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Strengthening FDA's Regulatory Readiness: Implementing Lessons Learned from the COVID-19 Pandemic

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POLICY BRIEF

Background: The U.S. Food and Drug Administration (FDA) is responsible for protecting public health by ensuring the safety and efficacy of the nation's medical products. FDA plays a critical role in supporting the development of new countermeasures needed to protect against dangerous public health threats, which is vital during public health emergencies. Amid the worst pandemic in more than 100 years, FDA effectively used its authorities and expertise to help the United States develop innovative countermeasures to protect American families and the rest of the world from COVID-19.

Congress has regularly given FDA specific authorities to authorize drugs, biologics, and medical devices for use as medical countermeasures during public health emergencies. Congress provided these authorities through the Project BioShield Act of 2004, and strengthened them under the Pandemic and All-Hazards Preparedness Act and its successors. As a part of our nation's preparedness framework, FDA also supports the development and review of medical countermeasures, which includes working with the National Institutes of Health, the Biomedical Advanced Research and Development Authority, the Centers for Disease Control and Prevention (CDC), other federal agencies, states, and innovators.

In response to the unprecedented demands brought on by the COVID-19 public health emergency, FDA has leveraged the authorities and tools Congress provided over the last 20 years to swiftly and nimbly respond to the pandemic. FDA has authorized more tests, treatments, vaccines, and other countermeasures for emergency use than ever before. Many of these countermeasures were developed and authorized in a matter of months or even weeks, without compromising safety and efficacy – a testament to FDA's collaboration with innovators, coordination with other agencies, and dedication to its mission.

As we take stock of lessons learned from the COVID-19 pandemic, we should build on FDA's leadership and experience to improve our readiness for future public health emergencies and to enable private sector partners to innovate quickly. Accelerating the development and review of countermeasures for future threats, improving the resilience of medical product supply chains, and strengthening FDA's regulatory readiness and operations will help ensure our nation is more resilient against future threats. Congress must leverage lessons learned to ensure FDA has the tools, and innovators have the regulatory certainty, necessary to develop the next wave of medical countermeasures and cutting-edge treatments for patients.

Building on Lessons Learned: Successes and Progress at FDA

During the COVID-19 pandemic, FDA has taken unprecedented steps to expedite the development and review of new vaccines, therapeutics, tests, and other devices to protect Americans. To date, FDA has authorized three vaccines, licensed one for individuals 16 years and older, authorized one vaccine booster dose, and continues to review additional vaccine data from ongoing studies. FDA has authorized 11 therapeutics and approved one to treat COVID-19 and related health outcomes in certain populations, and it has authorized more than 400 tests and sample collection devices to help combat and prevent the spread of the virus. The successful elements of FDA's agile approach should be a model for future public health emergencies, as well as a guide to establish policies and make decisions to help speed the development and review of innovative products in the future.

Accelerating the Availability of Countermeasures

Many of the vaccines and therapeutics authorized for COVID-19 use platform technologies that hold immense promise for our capacity to respond to future public health threats. Platform technologies are critical to advancing novel medical products that can be adapted to address multiple different diseases using a common base. Building on longstanding research, the groundbreaking COVID-19 vaccines incorporate platform technologies such as messenger RNA (mRNA) and viral vectors to create new vaccines tailored to prevent and mitigate the effects of COVID-19.¹ As we look to the future of biomedical research, platform technologies will play a key role in building an arsenal against new public health threats and creating new treatments or cures.

Innovators are already using the platform technologies that underpin FDA-authorized vaccines to develop new medical products like flu vaccines, as well as new therapeutic candidates targeting infectious diseases, oncology, immunology, and other areas.² Other manufacturers – encouraged by FDA’s receptive approach to platform technologies during COVID-19 – have announced significant investments in developing new medical products on mRNA-based platforms.³ Multiple therapeutics, such as monoclonal antibodies, were likewise developed using underlying platform technologies to rapidly design new COVID-19 treatments.⁴

The development and authorization of multiple safe and effective COVID-19 vaccines in less than one year is a remarkable and historic accomplishment, and a testament to American innovation and ingenuity built on decades of scientific research and development. FDA worked with vaccine manufacturers to swiftly develop and test these vaccines, upholding the agency’s gold standard of safety and efficacy without cutting corners. New vaccine development is a time-consuming and difficult process, often taking a decade or more.⁵ FDA worked with vaccine manufacturers with unprecedented speed and agility to streamline development and scale manufacturing at risk and in parallel, which included supporting multiple phases of preclinical and clinical testing concurrently, rather than sequentially.⁶ These flexible and creative approaches, compared to the often long and risky development process, helped lead to life-saving, safe and effective vaccines.

