. Langer. "Covid-19: Impact on Bioprocessing and Outsourcing." Contract Pharma. May 5, 2020.

22 Ibid.

23 National Academies of Sciences, Engineering, and Medicine 2020. Innovations in Pharmaceutical Manufacturing: Proceedings of a Workshop—in Brief. Washington, DC: The National Academies Press. https://doi.org/10.17226/25814.

experience during the pandemic will accelerate moves for more remote auditing and inspections using remote video and virtual reality platforms. The net effect may be more efficiency in the system, with regulators, consultants, contractors, etc., being able to limit time spent in travel and serve more customers with the time gained.[24]

International auditing guidelines allow for remote auditing; regulatory authorities are issuing guidance to better facilitate them during the pandemic; and experts are starting to direct and monitor remediation efforts remotely, using video, virtual reality, and other advanced tools.

Framework Element 1d: Distribution

The movement of raw materials and inputs within the supply chain, and the distribution of finished products, have been challenged by the COVID-19 pandemic. Observable issues have included the following:

- Government-based redirection or interception of materials and products, such as PPE, for which there were previous contracts.
- Large-scale purchases of existing medicines thought to be potentially effective against COVID-19 causing shortages for patients needing those medicines for their traditional indications. Most notable in the case of hydroxychloroquine.
- Shutdown of ports and slowdown of port operations related to staffing challenges.
- Major cutbacks in ability to transport products in the cargo holds of commercial passenger flights due to reduction in flights.
- Closures of land borders and increased delays and inspections at borders.

Some distribution challenges were experienced across manufacturing industries in general (not specific to life sciences) as the pandemic took hold. Between February 22 and March 5, the Institute for Supply Management received 628 responses to a survey of U.S. manufacturing (52 percent) and nonmanufacturing (48 percent) organizations.[25] Seventy-five percent of respondents reported supply-chain disruption in some capacity due to coronavirus-related transportation restrictions; and by the end of March, when resurveyed, this increased to 95 percent. Reduced Chinese manufacturing capacity was felt first, with Chinese manufacturing operating at only 50 percent of capacity by late February. Other Asian nations, European and North American manufacturing disruptions quickly followed.

Summary of Lessons Learned for Distribution:

- ***Multiple sources of critical supplies are beneficial.***
- ***Well-planned supply chains and distribution agreements may be interrupted.***
- ***Digital supply-chain monitoring is desirable and feasible.***

Lesson 1d.1: Multiple sources of critical supplies are beneficial.

While multiple governments are discussing potential regulations that would require critical biomedical products to be manufactured in their respective countries, the challenge is that a domestic outbreak can still be disruptive. Sustaining participation in international supply networks makes sense from a "hedging against risk" standpoint, and indeed the Institute for Supply Management reports that organizations that diversified their supplier base after experiencing tariff impacts could be better positioned to address the effects of COVID-19 on their supply chains.[26]

24 See discussion at: https://www.contractpharma.com/contents/view_experts-opinion/2020-05-18/Covid-19s-long-term-impact-on-drug-development-the-new-pragmatism/.

25 Institute for Supply Management. "Covid-19 Survey: Impacts on Global Supply Chains." March 11, 2020. https://www.ismworld.org/supply-management-news-and-reports/news-publications/releases/2020/covid-19-impacts-on-global-supply-chains/.

26 Ibid.

Life sciences products are complex and specialized, and it would be both expensive and technically difficult to re-shore industries that have developed sophisticated supply relationships based on national and regional core competencies and specializations rooted in both infrastructure and workforce know-how. Rather, the more reasonable option being discussed is to ensure that no single location has a monopoly on critical products. Modern digital supply-chain tools (discussed further below) provide an ability to manage multiple suppliers and more complex supply chains more efficiently, significantly improving the technical feasibility of inputs supply diversification.

Lesson 1d.2: Well-planned supply chains and distribution agreements may be interrupted.

The global spread of COVID-19 led to some aggressive actions by governments. As the pandemic spread, nations banned the international shipment of certain medical products, meaning companies could not honor existing contracts and orders from their international customers. As nations scrambled to secure PPE for frontline healthcare personnel and other essential workers, some government actions in terms of intercepting products ordered by others reached a level whereby nations accused each other of international piracy.

The pandemic generated a surge in demand for medical goods, exacerbated by panic buying, causing significant stress on supply chains. Fearing critical shortages and under immense public pressure, more than 80 jurisdictions implemented export restrictions to keep critical products within their borders. Though restrictions largely focused on PPE, biopharmaceuticals and diagnostic tests were also targeted, hindering the life sciences sector's ability to respond to the COVID-19 crisis. Export restrictions also made it difficult for some countries, especially those reliant on imported medical goods, to secure critical products. Peter Navarro, White House director of trade and manufacturing policy, suggested that "if we have learned anything from the coronavirus … it is that we cannot necessarily depend on other countries, even close allies, to supply us with needed items."[27] In response, the World Trade Organization (WTO) called export restrictions "dangerously counterproductive"[28] and G20 leaders earlier stated that "emergency measures … must be targeted, proportionate, transparent, and temporary."[29]

While many restrictions have now lapsed, to avoid future challenges, the EU and other economies have called to remove trade barriers that needlessly delay the distribution of medical goods and drive up their price. Notably, these steps would include the elimination of tariffs on certain biopharmaceuticals. Similar proposals have been seen in other regional forums, including the Asia-Pacific Economic Cooperation (APEC). Although tariffs have been declining over the last 20 years on biopharmaceuticals (4.9 percent in 2001 to 3.4 percent 2018), many jurisdictions continue to apply large duties and are expanding the number of treatments covered.[30] It is likely that, for PPE and certain other critical products, two mitigation pathways will be pursued to prevent reoccurrence of this challenge in the future:

- Nations, state governments, and large health systems will seek to build significant emergency preparedness stockpiles—stockpiles far larger than previously sustained. In the near- to mid-term, this will be a challenge as many of the products are still in short supply as the pandemic expands and a second wave is predicted for late in the year.

- Nations will collaborate with PPE manufacturers, and manufacturers of other

27 The Washington Post, "White House asks Congress for $1.8 billion to bolster coronavirus response." February 24, 2020. https://www.washingtonpost.com/business/2020/02/24/white-house-preparing-ask-congress-more-moneyfinance-coronavirus-response/).
28 World Trade Organization. April 24, 2020. https://www.wto.org/english/news_e/news20_e/igo_15apr20_e.htm.
29 World Trade Organization. March 30, 2020. https://www.wto.org/english/news_e/news20_e/dgra_30mar20_e.htm.
30 Philip Stevens and Nilanjan Banik. "Abolishing Pharmaceutical and Vaccine Tariffs to Promote Access." Geneva Network. July 2020. https://geneva-network.com/article/2020-pharmaceutical-tariffs/.

critical products, to build new manufacturing capacity dedicated to domestic supply.

It is also likely that companies will collaborate more in ensuring that supplies of critical products are available. During the pandemic, for example, the European Medicines Agency notes that pharmaceutical companies, which have been competitors, came together to secure critical, high-demand medicines for hospital intensive-care units by setting up the industry-single-point-of-contact (i-SPOC) system, which enables close monitoring of possible disruptions in supply.[31] Because collaborations have been effective in addressing pandemic needs, the changes in competition laws (or flexibility in their application) used to facilitate such collaborations should be evaluated as effective crisis response mechanisms for future use.

Lesson 1d.3: Digital supply-chain monitoring is desirable and feasible.

Digitally enabled, resilient distribution and supply chains will expand in the biopharmaceuticals and other medical product spaces as a result of the pandemic. Advanced supply-chain analytics and artificial intelligence (AI) systems, implementation of Internet of Things sensing and tracking systems, automated warehouses, and other technologies are already being deployed by many major biopharmaceutical and medical products manufacturers and distributors; and this trend will likely be accelerated post-pandemic as companies strive to build more resilient and transparent distribution and supply operations. Improved transparency across the supply chain will allow predictive analytics systems to identify pending supply bottlenecks and adjust inventories and order patterns to suit.

Amazon shows what can be accomplished through the use of digital supply-chain management and distribution tools. Delivering over 3.5 billion packages a year, Amazon carries over 12 million products and deals with thousands of individual suppliers. Amazon operates a digitally managed supply ecosystem that is able to be predictive, resilient, and transparent to their customers (who can track orders and make changes even when products are already shipped). Using AI and advanced analytics and robotics automation in warehouses and fulfillment centers, Amazon is on the leading edge of supply-chain technologies, and has a highly scalable and resilient business model—one that could expand, not contract, in the pandemic. Amazon's success is well recognized, and other industries are seeking to build similar capabilities.

Telemedicine models for clinical care, combined with home monitoring and wearable systems, will provide mechanisms that further facilitate efficient distribution of digitally enabled biomedical products to patients.

31 European Medicines Agency. "Update on EU actions to support availability of medicines during Covid-19 pandemic." April 10, 2020. ema.europa.eu.

