

FDA COVID-19 Pandemic
Recovery and Preparedness
Plan (PREPP) Initiative:
Summary Report
January 2021



Foreword

The COVID-19 pandemic represents the most profound disruption to daily life in generations. It has reshaped our lives, forcing us to adapt the ways in which we live and work, producing enormous economic hardships, and causing profound personal pain and tragedy – with more than 350,000 deaths and 20 million confirmed cases in the United States alone – and contributed to enormous economic dislocation all over the world.

The U.S. Food and Drug Administration (FDA or the “Agency”) has been at the forefront of the nation’s response to the pandemic. Our resourceful and resilient workforce of nearly 18,000 strong has continued to make unparalleled contributions and demonstrated unwavering commitment to promote and protect the health and safety of the American public. As the pandemic evolves, there are beacons of hope that we must not lose sight of, including the FDA’s emergency use authorization of COVID-19 vaccines, monoclonal antibody therapies, and rapid, more readily accessible tests for COVID-19, such as over-the-counter diagnostic tests.

The pandemic has presented new challenges for the entire health care community and all levels of government, including the FDA. To carry out our mission during the pandemic, we continue to make decisions guided by science and the best evidence, even when the complete safety and efficacy information of a given product may not yet be known or available at the time. We will revise our policies as our understanding of the science changes based on the rapidly evolving data on this previously unknown, highly contagious virus.

FDA continues to play a central role in the nation’s response and recovery. We have a responsibility to learn from our actions to focus on what we can – and must – do better for the future. Our experience so far has taught us that transparency and continuous improvement are the essential drivers of a successful response. With this in mind, we initiated and publicly launched the **COVID-19 Pandemic Recovery and Preparedness Plan (PREPP)** initiative in April 2020 and August 2020, respectively. The purpose of PREPP has been to identify opportunities that strengthen our on-going COVID-19 response and build the Agency’s resilience to respond to future public health emergencies. An external third party supported this initiative to generate insights through internal FDA interviews and external listening sessions, help progress immediate actions on several response priorities, and to summarize the work and ideas generated through this initiative into this report.

The ideas presented in this report serve as a summary of potential options for the Agency to consider and are deliberative, not exhaustive, and not binding. The potential actions reflect lessons learned from the response so far and serve as a basis for continued learning and progress through and beyond the current pandemic. For each potential priority area, the report provides objectives, potential actions and approaches, and example key metrics and measures. The report also describes several important risks and considerations that will inform the Agency’s decision-making on implementation and prioritization of the potential actions as resources may permit.

FDA takes its mission to protect and promote the public health very seriously. We are constantly reevaluating, revising, and strengthening what we do to ensure the health and safety of American patients and consumers. This report, which incorporates important new data and insights, provides ideas on ways that FDA can further adapt and progress its mission. As a next step in the PREPP initiative, Agency leadership will deliberate whether and how the Agency will proceed with the potential actions or other alternative approaches that could achieve the same public health objectives. In doing so, Agency leaders

will consider the relevance and merits and feasibility and risks of different courses of action to determine how to best advance the Agency's mission, utilizing our current authorities and funding.

The PREPP initiative represents science in action and is a testament to the hard work of FDA colleagues. We commend the entire FDA team for serving on behalf of the American public and their commitment to our many essential public health responsibilities. We want to thank Lowell Zeta (Senior Counselor to the Commissioner), Chaitali Patel (Senior Advisor, Office of the Commissioner), and the PREPP Core Working Team for your leadership and commitment to this work, as well as the PREPP Governance Committee who provided guidance over the last several months.



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Purpose of this document

The purpose of this report is to summarize the insights, supporting facts and work of the FDA COVID-19 Pandemic Recovery and Preparedness Plan (PREPP) initiative between July and December 2020. The substance of this report is informed by interviews with more than 70 FDA leaders and personnel, engagement with more than another 50 FDA subject-matter experts (SMEs), listening sessions with seven external stakeholder groups, and the review and analysis of documents, facts and other information gathered in the course of this initiative. An external third party prepared this objective summary report of the PREPP initiative on the basis of those activities.

This report describes ongoing and potential prospective actions to strengthen the Agency's COVID-19 response and build the Agency's resilience to respond to future emergencies. The report does not offer a retrospective assessment of the Agency's COVID-19 response, which continues at the time of this writing. Rather, PREPP has focused on identifying options for, and selectively progressing, prospective enterprise-wide response and resilience actions, including programmatic, process, and organizational innovations. The options described in this report build on the Agency's current efforts and in many cases may represent a continuation or progression of actions already ongoing or under consideration by FDA. The information included in this report does not contain nor does it intend to offer policy advice. The descriptions of ongoing and potential prospective actions are not exhaustive.