FDA also worked swiftly with sponsors to develop new COVID-19 therapeutics. Similar to FDA’s breakthrough designation programs, the agency engaged in early, frequent interactions with product developers to provide them with FDA’s scientific and clinical expertise to accelerate the availability of medicines for patients fighting COVID-19. FDA’s COVID Treatment Acceleration Program helped accelerate clinical studies, address complex manufacturing challenges, and enable rapid review of

¹ *The lightning-fast quest for COVID vaccines – and what it means for other diseases*, Nature (Dec. 18, 2020), <https://www.nature.com/articles/d41586-020-03626-1>.

² Moderna, *Moderna Announces First Participant Dosed in Phase 1/2 Study of its Quadrivalent Seasonal Flu mRNA Vaccine* (July 7, 2021), <https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-first-participant-dosed-phase-1-2-study-its>; Pfizer, *New RNA Technology Could Get the Flu Vaccine Right, Every Year*, https://www.pfizer.com/news/featured_stories/featured_stories_detail/new_rna_technology_could_get_the_flu_vaccine_right_every_year.

³ See, e.g., Sanofi, *Sanofi to acquire Translate Bio; advances deployment of mRNA technology across vaccines and therapeutics development* (Aug. 3, 2021), <https://www.sanofi.com/en/media-room/press-releases/2021/2021-08-03-07-00-00-2273307>; GlaxoSmithKline, *GSK and CureVac announce strategic mRNA technology collaboration* (July 20, 2020), <https://www.gsk.com/en-gb/media/press-releases/gsk-and-curevac-announce-strategic-mrna-technology-collaboration/>.

⁴ See sotrovimab from GlaxoSmithKline and Vir Biotechnology, Emergency Use Authorization 100, REGEN-COV (casirivimab and imdevimab) from Regeneron, Emergency Use Authorization 091, and bamlanivimab from Eli Lilly and Abcellera, Emergency Use Authorization 094, as examples of monoclonal antibodies that were created using platform technologies.

⁵ International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), *The Complex Journey of a Vaccine* (2019), https://www.ifpma.org/wp-content/uploads/2019/07/IFPMA-ComplexJourney-2019_FINAL.pdf.

⁶ GAO, *Operation Warp Speed – Accelerated COVID-19 Vaccine Development Status and Efforts to Address Manufacturing Challenges* at 23 (Feb. 2021), <https://www.gao.gov/assets/gao-21-319.pdf>.

regulatory submissions to expedite the development and authorization of new treatments for patients. To date, FDA's efforts have supported more than 640 drug development programs and reviewed more than 470 applications for new clinical trials.⁷

Smart, Flexible Regulation and Communication

FDA has taken a flexible, nimble approach to supporting the development and review of COVID-19 countermeasures, including encouraging creative clinical trial designs. FDA worked with sponsors to adapt clinical trial designs and tools to meet the needs of the pandemic response. These efforts allowed biomedical research to meet patients where they were, eliminating barriers to participating in clinical trials for life-saving treatments and therapies. FDA supported the use of decentralized clinical trial designs and issued temporary guidance documents that expanded the use of digital technologies to better facilitate remote clinical trials, which helped protect patient safety while modernizing the way data is collected and evaluated.⁸ In fact, one vaccine sponsor conducted approximately 90 percent of patient monitoring remotely during their pivotal trial.⁹ FDA has also enabled sponsors to use adaptive and other creative trial designs to study COVID-19 therapies, such as seamless or concurrent trials, and has used real world evidence to assess the safety and efficacy of authorized products as they transition to applications for full approval or licensure.