Framework Element 2: Talent (Human Capital)

The biomedical products ecosystem is powered by people. From the front-end of scientific discovery through to the back-end of highly skilled physicians and pharmacists providing products to patients, the biomedical sector is heavily dependent on highly skilled human capital. Highly skilled and intensively trained staff perform R&D, supervise clinical trials, manage the commercialization of innovations, operate and supervise manufacturing operations, sustain quality control and reporting to regulators, manage sophisticated supply chains (often requiring cold storage and distribution of perishable and time-sensitive products), and deploy the products in clinical settings.

It takes time to build the human capital needed to power a life sciences ecosystem. The amount of education and specific skills training required for these jobs is such that life sciences ecosystems cannot be rapidly scaled from scratch, and educators and workforce development professionals need to be proactive in building workforce supply systems that are predictive of need and responsive to input from life sciences companies.

The life sciences ecosystem evolves, and the education and skills of the workforce have to evolve with it. The rise of biotechnology, for example, required a new set of R&D and, especially, production skills that differed significantly from traditional chemistry-based small molecule drugs. Advancements in genomics and related fields are advancing opportunities for personalized medicine and custom compounding, and manufacturing is expanding in alternative production platforms that will require education in new technologies. In addition, the ongoing convergence of advanced analytics and digitalization with life sciences is placing a premium on highly educated personnel skilled in new (to life science) areas such as machine learning and AI, informatics, advanced statistical analysis, software engineering, and robotics process automation. **Competition for much of this talent is very high; and biomedical industries have to compete with other sectors for the talent, particularly in digital, computational, and analytics fields.**

The pandemic has changed the way that many people conduct their work. Remote work, enabled by efficient telecommunications and digital systems, has proven itself to be quite feasible and productive for many jobs. It seems likely that a significant component of work will remain remote and distributed for companies, and this may require changes in the way work is managed and personnel are trained.

Summary of Lessons Learned for Talent:

- *Scaling a life sciences workforce requires foresight and a long time horizon.*
- *Protection of workforce and contingency planning should be emphasized.*
- *Advancement of life sciences, digital, and advanced analytics convergence skills is required.*

Lesson 2.1: Scaling a life sciences workforce requires foresight and a long time horizon.

The single largest challenge for scalability in life sciences ecosystems, especially scalability during pandemic conditions, is the workforce. As noted above, a large proportion of life sciences ecosystem workers are highly-educated and technically-skilled workers—workers with capabilities that took considerable time to acquire. Thus, ramping-up a supply of workers for the sector is not something than can be accomplished quickly. This especially holds true during a pandemic when movement of people, especially internationally, becomes challenging.

One of the best practices observed in workforce development for the sector is investment in specialized training facilities for bioprocessing that duplicate the facilities used in industry (and

typically engage industry in their design and curriculum). An example of this is in North Carolina in the United States where the Biomanufacturing Training and Education Center (BTEC) has been developed on the campus of North Carolina State University. BTEC is a cross-disciplinary instructional center providing education and training for skilled professionals needed in the biomanufacturing industry. It is equipped with industry standard equipment, helping to build industry-transferable skills in those trained at the facility. One of the benefits of BTEC is that potential workers can be trained in the facility in parallel with a new biomanufacturing facility being constructed in North Carolina, thereby ensuring that a workforce is ready to go once a new production facility is commissioned. Another example of such a training facility is the Jefferson Institute for Bioprocessing (JIB) at Thomas Jefferson University in Pennsylvania. JIB conducts education and training for biopharmaceutical processing, combining commercial single-use processing equipment with the internationally recognized National Institute for Bioprocessing Research and Training curriculum.

While these, and other, specialized training centers represent a solution for workforce scaling in normal times, they are less viable as an option during a pandemic. BTEC, for example, has not been operational during the pandemic and its on-site training programs were suspended. The solution in the future will likely require implementation of remote education and training resources, supported by advancements in education technology (EdTech). Advancements in virtual and augmented reality, digital models of equipment, and gamification of learning can enable students and trainees to interact with their training content in simulated environments when attendance at physical training facilities is limited by social-distancing requirements.

Training in bioprocessing, and new technologies in bioprocessing, will be particularly important for pandemic preparedness. Industry responses to a survey by BioPlan indicate that "R&D and manufacturing will compete for limited staff with the cellular and gene therapies sectors, as new facilities come online. Expect bioprocessing expertise and even technicians to be increasingly in short supply, with recruiting more difficult and salaries increasing."[32]

Lesson 2.2: Protection of workforce and contingency planning should be emphasized.

While many of us have had the ability to work from home during the pandemic, countless "essential workers" have continued to go into their places of work. While the frontline clinical healthcare workforce has been rightly recognized and celebrated for their selfless commitment to working during the crisis, and the bravery they have shown in the face of potential virus exposure, many other critical infrastructure workers who have remained on the job may not be as well recognized. Among these pandemic heroes are thousands of workers within the life sciences ecosystems—workers who have continued to perform R&D and new product innovation for the pandemic response; clinical personnel who have continued to operate critically important trials; pharmaceutical and biologics manufacturing workers keeping the production of medicines, vaccines, and diagnostics flowing; and distribution and transportation workers ensuring that critical biomedical products get to where they are needed.

One of the key lessons from the pandemic is the importance of having in place plans to provide for the protection of these workers and an ability for sustaining access to critically important PPE to protect workers on the job. Organizations and companies have been creative in shift development and work scheduling to promote social distancing on the job and have called on their information technology departments for supporting remote working for personnel with positions that could be handled remotely. Given the scarce and critically important skills of life sciences workers, and the importance of the products they produce, a high

32 Ronald A. Rader and Eric S. Langer. "Covid-19: Impact on Bioprocessing and Outsourcing." Contract Pharma. May 5, 2020.

priority should be placed on securing protective equipment supplies for their health and safety during infectious disease events.

Lesson 2.3: Advancement of life sciences, digital, and advanced analytics convergence skills is required.

Longer term, it is likely that the challenges posed by the scalability of workforce (as well as the issues of protecting workers during an infectious disease pandemic) will be a driver of interest in automating manufacturing and warehousing systems. Futurists envision "lights out" automated facilities able to operate 24/7, with maintenance performed using robotics, and human monitoring of systems performed remotely. At a minimum, it is likely that the trend toward digitalization of manufacturing processes and the monitoring of these processes will continue apace, and that work will continue to shift from requiring manual skills to more technical/digital skills. McKinsey notes as follows:

> *As the adoption of digital and analytics tools and automation increases, pharmaceutical-operations organizations may have a greater need for talent that can program, operate, and interpret data from these new technologies. This will require significant up-skilling and capability-building efforts alongside ongoing strategic planning.*[33]

Jun Huang, director of the Process Monitoring, Automation, and Control Group at Pfizer Global Technology & Engineering, recently noted that Pfizer is "recruiting data architects who can build data infrastructure or central repositories, data engineers who can transform or aggregate data into a suitable format, and data scientists who can build models and analyze data."[34]

For those concerned with the future performance of their life sciences economic clusters, there should be little doubt that core competencies in advanced data analytics, including AI, will have a critical impact on ecosystem performance. Core competencies in advanced data analytics represent an increasingly essential driver of regional competitiveness and will only become more so in the future. Because it takes time to impart education and skills in analytics and data science, national and regional leaders need to pay special attention to digital literacy. A recent report for BioCrossroads in Indiana in the United States notes as follows:

> *Mathematics and English have long been foundational in our education – rightly seen as essential cross-cutting core competencies that provide the ability to comprehend content in other disciplines and successfully navigate the worlds of work and society. The changing landscape may also require adding Digital literacy to the existing foundation. Digital technology and data pervade modern economic and societal activity and are at the core of most expanding job markets. A key sub-component of this skill set involves Data Analytics – providing capacity to understand, process, manage and use sets of digital information.*[35]

It is also notable that the pace of digitization means that pure reliance on public education systems to build a responsive workforce may be too slow. The report for BioCrossroads notes as follows:

> *The pace of digitally enabled change and the breadth of advanced analytics adoption across industries will be such that skills required cannot be accommodated solely by new entrants to the workforce (those currently coming through the K-12 and traditional higher education*

33 McKinsey & Company. "Pharma operations: the path to recovery and the next normal." https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/pharma-operations-the-path-to-recovery-and-the-next-normal.

34 National Academies of Sciences, Engineering, and Medicine 2020. Innovations in Pharmaceutical Manufacturing: Proceedings of a Workshop—in Brief. Washington, DC: The National Academies Press. https://doi.org/10.17226/25814.

35 Simon Tripp, Ryan Helwig, and Joseph Simkins. "Artificial Intelligence and Advanced Analytics in Indiana: An Initial Discussion of Industry Needs and University Capabilities." TEConomy Partners, LLC. January 2020.

pathways). It will also be necessary to train and re-skill many in the incumbent workforce, and indeed, the rate of technological change will likely require personnel to re-skill or upgrade skills with increasing regularity, multiple times over their career-span. This requirement will place a premium on having the educational fundamentals that facilitate a life-long learning mindset and access to multiple modalities of affordable and timely education delivery.[36]

Karen Balss at Janssen Pharmaceuticals echoes this in comments to the National Academies, emphasizing "the importance of taking advantage of internal talents and providing training opportunities for current staff rather than searching for talents outside."[37]

Framework Element 3: Capital

Life sciences ecosystems are funded by a diversity of funding sources, and the makeup of these funding sources varies across the value chain. Government (especially) and philanthropic funding dominate at the very earliest precompetitive stages of research, while private-sector funding takes the lead in advancing drug discovery and development and advancing potential therapeutics, vaccines, etc., into trials and commercialization. If the commercialization pathway takes the form of new company development to advance a product or technology, private risk-capital markets (and to a lesser degree government small and emerging business supports) come into play. If the commercialization pathway is via an existing biopharmaceutical or medical product corporation, then companies have access to funding from equity markets, loan sources, or internal funding from ongoing operations.