FDA has used the flexibility provided under the Emergency Use Authorization (EUA) authorities to issue “umbrella” EUAs to quickly authorize categories of medical products, particularly devices and personal protective equipment. These actions incentivized the rapid development of COVID-19 tests, after an initial delay caused by issues surrounding CDC-produced tests, and increased manufacturing of personal protective equipment, ensuring more Americans had access to these critical tests and medical supplies during the response.

During the COVID-19 public health emergency, FDA quickly published guidance and other regulatory documents to provide crucial feedback to innovators and clinicians facing unprecedented uncertainties. Early and frequent interactions with sponsors to provide clear, consistent, and timely feedback helped speed the development and availability of medical countermeasures to turn the tide on the pandemic response.

Addressing Challenges Identified In the COVID-19 Response

While FDA rose to the challenge in its efforts to accelerate the development and review of medical countermeasures, other aspects of the agency's performance during the COVID-19 pandemic highlight challenges that should be addressed to improve FDA's regulatory readiness and better equip the agency for future public health emergencies.

Getting Tests to Americans in a Timely Manner

The failure to develop a broadly available, effective test early in the pandemic was one of the biggest gaps in our preparedness framework. During the earliest stages of the pandemic, protocols were not in place for

⁷ FDA, Coronavirus Treatment Acceleration Program (CTAP) (current as of Sept. 13, 2021), <https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap>.

⁸ See, e.g., FDA, *Enforcement Policy for Non-Invasive Remote Monitoring Devices Used to Support Patient Monitoring During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency* (Updated Oct. 2020), <https://www.fda.gov/media/136290/download>.

⁹ *Inside the Pfizer/BioNTech COVID-19 vaccine trial: 'We knew the world was watching and waiting for results'*, Biopharma-Reporter (March 3, 2021), <https://www.biopharma-reporter.com/Article/2021/03/03/Inside-the-Pfizer-BioNTech-COVID-19-vaccine-trial-Insights-on-speed-agility-and-digital-development>.

FDA to leverage the full horsepower of the laboratory infrastructure in the United States. On January 21, 2020, CDC confirmed the first case of COVID-19 in the United States.¹⁰ Days after the declaration of a public health emergency by Department of Health and Human Services Secretary Azar on January 31, FDA issued on February 4 the first EUA for the diagnostic test developed by the CDC to be used at qualified public health laboratories.¹¹ CDC's test, however, was critically flawed, and was developed in a laboratory that failed to meet basic quality standards.¹² Throughout February 2020, as COVID-19 rapidly spread across the country, CDC's flawed test was the *only* authorized test available.¹³

CDC's insistence that they, and they alone, develop diagnostic tests in the early days of the pandemic prevented early engagement from the laboratory community to develop tests to diagnose and detect the virus. FDA's delays in expanding testing availability and capacity resulted in important time lost early in the pandemic. While multiple laboratories and innovative test developers across the country were otherwise ready to detect and diagnose this emerging virus, FDA required laboratory test developers to submit an EUA application for each individual test. In February 2020, with no reliable tests on the market, FDA *stopped* some laboratories from using their tests to help diagnose COVID-19 and detect SARS-COV-2.¹⁴

On February 29, more than four weeks after the public health emergency was declared, FDA tapped into existing commercial and academic laboratory capacity, authorizing certain certified clinical laboratories to develop and use their own COVID-19 tests, on the condition they notify FDA that they had validated their test and submit certain information to FDA within 15 days.¹⁵ FDA's overly strict and initially inflexible criteria did not encourage innovative test development and instead limited the tests available to the public and health care providers to help detect, diagnose, and surveil for COVID-19. Instead of restricting the availability of important tools that could have been used to slow the spread of the disease, FDA should have acted immediately to work with laboratories and test developers to innovate and help scale up our nation's testing capabilities.