While the above pathways for funding generally work well in supporting a highly active life sciences commercialization market, the COVID-19 pandemic has highlighted some weaknesses when it comes to funding and capital access in infectious diseases. Developed nations have tended to be more concerned with chronic illness in the research they fund, largely because chronic disease presents the greatest burden to the populations of developed nations and the health systems that serve them (whether public or private). COVID-19 has highlighted vulnerabilities in an R&D system heavily focused on chronic disease and has greatly increased awareness of the health and economic threat that emergent and novel infectious diseases still pose for both developed and developing nations when they are caught unprepared.

Summary of Lessons Learned for Capital:

- ***Research grants and development support set a key foundation for rapid innovation.***
- ***Public co-investment can be a significant catalyst.***
- ***Inter-industry partnerships and collaborations make a difference.***
- ***Public markets may infuse capital.***
- ***Venture capital (VC) and angel investor activity prime the pump of innovation.***

Lesson 3.1: Research grants and development support set a key foundation for rapid innovation. The earliest phases of research, especially (but not limited to) fundamental research, are supported by governments and, to a lesser degree, by philanthropic organizations worldwide. In the United States, funding by federal funding agencies, such as the National Institutes of Health (NIH) and the National Science Foundation (NSF) is a critically important element in the funding equation. In research in infectious diseases, the importance of

36 Ibid

37 National Academies of Sciences, Engineering, and Medicine 2020. "Innovations in Pharmaceutical Manufacturing: Proceedings of a Workshop— in Brief." Washington, DC: The National Academies Press. https://doi.org/10.17226/25814.

Examples of Actions by National R&D Funding Organizations

- In **Australia**, the National Health and Medical Research Council (NHMRC) issued an A$22 million call for proposals for COVID-19 R&D.
- In **Brazil**, the National Council for Scientific and Technological Development (CNPq) mobilized a paid call for R&D proposals resulting in support for 90 research projects funded by R$45 million.
- The **Canadian** government allocated C$23 million for the pre-existing Vaccine and Infectious Disease Organization–International Vaccine Centre at the University of Saskatchewan to accelerate development of a vaccine based on plant-produced antigens. The government also allocated C$114.9 million to the Canadian Institutes of Health Research to support rapid development grants for COVID-19 solutions.
- The **Chinese** government supported 83 emergency R&D programs. Support to businesses, universities, and research institutes was directed to supporting work in five core areas: clinical treatment, new medicines and vaccines, testing techniques and products, viral etiology and epidemiology, and animal model construction.
- In **France,** the ANR (National Agency for Research) issued a "flash" call for R&D proposals to address COVID-19. The call resulted in 270 submissions, with €3 million going to 86 projects, supplemented by further funding from the private nonprofit Foundation for Medical Research for a total of €14 million.
- **Germany** advanced multiple funding streams to support basic, clinical, and applied COVID-19 research. These included: €145 million to the Coalition for Epidemic Preparedness Innovations (CEPI) and €1.5 million to the WHO Solidarity Trial of alternative therapeutics; €750 million to strengthen and accelerate vaccine development; €15 million for developing therapeutics and improving understanding of the virus; and €150 million for establishment of a new research network to pool the research strengths of German medical schools, and establish a central infrastructure including a patient database to identify and reinforce best practices.
- **Japan** allocated an unspecified amount of R&D funds under its COVID-19 supplemental budget of ¥117 trillion ($1.1 trillion). Funds are to be directed to R&D for therapeutic medicines and vaccines and an increase of production and stockpiling of 2 million doses of Avigan.
- A COVID-19 **Africa** Rapid Grant Fund of €4.75 million has been established with 15 participating African countries. South Africa's National Research Foundation is a major funding supporter.
- The government of **Sweden** allocated approximately 100 million krona to the Swedish Research Council to expand initiatives in virus and pandemic research. The government also provided recipients of existing grants an option to repurpose their supported work to address COVID-19 .
- **UK** Research and Innovation, together with the National Institute for Health Research, and the Medical Authority, issued a joint call for R&D proposals for COVID-19. Fourteen million pounds was allocated to 21 accelerated research projects. Innovate UK also stood up a £1.25 billion package for innovative commercialization projects for COVID-19 by UK firms.

government and philanthropic funding has been particularly important, whereas major industry research activity has been more focused on the large-scale challenges associated with chronic diseases. Writing in Contract Pharma, Paul Bridges and Sheela Hegde note the following:

> *For many years now, funding for R&D in infectious disease treatments or vaccines has come mainly from government entities, such as the U.S. National Institute of Allergy and Infectious Diseases, and philanthropic organizations, including the Bill & Melinda Gates Foundation. The biopharma industry has invested its development dollars in other areas, and infectious disease programs currently represent less than 2 percent of the overall development pipeline.*[38]

It is likely that the COVID-19 pandemic will prove to be a wake-up call for research funders and will result in governments allocating a greater portion of their life sciences research funds toward addressing infectious diseases. Industry has, for logical business reasons, primarily focused on chronic diseases. In infectious diseases, products have generally not been reimbursed at levels conducive to intensive innovation. Generic antibiotics dominate, and vaccines are a more challenging market because a vaccine is typically administered only once or twice to a patient across their life span.

Bridges and Hegde note the following:

> *To spur greater investment in infectious disease, policymakers will need to address both "push" and "pull" incentives. While funding grants (push) and regulatory incentives can help companies de-risk the early stages of development, they do not address the low return on investment... Pull incentives would create more certain and attractive returns for successful antibiotic development. These could include market-entry rewards, such as payments over multiple years to companies after approval or transferable vouchers that would extend the exclusivity period on other drugs in a company's portfolio.*[39]

Lesson 3.2: Public co-investment can be a significant catalyst.

A specific trend observable in the response to COVID-19 has been the quick engagement of government in developing funding mechanisms to boost capital flows to industry that can help more rapidly advance relevant products in development and de-risk industry exposure for potential development challenges.

In the EU, for example, the European Commission has been funding projects to develop vaccines, treatments, and diagnostics via grants from Horizon 2020 and the Innovative Medicines Initiative (IMI). Through these mechanisms, the EU announced up to €45 million (US$48.8 million) in public funding. The IMI expects pharma companies to pitch in more money to make a total investment of €90 million (US$97.7 million).

In the United States, the federal government's Biomedical Advanced Research and Development Authority (BARDA) is providing substantial financial support to help companies dramatically accelerate the development of promising vaccines and therapeutics against COVID-19, even to the extent of helping to support manufacturing investments in advance of a proven product (an unprecedented, but necessary, forward-looking step to take, given the health and economic damage being wrought by the coronavirus). The following are examples of the significant funding being provided by BARDA:

38 Paul Bridges and Sheela Hegde. "COVID-19's Long-Term Impact on Drug Development: The New Pragmatism." Contract Pharma. May 18, 2020. https://www.contractpharma.com/contents/view_experts-opinion/2020-05-18/covid-19s-long-term-impact-on-drug-development-the-new-pragmatism/.

39 Ibid.

International Funding for Scale-up and Manufacturing

- In Brazil, the government issued a credit line of R$600 million to support companies in scaling-up products and devices. Among the results is a 10-minute diagnostic launched by Hi Technologies.
- The National Research Council of Canada agreed to upgrade its Human Health Therapeutics facility in Montreal to facilitate manufacturing of a CanSino vaccine candidate.
- In the UK, the government accelerated the development of a Vaccine Manufacturing and Innovation Centre (VMIC), allocating an incremental £93 million so that the facility can open in 2021, a year ahead of schedule. The government also allocated an additional £38 million for distributed or virtual support of vaccine manufacturing competencies in the country, in advance of the VMIC opening. The UK also invested in the National Biologics Manufacturing Centre in Darlington, which is slated as a manufacturing site for Imperial College's mRNA candidate vaccine.

- $2.5 billion in support to help Moderna develop manufacturing capacity for its mRNA-based Covid-19 vaccine.[40]
- $1.2 billion in investment alongside Astra-Zeneca for accelerating clinical testing and advancing manufacturing for its ChAdOx1 COVID-19 vaccine candidate.[41]
- $2 billion in investment with Sanofi Pasteur and GSK to advance recombinant SARS-CoV-2 Protein Antigen + AS03 Adjuvant-based vaccine candidate.[42]

As of September 8, 2020, the BARDA website reporting on its co-investment support for advancing COVID-19 countermeasures[43] lists 59 investments including work to advance solutions at universities, device companies, diagnostics companies, biopharmaceutical firms, and vaccine manufacturers.