Ensuring a Resilient Supply Chain

As COVID-19 spread domestically and worldwide, the United States experienced shortages of certain critical medical products and supplies needed to provide care and protect health care providers, patients, and the public. Supply challenges resulted in significant shortages of personal protective equipment, jeopardizing our frontline health care workers.¹⁶ Preexisting drug shortages were exacerbated by

¹⁰ Centers for Disease Control and Prevention, *First Travel-related Case of 2019 Novel Coronavirus Detected in United States* (Jan. 21, 2020), <https://www.cdc.gov/media/releases/2020/p0121-novel-coronavirus-travel-case.html>.

¹¹ FDA, Emergency Use Authorization for CDC 2019-Novel Coronavirus (2019-nCoV) RealTime Reverse Transcriptase (RT)-PCR Diagnostic Panel for the presumptive qualitative detection of nucleic acid from the 2019-nCoV (Feb. 4, 2020).

¹² See, e.g., *C.D.C. Labs Were Contaminated, Delaying Coronavirus Testing, Officials Say*, The New York Times (Updated May 7, 2020), <https://www.nytimes.com/2020/04/18/health/cdc-coronavirus-lab-contamination-testing.html>; *Inside the coronavirus testing failure: Alarm and dismay among the scientists who sought to help*, The Washington Post (April 3, 2020), <https://www.washingtonpost.com/investigations/2020/04/03/coronavirus-cdc-test-kits-public-health-labs/?arc404=true>; *America Needed Coronavirus Tests. The Government Failed.*, The Wall Street Journal (March 19, 2020), <https://www.wsj.com/articles/how-washington-failed-to-build-a-robust-coronavirus-testing-system-11584552147>.

¹³ See Government Accountability Office, *COVID-19: Continued Attention Needed to Enhance Federal Preparedness, Response, Service Delivery, and Program Integrity* at 17-18 (July 2021), <https://www.gao.gov/assets/gao-21-551.pdf>.

¹⁴ See, e.g., *'It's Just Everywhere Already': How Delays in Testing Set Back the U.S. Coronavirus Response*, The New York Times (Updated March 16, 2021), <https://www.nytimes.com/2020/03/10/us/coronavirus-testing-delays.html>. See also *Scientists baffled by decision to stop a pioneering coronavirus testing project*, Nature (May 22, 2020), https://www.nature.com/articles/d41586-020-01543-x?utm_source.

¹⁵ FDA, *Coronavirus (COVID-19) Update: FDA Issues New Policy to Help Expedite Availability of Diagnostics* (Feb. 29, 2020), <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-new-policy-help-expedite-availability-diagnostics>.

¹⁶ See, e.g., *Hospitals Facing Coronavirus Are Running Out of Masks, Other Key Equipment*, The Wall Street Journal (March 18, 2020), <https://www.wsj.com/articles/hospitals-facing-coronavirus-are-running-out-of-masks-other-key-equipment-11584525604>.

pandemic-related global supply challenges,¹⁷ and global and nationwide demand for key products like reagents and testing supplies limited and further strained the health care system's capabilities and capacity to care for patients.¹⁸ Additionally, American reliance on foreign suppliers highlighted national security and public health risks, as countries like China interfered with and restricted exports of critical products to the U.S.¹⁹

While FDA often holds key supply chain information for approved or cleared medical products, it has a limited role in commercial supply chain operations. In learning from the challenges of this pandemic response, it is critical to strengthen the resilience and improve the sustainability of medical product supply chains to reduce the likelihood and severity of supply disruptions during future public health emergencies. Additionally, greater insight into medical supplies in jeopardy of shortage during a public health emergency will be important to ensure such information is communicated swiftly and to appropriate decision-makers to mitigate and prevent supply risks.

Modernizing Inspections

FDA's experience during the pandemic also highlighted opportunities to modernize its inspections to improve oversight over product safety and effectiveness and ensure that new medical products get to patients as quickly as possible. For a significant part of the COVID-19 pandemic, FDA was unable to conduct in-person inspections. The lack of inspections resulted in delays of approvals for critical medical products and created challenges in conducting the agency's normal risk-based oversight of product safety. For example, 68 products had their applications delayed due solely to a lack of inspection, depriving patients of these innovations in a timely manner.²⁰ FDA conducted far fewer inspections than it would have absent the pandemic. As FDA transitions back to conducting in-person inspections, it must work through a backlog of thousands of outstanding inspections. Both in the immediate future and moving forward, FDA must use every tool, including alternatives to in-person inspections, to ensure that life-saving products are safe, effective, and available to patients in as timely a manner as possible.

Vision for the Future

The COVID-19 pandemic presented an extraordinary challenge to FDA, and FDA largely rose to the occasion. To build on the successes achieved during the COVID-19 response, Congress should codify and improve FDA's capacity to accelerate the development and review of medical countermeasures for future public health threats. FDA should continue to encourage flexible and creative clinical trial designs, modernize data collection and evaluation, and support greater use of platform technologies and real world evidence to enable swifter development of safe and effective medical products. We should take steps to improve the resilience of medical product supply chains against future disruptions, better leverage labs and test developers to improve rapid availability of testing for emerging infectious diseases, and adopt FDA's best practices that emerged during the pandemic related to providing guidance to and interacting with sponsors.

¹⁷ See, e.g., *COVID-19 and Drug Shortages: A Call to Action*, J Manag. Care Spec Pharm (Aug. 2020), <https://www.jmcp.org/doi/full/10.18553/jmcp.2020.26.8.945>.

¹⁸ See, e.g., *COVID-19 Testing Is Hampered By Shortages of Critical Ingredient*, The Wall Street Journal (Sept. 22, 2020), <https://www.wsj.com/articles/covid-19-testing-is-hampered-by-shortages-of-critical-ingredient-11600772400>.

¹⁹ See Congressional Research Service, *COVID-19: China Medical Supply Chains and Broader Trade Issues* (Updated Dec. 23, 2020), <https://crsreports.congress.gov/product/pdf/R/R46304>; *China's Export Restrictions Strand Medical Goods U.S. Needs to Fight Coronavirus, State Department Says*, The Wall Street Journal (Apr. 16, 2020), <https://www.wsj.com/articles/chinas-export-restrictions-strand-medical-goods-u-s-needs-to-fight-coronavirus-state-department-says-11587031203>.

²⁰ FDA, *Resiliency Roadmap for Inspectional Oversight* (May 2021), <https://www.fda.gov/media/148197/download>.

RECOMMENDATIONS

Accelerate the Development and Review of Medical Countermeasures: During the COVID-19 pandemic, FDA took unprecedented steps to allow for the expedited development and review of new vaccines, therapeutics, tests, and other devices. FDA cannot turn back to its business-as-usual processes in place prior to the emergence of COVID-19, and instead must build on these successes to provide American patients with devastating diseases new hope and improve our public health preparedness.

- *It is critical that FDA continue to accelerate development timelines, and streamline review, of countermeasures for future potential threats by advancing FDA's recognition of platform technologies, leveraging cross-agency scientific resources, and providing clear and predictable pathways for test developers.*

Improve Medical Product Supply Chain Resilience: The COVID-19 pandemic revealed opportunities to improve the resilience and sustainability of medical product supply chains to reduce the likelihood and severity of disruptions during future public health emergencies. While other aspects of our preparedness framework, such as the Strategic National Stockpile, more directly address supplies available to respond during a public health emergency, targeted reforms at FDA can contribute to more resilient supply chains.

- *Improve the resilience and sustainability of medical product supply chains by simplifying regulatory processes related to certain manufacturing facilities, incentivizing novel ways to manufacture medical products, and modernizing FDA's use of remote tools to conduct inspections.*

Apply Lessons Learned to Strengthen FDA's Regulatory Readiness: Finally, FDA exercised significant regulatory flexibilities during the pandemic which can inform long-term and sustainable improvements to FDA's regulatory readiness and operations. These lessons from the current public health emergency can be turned into best practices at the agency and implemented more broadly.

- *Apply lessons learned to strengthen FDA's regulatory readiness and operations, providing more clear and predictable roadmaps for innovative clinical trial designs and enhancing FDA's guidance and communication practices to increase real-time communications with sponsors.*