It should be noted that these government investments represent a co-investment. Industry itself is making large-scale at-risk investments, and self-funding major capital undertakings in advance of having fully proven products. This is unprecedented in terms of the risk being taken and the willingness of the life sciences industry to extend itself, given the urgency of the situation for humanity. Phyllis Arthur, vice president for infectious diseases and diagnostic policy at Biotechnology Innovation Organization (BIO), notes as follows:

> *This is unique. Normally, companies would not invest in their manufacturing scale-up until they were deep into phase 2 and starting phase 3. They'd have more clarity that a product was going to work.*[44]

Without the luxury of time to achieve such clarity, the industry has stepped out on a financial limb in efforts to advance a cure.

40 Moderna Base Award Amount $430,298,520 (April 16, 2020); Mod/Option 1 Amount $53,000,000 (May 24, 2020); Mod/Option 2 Amount $471,596,459 (July 25, 2020); Mod/Option 3 Amount $1,525,000,000.00 (August 11, 2020). Source: https://medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx?filter=vaccine.

41 Ibid.

42 Base Award Amount $30,775,336.46 (April 10, 2020); and Mod/Option 1 Amount $2,042,000,000.00 (July 30, 2020). Ibid.

43 Ibid.

44 Olivia Goldhill. "The US is spending hundreds of millions to make experimental coronavirus vaccines." Quartz. April 22, 2020. Accessed online at: https://qz.com/1842490/us-invests-hundreds-of-millions-to-produce-Covid-19-vaccines/.

Lesson 3.3: Inter-industry partnerships and collaborations make a difference.

In addition to government-sourced funding supports, industry has entered into inter-firm business collaborations and formal partnerships to more rapidly advance coronavirus vaccine and therapeutic candidates. Large biopharmaceutical companies have partnered to leverage their respective intellectual property (IP) and proprietary technology platforms, a level of collaboration and potential financial exposure that likely would not have been pursued were it not for the urgency of the pandemic.

Similarly, smaller and emerging biotech and pharmaceutical early-stage ventures are teaming with large biopharmaceutical companies to gain access to their development, production, and distribution expertise and networks. Again, these earlier-stage companies would have been more likely to have cautiously advanced their products and more closely held their IP were it not for the urgency of the pandemic. Some of these partnerships and collaboration decisions may well not be optimized from a financial return perspective for the participating companies, but they are being advanced anyway because not to do so puts lives at risk in delaying potential solutions to the COVID-19 pandemic.

Lesson 3.4: Public markets may infuse capital.

Equity markets have proven to be a source of rapidly injected cash into companies announcing promising candidate vaccines and therapeutics for COVID-19. Multiple publicly traded companies with candidate products (especially those that

The European Union's Central Response

As a formal component of the overall €16 billion EU-level response to the crisis, the European Commission's strategy for vaccine development released in June included the following:*

- A pledge of €1 billion from the current Horizon 2020 research program, of which €350 million was dedicated to projects on vaccine development through a series of emergency calls and enhanced flexibility in existing projects.
- An Accelerator Pilot managed by the European Innovation Council (EIC), the agency for investing in company-based innovation, resulting in €148 million being placed in projects run by 36 companies with relevant projects. (The EIC is set to become part of the succeeding research framework program, Horizon Europe, which will run from 2021 through 2027). *
- Commitment of €400 million in lending capacity through the European Investment Bank to buy down the risks of high-stakes vaccine development in exchange for secured supplies, resulting in loans of €100 million to BioNTech and €75 million to CureVac.
- Building on previously funded programs such as the European Virus Archive, TRANSVAC2, the European Infrastructure for Translational Medicine, and the European Clinical Research Network.*
- Funding of €100 million toward large-scale, multicenter trials through CEPI.
- Development of a COVID-19 data portal* for sharing of research results.

** European Commission. EU research and innovation supporting vaccine development for COVID-19. June 17, 2020. Online at: https://ec.europa.eu/info/sites/info/files/research_and_innovation/research_by_area/documents/ec_rtd_cc-vaccine-development_factsheet.pdf.*

Figure 7: COVID-19 Therapies in Development by Originating Company Headquarters

Source: Analysis by BIO

are able to report robust preclinical results or, especially, success in early-stage clinical trials) have seen their stock prices increase substantially upon public announcements of results. Increases in company share prices provide a capital cushion to companies, providing cash for capital investments and acquisitions (if the company owns substantial shares in its own stock) and enhanced retention of talent (for those employees who have stock options). Enhanced company value also provides assurance to commercial lenders who may be approached to fund capital investments for scaling-up a company's products and operations.

Lesson 3.5: VC and angel investor activity prime the pump of innovation.

One of the reasons why the United States has been a leader in advancing candidate biopharmaceutical products (see Figure 7) is its access to a robust domestic network of early-stage capital providers. TEConomy and BIO note the following in their recently released 2020 joint report on the U.S. life sciences ecosystem:

> *The availability of investment capital is critical for advancing and sustaining industry development; and for an innovation-intensive and science-driven industry such as the biosciences, it is especially important for companies navigating lengthy time horizons to achieve commercial viability. Access to seed- and early-stage capital is especially important to sustain product development and where relevant, to conduct and meet rigorous pre-clinical and clinical testing requirements.*[45]

Having access to a rich resource of early-stage capital primes the pump in terms of building entrepreneurial companies that may address health challenges. In 2019 alone, analysis of Pitchbook data by TEConomy shows that U.S.-based companies in drug discovery and development, pharmaceuticals, medical biotechnology, and diagnostics

45 TEConomy Partners and BIO. The Bioscience Economy: Propelling Life-Saving Treatments, Supporting State & Local Communities. 2020. https://www.bio.org/sites/default/files/2020-06/BIO2020-report.pdf.

received $18.3 billion in risk capital investments. A total of 1,037 companies were funded with 1,225 investment deals made by VC firms, angel investors, and seed-stage funders.

The key lesson to be learned is that there are pandemic countermeasure advantages, as well as economic development advantages, in building entrepreneurial life sciences ecosystems that are supported by a substantial pool of active risk-capital providers. It should also be noted that the development of VC and angel capital providers is further enabled in nations by having access to strong publicly traded stock markets, which provide key liquidity (or "exit") events for early-stage investors when companies undertake initial public offerings (IPOs). The United States accounted for circa 50 percent of global VC investments in 2019, with other highly active nations including Israel, Sweden, the United Kingdom, Germany, France, and China.

It must also be recognized that investment capital is extremely hard to attract without robust protections for IP. Patent protection, and a well-structured legal system for defense of patents, is very much a requirement for sustaining investment momentum in life sciences markets.

Framework Element 4: Policies and Regulation

Policies and regulations enacted by governments represent a cross-cutting series of factors that have an impact across the value chain of the life sciences industry. Perhaps no other industry is as heavily regulated and influenced by public policies globally, and at the individual nation level, as is the human life sciences sector. Products for clinical application have profound implications for human health, and thus carefully constructed regulatory systems have evolved to govern and ensure the efficacy and safety of biomedical products (especially those that enter or touch the patient).

The COVID-19 pandemic has highlighted elements of the policies and regulations framework that have worked well and has generally shown regulators to be quite responsive and flexible in the face of the unprecedented real-time threat of the coronavirus. At the same time, however, the pandemic has also highlighted areas in need of improvement or revision based on barriers generated to more effective and timelier pandemic response.

Overall, as shown in this report, life sciences ecosystems across the globe have been extraordinarily responsive to the pandemic, activating and advancing production in diagnostics and therapeutics and accelerating R&D for vaccines and therapeutic products. Manufacturers of biopharmaceuticals, medical devices (such as ventilators), PPE and other critically needed products have worked round the clock to boost production—working even while the pandemic impacted their own communities. Regulatory bodies have been working equally hard in accelerating reviews of critical R&D projects and innovations and developing programs designed to provide rapid response to questions and inquiries from researchers and manufacturers.

The life sciences ecosystem has evolved in response to scientific advancements, market needs, business realities, and public policies. It is generally a well-refined ecosystem, and care must be taken with decisions that may disrupt ecosystem operations. The pandemic has certainly generated a rude awakening as to the damage that can be wrought to health and the economy by a fast-spreading novel virus, and it may be tempting for governments or other actors to seek to quickly make changes in the system that they believe will fix problems they observed in their individual nations. However, turning the dials on a refined and balanced system without understanding the ramifications of a change in one area on other areas, or the system overall, carries risk. A topline caution to policymakers and regulators is to be cautious and considered in the development of policies and procedures that will impact the ecosystem's equilibrium unless there is certainty in positive outcomes to be achieved.

There is already discussion in some markets of quite significant actions that governments and other parties are considering, and the following are some cases in which such actions have been taken:

- Requiring domestic production of medicines or other medical products that are currently imported.
- Requiring the transfer/licensing of IP from an originating firm to an in-country domestic manufacturer in order for the product to be sold in the nation.
- Banning or severely restricting the export of critical medical products and technologies, or government interception of contracted goods.
- Actively attempting to "poach" companies with promising technologies from their originating countries in order to relocate them and capture their innovations.

For the most part, such actions have been in the minority, and public bodies have generally been thoughtful and professional in the policies being adopted or considered as the pandemic progresses. Actions taken have been diverse, and it is beyond the scope of this document to cover them all, but a number of the most important lessons learned are highlighted below.

Summary of Lessons Learned for Policies and Regulation:

- *It is important to sustain the existing ecosystems characteristics that are favorable to life sciences ecosystem operations.*
- *Centralized, preplanned, and well executed rapid national response strategies are critically important.*
- *Regulatory flexibility is required in emergency situations.*
- *Liability and other risk mitigation should be addressed.*
- *Commitment to building strategic stockpiles and government purchasing is required.*
- *Disinformation and misinformation must be proactively addressed and managed.*
- *Government can facilitate the implementation of new biopharma production technologies.*

Lesson 4-1: It is important to sustain the existing ecosystem characteristics that are favorable to life sciences ecosystem operation.

In responding to a crisis, care must be taken to avoid actions that may undermine existing favorable ecosystem characteristics. Many of the "fundamentals" that underpin successful life sciences ecosystems are influenced by government policies and regulations, including, for example:

- Government funding for research
- Favorable tax treatment of private sector R&D investments.
- Nationally funded "big science" infrastructure assets operated as user facilities to advance basic and applied research.
- Robust intellectual property protections and enforcement.

- Funding for K-12 and higher education systems, and training programs for a life sciences workforce.
- Operation of predictable and scientifically-based regulatory systems
- Maintenance of free and fair international trade.

While each of the above is important, intellectual property protections (IP) are particularly critical for life sciences innovation commercialization. Robust IP protections and enforcement are essential for companies that may spend billions of dollars to conduct the R&D, trials, and establish manufacturing to bring novel biopharmaceuticals, vaccines, and other therapeutic products to market. IP protections have also shown themselves, during the pandemic, to be effective protections that enable companies and organizations to collaborate. Innovators can work together on coronavirus solutions, secure in the knowledge that IP protection allows their individual R&D investments and rights to be preserved.

The cost of responding to a pandemic, and fiscal challenges generated through economic slowdowns, place substantial pressures on government budgets. However, government plays a central role in supporting basic and investigative research that "primes the pump" for applied innovations. Sustaining funding for ongoing government sponsored research is critically important.

Lesson 4.2: Centralized, preplanned, and well executed rapid national response is required.
With a fast-spreading virus, it is imperative that mitigation actions stay ahead of the spread. Nations in Southeast Asia that were impacted by the SARS outbreak in 2003 learned this lesson, and both Taiwan and Korea, for example, captured their lessons-learned and developed a formal response strategy and action plan for when the next major pandemic would emerge. The actions laid out in the Taiwanese and Korean response plans swung into action very early as the coronavirus started to spread in China. Under these strategies, travel restrictions were quickly implemented; and recent passengers from originating destinations were traced, contacted, and quarantined—and those with whom they had contact were notified and quarantined also. Taiwan, for example, established a central National Health Command Center after SARS and activated it as soon as reports of COVID-19 surfaced. Executing its plan, Taiwanese health officials quickly boarded aircraft arriving from Wuhan China to assess passengers for symptoms before allowing them to deplane; and by January 5, Taiwan was tracing people who had traveled to Wuhan within the previous 14 days and then quarantining any contacts with signs of a respiratory infection. Taiwan's plan also prioritized personal protective shipments to frontline health providers and, in parallel, ramped up production or supplies purchasing to enable distribution to the general population. Korea acted similarly quickly, and its plan called for quickly developing diagnostic tests for the coronavirus, scaling them quickly and putting in place drive-through testing centers. Singapore was likewise effective in its early response.

Countries that did not have a predeveloped plan that they could rapidly execute found themselves on the back foot, trying to play catch-up to viral spread. Some adopted the playbook of those with a plan and had relative success with this copy-based approach—including quickly approving, adopting, and rolling out diagnostics proven in the forerunner fast-moving nations. Others were slow in response, for whatever reason, either not having a central plan for a pandemic, not executing previously developed response plans (perhaps because they were developed by a previous out-of-favor administration), or deciding to cede control over response to subnational regional or state authorities. The key lesson to be learned from COVID-19 is that speed is of the essence and, to move fast enough, a formal national plan must be in place and executed. Trying to pull together a novel plan in real time as a highly infectious disease takes hold has largely been shown to be ineffective by the current pandemic.

Lesson 4.3: Regulatory flexibility is required in emergency situations.

It can take months to advance research proposals, clinical trial plans, or product approvals through established regulatory approval processes. In non-emergency conditions, that timing can be absorbed; but, in a fast-moving pandemic, a slow moving regulatory system that is inflexible in its processes or protocols will be an impediment to advancing innovations and potential solutions. Actions taken by agencies in the United States to COVID-19 and diagnostics, for example, have illustrated both good and less-than-ideal actions:

- The FDA has been highly responsive and taken unprecedented actions to help researchers and companies advance products and technologies to address COVID-19. The agency issued multiple Emergency Use Authorizations (EUAs) that expedited review of diagnostic test kits and authorized their use for cases involving COVID-19. Also, as noted in the Clinical Trials section of this report, the CTAP program at FDA provided a novel process to rapidly advance innovations and trials for COVID-19.
- The Centers for Disease Control (CDC) decided not to use diagnostic tests already developed and in use in other nations, or the WHO's promoted test, and instead followed its preferred course to develop its own test. Unfortunately, the CDC-developed test had problems when implemented, resulting in a significant delay in rolling out an approved U.S. test for labs across the nation to use.

A report by FTI Consulting captures many of the FDA's actions during the pandemic, serving to illustrate the fact that the agency has been both responsive and flexible to the real challenges posed by the pandemic.[46] It is noted that FDA actions included the following:

- Working with manufacturers to expedite the initiation of clinical trials of COVID-19 vaccines as well as subsequent review and approval.
- Evaluating approved, currently available drugs, such as Actemra (approved for rheumatoid arthritis), for repurposing to treat COVID-19.
- Actively reaching out to pharmaceutical manufacturers to identify potential drug shortages.
- Exercising enforcement discretion to allow multiple laboratories to develop COVID-19 tests.
- Working through disruption of inspections of drug and medical supply firms in China that followed the U.S. State Department's travel advisory for that country. Approximately 100 scheduled inspections in February and March were placed on hold. Consequently, FDA has stated that it will use, where appropriate, the agency's authority to request records from firms "in advance or in lieu of" drug surveillance inspections in China.
- Active monitoring of marketing materials to protect the public from false and misleading information. The FDA has issued multiple Warning Letters to companies promoting unproven or fraudulent products for combatting COVID-19.
- Relaxing compounding oversight for some of the drugs in high demand for the most severe COVID-19 patients. The drugs include sedatives (e.g., fentanyl and ketamine) used during intubation, as well as antibiotics such as vancomycin.

The U.S. government has also been proactive in easing some of its anti-trust limitations for companies working together to advance products to combat COVID-19.

46 FTI Consulting. Covid-19: *Impact on Global Pharmaceutical and Medical Product Supply Chain Constrains U.S. Production*. https://www.fticonsulting.com/~/media/Files/us-files/insights/articles/2020/mar/Covid-19-impact-global-pharmaceutical-medical-product-supply-chain.pdf.

Examples of Government Approaches to Regulatory Flexibility and Speed of Response in the Covid-19 Pandemic

- The Brazilian Registry of Clinical Trials announced intent to fast-track approval of COVID-19 trials, with a target of 48 hours for turnaround.
- Health Canada approved 37 COVID-19–related clinical trials, in the process allowing a wider range of health professional and investigator classifications to be involved, rather than only drug manufacturers. It has also approved, on an expedited basis, importation of drugs and devices.
- In Korea, the Ministry of Science and ICT announced its intention to reduce from one or two months to less than one week the time that would be required, under existing procedures, for institutional IRB approval of COVID-19–related clinical trials. The Ministry of Food and Drug Safety developed its "Go Expedited Review Program (GERP)" to support rapid commercialization of innovations for COVID-19.
- Multiple trials were launched in the UK in record time as a consequence of fast-track review by the Health Research Authority.
- Regulatory agencies in multiple countries have enabled virtualization of clinical trials through digital health technologies, and extended the use of digital technologies for virtual regulatory inspections (in areas such as Good Clinical Practice and pharmacovigilance inspections), and electronic files submission of Certificates of Pharmaceutical Products and Good Manufacturing Practices.

Lesson 4.4: Liability and other risk mitigation should be addressed.

Even with many years of R&D and trials development, there are times when a pharmaceutical approved for sale is found to produce exceptionally rare side effects not encountered in trials. Human biology is complex; and factors, such as genetic diversity, rare allergies, and differences in environmental factors people encounter, can produce unforeseen adverse drug events. The extreme humanitarian need for therapeutics to treat COVID-19 infection, and vaccines to prevent infections, is justifiably requiring R&D and trials management teams to advance products as rapidly as possible within the bounds of established protocols. Candidate vaccines and therapeutics have been advanced to human trials at an unprecedented pace upon regulatory consultation and with regulatory permission, and selfless volunteers have come forward to participate in trials. There is a possibility that the accelerated pace of development and production of COVID-19 medical countermeasures may result in some adverse events in the future. Governments should consider special legislation for COVID-19 treatment and vaccine manufacturers to mitigate legal liability for companies or establish ways to transfer potential liability to government to mitigate corporate risk based on companies accelerating development for the public good.

There are other risk factors for companies in this fast-moving environment that governments should also consider and address. Companies are making unprecedented financial decisions to invest in production facilities, for example, prior to having a fully proven and approved product. Companies risk having stranded assets if their product is ultimately unsuccessful against the virus, and negative financial ramifications of this may lead to later shareholder suits or other issues. Again, legislation should be considered to cover this risk. Rapid construction of new plants may also lead to other liabilities (such as environmental issues or other factors) that may also need to be addressed to reduce or remove company liability.

Innovation in the Pandemic. Nonprofit Battelle Memorial Institute Invents Containerized Decontamination Units for N95 Masks

One of the notable innovation success stories during the pandemic was the creativity and engineering skills at Ohio-based Battelle, which rapidly designed, engineered, and manufactured unique systems based on shipping containers, using vaporized hydrogen peroxide, to decontaminate the protective equipment (such as N95 masks) being used by frontline healthcare workers in COVID-19 hot spots. As of June 30, Battelle had CCDS Critical Care Decontamination Systems operating at 50 sites across the United States and the systems had decontaminated over 1.2 million masks.

Lesson 4.5: Commitment to building strategic stockpiles and government purchasing is required.

Multiple nations found that they had insufficient inventory of PPE, ventilators, and other medical supplies needed to address the scale of the COVID-19 pandemic. The current pandemic was created by a virus with an R (its effective reproduction number or its effective capacity to spread) that is higher than seasonal flu but much lower than many other infectious diseases, such as measles, for example. Still, the R of the coronavirus stretched the healthcare systems and intensive care units in hospitals in hot spot locations to the breaking point. Existing stockpiles and supply chains for PPE, especially, were found to be insufficient, and frontline healthcare workers in many locations were reduced to reusing PPE that was designed only for one-time use.

As best practice moving forward, each nation will need to assess the appropriate level of stockpiling (of PPE, medical devices, critical medicines, etc.) that will be necessary to develop based on the experience of COVID-19 and take into consideration the possibility that a future pandemic may have an even higher R than COVID-19. Having portable decontamination systems (see sidebar) that may be shipped to hot spots may also be a consideration.

Lesson 4.6: Disinformation and misinformation must be proactively addressed and managed.

Making rational, scientifically based decisions in a fast-moving dynamic health event is difficult enough—but, it is rendered even more difficult if misinformation, or deliberate disinformation, is spread to impacted populations. The risk of mis/disinformation impacting decision making is one of the reasons why having a predeveloped strategic action plan, rooted in scientific evidence and best practices, that is mandated for use when an event presents, is so important—it helps remove political pressures, fast-moving opinions, and distractions from the equation.

Combatting mis/disinformation is a challenge that is expanding under proliferation of social-media and other communications platforms that can quickly disseminate non-refereed or inadequately reviewed content. It is a challenge that extends far beyond pandemic response and is a thorny issue to address with the inherent paradox of balancing freedom of speech issues, personal freedoms and responsibilities, and collective public health needs. The reality is that each country is different in its social norms, response of citizens to authorities, and the powers invested in its government; and individual nations will likely need to engage not only epidemiologists and public health experts in their pandemic action plan development but also sociologists, anthropologists, psychologists, and political scientists.

Everyone lives with restrictions on their personal behavior. In the United States, one needs a driver's license to operate a car and must follow rules of the road for the safety of themselves and the public. Rules have been adopted on where smoking is allowed and where it is not. One also may not shout fire in a crowded movie theater when there is no fire. Other countries have more restrictions on acceptable behaviors based on their own cultures, social norms, and experiences. Developing a universal lesson learned for mis/disinformation under the COVID-19 pandemic is, for the above reasons, difficult to do. But, perhaps most could agree as follows:

- Deliberately spreading false information that would be harmful to public health should have consequences for the individual or organization that knowingly originates a claim that will cause increased exposure to infections.
- Deliberate noncompliance with lawfully enacted restrictions or public policies designed to foster public safety in a pandemic should have consequences. If deliberate noncompliance results in a proven contagion spike event, then consequences should be elevated.

What the "consequence" should be is a matter for individual national legislative and judicial systems to address; and they should be deliberated in advance of a pandemic event, incorporated into a pandemic event strategic action plan, and communicated to the public. As part of a global community, nations themselves have a responsibility to act appropriately also. National borders are porous, and viruses do not respect them. COVID-19 shows that poor containment in one location can spill over to affect neighbors, and again, international agreement may need to be reached on future consequences.

Lesson 4-7: Government can facilitate the implementation of new biopharma production technologies.

As noted earlier in this report, biopharmaceutical production technologies are evolving, and the COVID-19 pandemic may accelerate the evaluation and adoption of emerging production technologies such as single-use systems and continuous manufacturing. Best practice will be for regulatory agencies to monitor emerging technologies and to prepare scientifically and technically for innovative technologies as they are being developed and piloted. Janet Woodcock, director of the U.S. FDA's Center for Drug Evaluation and Research (CDER), has noted that "industry's reluctance to embrace new technologies … is probably related to expected regulatory obstacles with FDA and other regulators, and promotion of broad adoption of advanced manufacturing will likely require incentives."[47] Dr. Woodcock noted that there is a "need for advances in regulatory policy given that the agency is unsure how some of the innovative ideas will fit into the regulatory framework."[48]

47 National Academies of Sciences, Engineering, and Medicine 2020. *Innovations in Pharmaceutical Manufacturing: Proceedings of a Workshop—in Brief*. Washington, DC: The National Academies Press. https://doi.org/10.17226/25814.

48 Ibid.

Framework Element 5: Customers and Markets

The long-term effects of the pandemic on the delivery of healthcare and the market for medical products remain to be seen. At this point in time, there are, however, four lessons learned that are important to consider.

Summary of Lessons Learned for Customers and Markets:

- *Virtualization or digitalization of healthcare has accelerated.*
- *Universal, patient-centric access to care, diagnostics, therapeutics, and vaccines must be facilitated.*
- *There will be growth in product and service market niches rooted in pandemic preparedness and response.*
- *Long-term health implications for patients recovering from COVID-19 are, as yet, unknown.*

Lesson 5.1: Virtualization or digitalization of healthcare has accelerated.

It does appear that "virtualization" of person-to-person interactions (e.g., physician telemedicine consults with patients) has accelerated during the pandemic, and this is likely to be a continuing trend within the healthcare delivery environment. This assumes that post-pandemic study of the effectiveness of such virtual consult systems proves that they were of benefit and did not negatively impact health outcomes.

In general, it seems that accelerated advancement in the digital transformation of healthcare more broadly has been stimulated by the pandemic. This likely has implications for the following:

- More efficient use of clinician time.
- Reduced exposure of patients and clinicians to pathogens in clinical settings via reduced physical interactions.
- Enhanced development of, and acceptance of, home health solutions and wearable health monitoring devices.
- Increased use of online pharmacy ordering and home delivery of prescribed and over-the-counter pharmacy products.
- More virtual, and less face-to-face, interactions between medical product sales representatives and clinicians.

A key advantage of the virtual and digitalized delivery of healthcare is that this mode of interaction is inherently efficient for the capture of data—data that can then be used for analysis and systematic improvement of healthcare and health outcomes.

Lesson 5.2: Universal, patient-centric access to care, diagnostics, therapeutics, and vaccines must be facilitated.

When it comes to human transmissible diseases, there is substantial imperative to ensure that all potentially impacted members of a population have access to healthcare services and resources. If the public or private market is unable to deliver diagnostics, therapeutics, or vaccines to specific subpopulations, these subpopulations are likely to become reservoirs for the ongoing spread of the subject disease. Barriers to universal access to necessary healthcare resources have been highlighted by COVID-19, most notably in terms of the following:

- Variation in the ability, or willingness, of populations to pay for tests, therapeutics, or other interventions.
- Substantial geographic and socioeconomic disparities in access to healthcare.

Long term, the resolution of health disparities—working to smooth the landscape of patient access—will be beneficial to overall public health. In the near term, public health has been served by governments quickly moving to assure their populations that the government or third-party payers would fully cover costs of testing, diagnostics, and treatments. Most governments are

Collaborating to Advance Vaccine Access for All Nations

An output of the June 2020 Global Vaccine Summit hosted (virtually) by the UK, COVAX is a multinational collaborative designed to support rapid vaccine advancement and avert counterproductive competition between countries. The overall financing arrangement—under which higher-income countries will buy in advance for their own needs and contribute a cross-subsidy that supports the needs of low- and lower-middle income countries—is known as the COVAX Facility. COVAX is co-led by Gavi, CEPI, and WHO, working in partnership with developed and developing country vaccine manufacturers.

CEPI notes that "the overall aim of COVAX is to accelerate the development and manufacture of Covid-19 vaccines, and to guarantee fair and equitable access for every country in the world. It will achieve this by sharing the risks associated with vaccine development, and where necessary investing in manufacturing upfront so vaccines can be deployed at scale as soon as they are proven to be safe and effective, and pooling procurement and purchasing power to achieve sufficient volumes to end the acute phase of the pandemic by 2021."

As of July 31, $600 million toward the targeted $2 billion urgently needed minimum for Advance Market Commitments had been raised through the COVAX Facility. The COVAX Facility is pitched as a global insurance policy. Participation gives all interested governments—regardless of income level and ability to pay full freight—a guaranteed share of any future successful vaccine production that will be allocated by Gavi in a fair and equitable way across nations. The goal is to cover the most vulnerable 20 percent of the participating countries' population (and also healthcare workers).

similarly planning to cover the cost of vaccines for patients, while nonprofits and transnational organizations are stepping forward to help fund patient access for developing nations that lack the financial resources to fully implement required access programs.

Some commercial enterprises and partnerships have stated that they will be supplying vaccines on a cost recovery basis only—not seeking to receive profits from their R&D and commercialization efforts. While this is admirable, it may not be in the long-term interest of building responsive infectious disease and associated product development ecosystems. A profit incentive will be required to sustain long-term commitment to expensive life sciences R&D needed to address infectious diseases and associated public health events. It may be that COVID-19 is a one-time event—but the likelihood is that this will not be the last fast-moving pandemic to be seen. Infectious disease has tended to be an area of life sciences commerce that has received lower levels of commercial R&D attention than chronic disease (for the basic reason that ongoing chronic diseases sustain long-term patient demand for therapeutics and thus a sustained market, whereas infectious disease outbreaks are singular events and vaccines may be administered only periodically, with long time spans between original vaccination and a required booster shot). Given the more challenging commercial market characteristics of infectious diseases, increased funding support and engagement by government funding sources will be important to help pull through a greater volume of research and commercial products. A mechanism being deployed to accomplish this by governments is the structuring of advanced purchase agreements with biopharmaceutical companies. This is extremely helpful in mitigating some of the significant risk that companies are taking in greatly accelerating product development and, in some cases, developing manufacturing capacity in advance of having a fully proven product.

Lesson 5.3: There will be growth in product and service market niches rooted in pandemic preparedness and response.

It is probably safe to predict that the market for products used in the decontamination or sanitation of surfaces will see a sustained increase in demand. Similarly, the use of certain PPE, especially face masks, will become more accepted in daily life worldwide (akin to the cultural acceptance of their use in Southeast Asian nations).

There will also be an increase in demand for multiple medical and healthcare products to replenish and maintain national strategic stockpiles of medications (diagnostics, critical therapeutics, and vaccines) and supplies found to be relevant to specific or general pandemic response. Individuals and families are also likely to create moderate home stockpiles based on experiences with hard-to-find products during the pandemic.

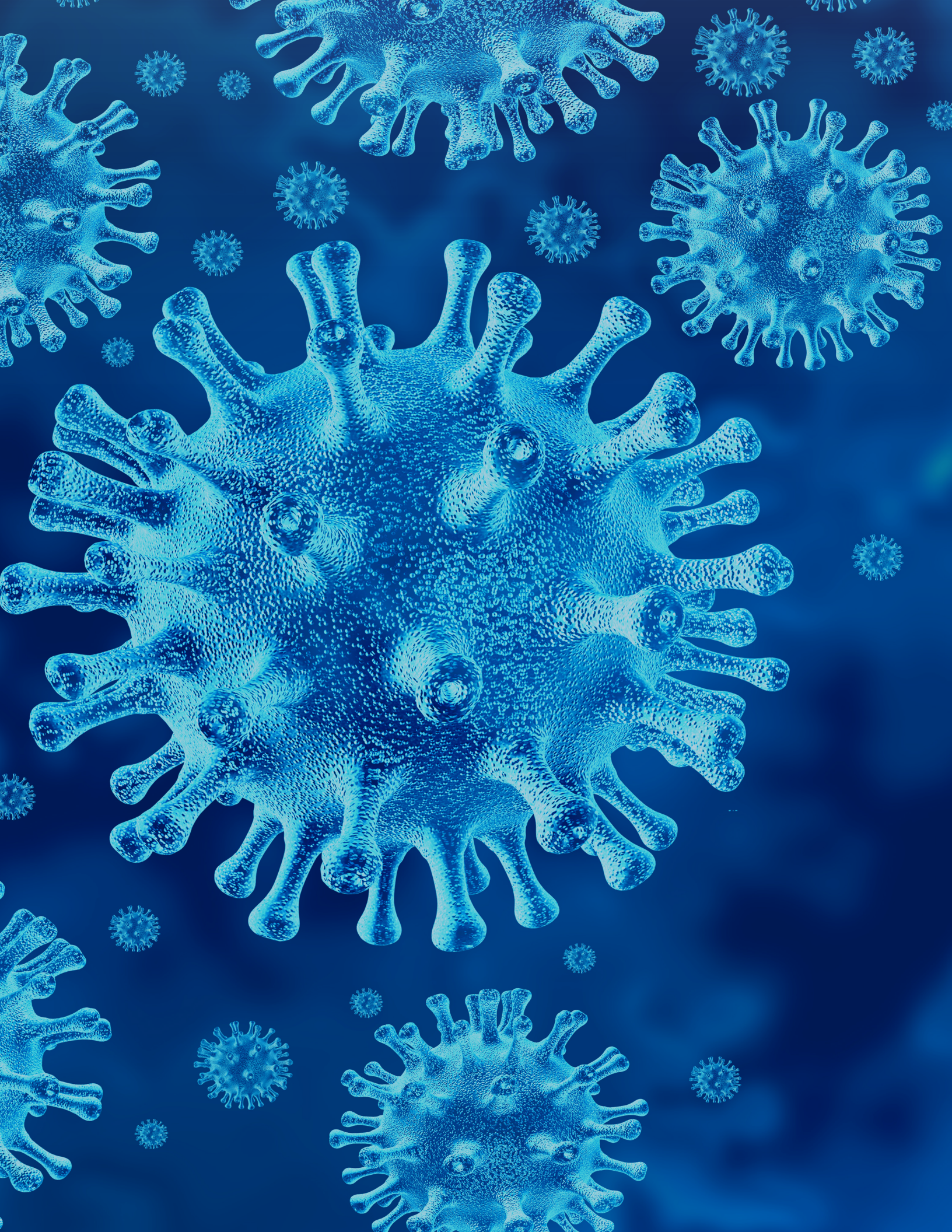
There is also a potential for seasonality to infections and for reemergence of COVID-19 cases in places where it has been previously suppressed. Potential waves, or smaller ripples of resurgence, need to be considered in mid- and long-term planning of production and purchasing strategies for all products needed in pandemic response. Policymakers will need to consider implications of seasonality or future infection events for their health budgets.

Lesson 5.4: Long-term health implications for patients recovering from COVID-19 are, as yet, unknown.

An unknown factor is what will be the long-term health implications for patients in their recovery from acute cases of COVID-19. Many patients may experience chronic illness as a result of lasting damage to their lungs and other organ systems as a result of severe forms of the illness. There is also an expanding base of patients experiencing what has come to be called "Long COVID" or "Long-Haul COVID," a sustained experience of a diversity of negative health effects, noted by Mayo Clinic to include long-term fatigue, headaches, vertigo, difficulties with cognition, hair loss, and cardiac issues, in addition to diminished cardiorespiratory fitness.[49] There may also be unknown health impacts associated with even milder forms of the disease that did not require hospitalization.

The reality is that "we don't know what we don't know" at this stage. The ongoing pressures of COVID-19 on patients, on healthcare systems, and on healthcare costs remain to be seen, and new lessons learned will no doubt appear. Long-term monitoring of survivors and subpopulations should be conducted to inform public health.

49 DeeDee Stiepan. "Long-term symptoms, complications of COVID-19." Mayo Clinic News Network. August 3, 2020. https://newsnetwork.mayoclinic.org/discussion/long-term-symptoms-complications-of-Covid-19/.



Conclusions

The COVID-19 pandemic has had a worldwide impact, creating societal and economic challenges of a scale not seen in a very long time. Typically, a crisis will bring forth lessons learned in terms of what was handled well and where gaps or flaws in response mechanisms were observed. Such is certainly the case in global, national, and regional responses to COVID-19.

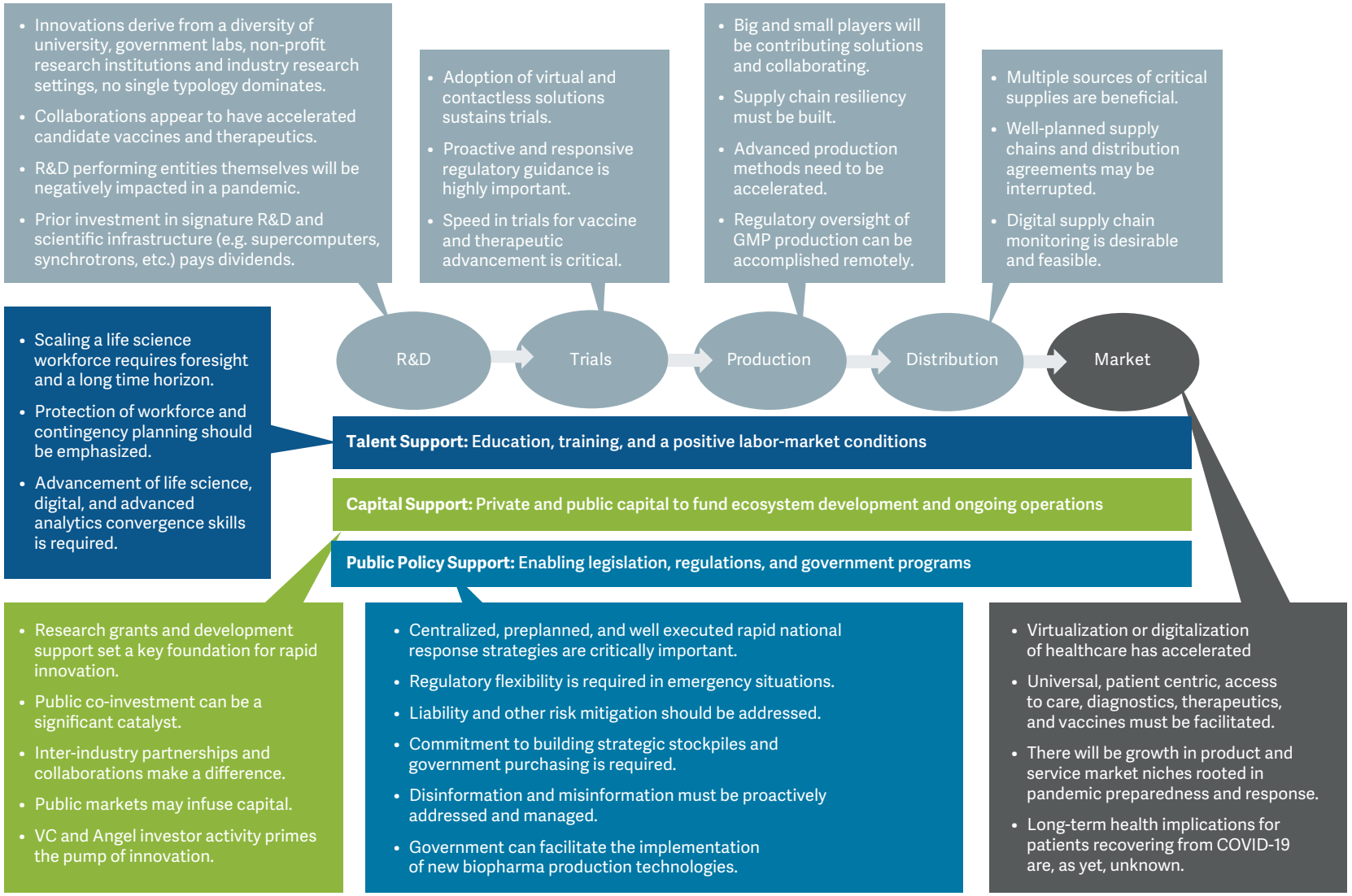
Review, herein, of lessons learned across the pandemic used a structured approach to examination of issues and observations across each main element of life sciences ecosystems. This approach enables readers to home in on those issues of most relevance to their specific interests or roles across the ecosystem. Figure 8 provides a quick-reference summary of lessons learned placed in the context of each core element of the ecosystem.

In reviewing these lessons learned across life sciences ecosystems, TEConomy finds that five key themes emerge as particularly important takeaways from this project. Associated with these themes are five recommendations for policymakers:

1. **Prior investments and advancements toward a robust life sciences ecosystem matter greatly in responding to a pandemic.** The fact that, in the face of the COVID-19 pandemic, so many vaccine candidates and drugs have been brought forward into testing, trials, and emergency use is a heartening achievement, and is a testimony to the foresight of those who have developed, work in, and support the complex life sciences R&D and industry ecosystems around the world. The complexity of the ecosystems that must be in place to advance R&D, product development, and production and distribution of biopharmaceuticals, vaccines, and diagnostics is such that they cannot be stood up from scratch in a real-time situation. They must already be in place, fully operational, well proven, and well funded, in advance of an emergent need.

   ***Recommendation**—Policymakers must prioritize and sustain investments in life sciences research infrastructure, workforce development, and advanced production systems. Enacted policies and regulations must support life sciences ecosystem development at scale and sustain favorable ecosystem operating conditions.*

Figure 8: Lessons Learned During the COVID-19 Pandemic Across Life Sciences Ecosystems



Source: TEConomy Partners, LLC.

2. **Promotion of collaborations is key to quickly mobilizing and pursuing new medical innovations.** Public- and private-sector collaborations, and inter-industry collaborations, have played a key role in rapidly advancing innovations for pandemic response. These collaborations often build upon the complementary and robust roles of public-supported academic research in basic research together with industry expertise in applied discovery, development, and clinical testing that routinely take place in high-functioning life sciences ecosystems. What the response to the COVID-19 pandemic has vividly demonstrated is the benefit of collaboration, even between previous competitors, whereby different, but complementary, R&D and industrial strengths and capacities can be brought together for advancing medical innovations.

   ***Recommendation**—Policymakers should develop and align incentives to encourage collaborations that will advance and speed the development and commercialization of medical innovations and take advantage of the full capacities found across life sciences research institutions and industry.*

3. **The convergence of digital technology with life sciences helps accelerate innovations and supports ecosystem resiliency.** One broad benefit of the COVID-19 pandemic has been the acceleration in the use of digital technologies across all stages of life sciences development. Digital technologies are proving effective in speeding up research insight and innovation, sustaining trials and regulatory oversight, building supply-chain transparency, and facilitating safer (remote) clinical healthcare interactions.

   ***Recommendation**—For the future, policymakers should continue to promote the use of digital technologies in R&D, clinical testing, supply-chain management, and healthcare delivery and seek ways to further the integration across distinct activities to improve the effectiveness of life sciences ecosystems.*

4. **Flexibility in government regulatory approaches is making a difference.** Given the typical drug and vaccine development timelines of at least 10 years, the speed of the overall response mounted by the global life sciences community to COVID-19 is nothing short of astonishing. This has been, in part, accomplished because of flexibility shown in regulatory processes by government. Perhaps the most-publicized area of flexibility is in the clinical testing of potential vaccines and therapies through mechanisms such as emergency use authorizations, compassionate use, conditional market authorizations, and short timeframe approvals, while still allowing for thorough scientific evaluation of a medicine's benefits and risks. Other less publicized forms of flexibility have also been advanced in the use of digital technologies in clinical trials monitoring, remote manufacturing inspections, ability to make changes in suppliers, and allowance for joint ventures and other collaborations.

   ***Recommendation**—Policymakers should consider how increased flexibility with accountability can be achieved on a more regular basis as a means for ensuring unmet medical needs are addressed to improve patient lives.*

5. **The existing business environment for innovation in life sciences ecosystems has proven to be highly agile and able to be effectively leveraged through the COVID-19 pandemic.** In challenging times there is a strong impetus for government to be seen to be "doing something." COVID-19 has certainly required critical government interventions and actions, but it is important to recognize that care must always be taken to avoid actions that may undermine the favorable ecosystem characteristics needed to maintain

life sciences advancements and innovation. There are multiple "fundamentals" that are influenced by governments that must be sustained in order for life sciences ecosystems to flourish, for example:

- Substantial commitment of government funds to supporting R&D through well-funded research grant funding agencies, together with favorable tax treatment of private sector R&D investments.
- Sustaining effective rules against trade barriers, and facilitating international trade, to enable resilient and flexible supply chains to operate that reliably meet demand for medical products.
- Operation of a flexible, science-based regulatory system.
- Maintaining predictable and sustainable payer pricing systems that balance the need to manage health care payer costs with the need for return-on-investment for innovative life sciences companies.
- Robust intellectual property protections.

The last bulleted fundamental is particularly critical. One of the core elements for life sciences innovation is having in place robust intellectual property (IP) protections for knowledge, ideas and data required for advancing novel medicines that are consistent with international treaty obligations and align with best practices. These IP protections are essential when it may cost billions of dollars in private investment to bring a novel medicine to market. Beyond ensuring private investment funding, IP protections are proving to be effective in enabling collaborations to take place between organizations with solutions to different pieces of the puzzle (even among traditionally competing firms). With robust IP protections, innovators can collaborate and work together to advance such solutions, knowing that their R&D efforts, inventions, and creativity are secure. Government funding support for research is similarly important, and global life sciences ecosystems have responded well to government incentives aimed at furthering R&D into novel antivirals and vaccines and increasing production capacities.

***Recommendation**—Policymakers need to ensure that the core elements of high-functioning life sciences business environments are in place to facilitate innovation advancement. Some of the key elements to be advanced include strong IP protections, operation of a flexible science-based regulatory system, and provision of secure market access for innovative medicines.*

The coronavirus caught humanity's leadership off-guard in many places across the globe this time. When the next high-threat infectious disease emerges (and such an emergence is all but a certainty and just a matter of time) all need to be better prepared. Funding, building, reinforcing, and sustaining robust life sciences ecosystems is a key component of that preparation, and the above themes and recommendations are proffered as important elements for consideration in building resiliency and responsiveness into critically important life sciences systems.

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