Some of the facts and ideas described in this report may already be outdated, given the rapidly evolving context of the pandemic. Statements of expectation, forecasts, and projections are based on assumptions that may not remain valid. As a result, the actual results achieved, if actions are pursued, may not correspond to any statements of expectation, forecasts, or projections.

The ideas presented in this report, including "actions to consider," "milestones, metrics or measures (examples)," and "considerations," are intended to serve as potential options for the Agency to consider to achieve its public health objectives. These ideas are deliberative, not exhaustive, not binding and not intended to impose additional obligations on FDA. Agency leadership and personnel should consider these potential actions taking into account the Agency's unique and evolving context and priorities, the relevance, implementation feasibility and risks associated with specific actions (including resource and funding constraints), and other factors to determine appropriate courses of action, including alternative approaches to achieve the objectives described in this report. Implementation requirements for potential actions could include but are not limited to changes to the Agency's statutory authorities, increased personnel capacity, new funding, and mutual prioritization by other U.S. government agencies. The PREPP initiative has not yet assessed practical implementation requirements associated with the potential actions described.

The depth of individual issue analysis in the course of PREPP was limited by three practical considerations. First, this work does not represent exhaustive input from internal FDA personnel, as the Agency was and is still engaged in leading COVID-19 response actions. FDA personnel have therefore focused on the response and the Agency's many other non-COVID-19 responsibilities, offering their time and perspectives to the PREPP initiative as their capacity has permitted. Second, the scope of data collected was limited because additional collection could have detracted from the Agency's ongoing COVID-19 response. Third, the PREPP Core Working Team solicited perspectives from external stakeholder groups representing medical professionals, academic research, food and medical product industries, and leading think tanks, but this input does not represent the full breadth of possible stakeholders, including patient advocacy and consumer groups. FDA could seek perspectives from additional stakeholder groups as it contemplates the potential actions described in this report.

Section 1. Executive Summary

1.1 Introduction

The global COVID-19 pandemic continues to be a public health crisis of unprecedented scale and severity, with more than 350,000 deaths and 20 million cases in the United States as of January 5, 2021.¹ The U.S. response to the pandemic has been multi-faceted and involves government organizations at the federal, state and local levels. The U.S. Food and Drug Administration (FDA or the “Agency”) plays a critical role in the whole-of-government effort to address the pandemic on many fronts, including, for example, expediting access to safe and effective COVID-19 medical countermeasures for the detection, protection against, and treatment of COVID-19, supporting the stability and quality of medical product and food supply chains, and ensuring that the Agency’s decisions are guided firmly by science and follow an open and transparent process to support public confidence and the appropriate use of the authorized products.

In fulfilling this role since the declaration of the public health emergency (PHE) by the Department of Health and Human Services (HHS), FDA has taken a range of policy, programmatic and operational actions in close collaboration with U.S. government partners and external stakeholders representing industry, academia, patients and the healthcare community. Among many other actions, FDA has:

- Published more than 65 industry guidance documents (“guidances”) related to COVID-19.² The Agency has updated and revised these guidances as circumstances have evolved in the course of the PHE to provide FDA stakeholders with regulatory clarity and flexibility on a broad range of issues.
- Reviewed over 2,300 emergency use authorization (EUA) requests and issued over 600 EUAs for medical countermeasures to combat COVID-19.³ These countermeasures include therapeutics, vaccines, tests, PPE, ventilators, and other devices to meet patients’ needs and prevent, diagnose and treat COVID-19.
- Reviewed and conducted inspectional activities in relation to nearly 400 COVID-19 therapeutic candidates⁴
- Issued over 150 warning letters to companies to enforce the safety and quality of COVID-19-related products and prevented or removed more than 1,200 fraudulent COVID-19 products from the market.⁵

FDA’s continued COVID-19 leadership is enabled by its workforce, who continue to demonstrate an unparalleled commitment and diligence to the Agency’s essential public health responsibilities. Indeed, the Agency has mounted its COVID-19 response on top of its work to advance non-COVID-19 related priorities, such as ongoing user fee commitments and goals. The well-being, resilience and flexibility of FDA personnel are essential for the Agency to continue to play a leading role in responding to the pandemic.

¹ CDC [COVID-19 Data Tracker](#), accessed Jan. 5, 2021

² [FDA COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholder](#)

³ CDRH data provided on Jan. 4, 2021; [2020 at FDA: A year of unparalleled contributions to public health](#).

⁴ FDA [Coronavirus Treatment Acceleration Program](#) (CTAP), accessed Dec. 23, 2020

⁵ [FDA COVID-19 Response, At-A-Glance Summary](#) as of Dec. 21, 2020

1.2 Pandemic Recovery and Preparedness Plan (PREPP) Initiative

FDA Commissioner Stephen M. Hahn initiated the **Pandemic Recovery and Preparedness Plan (PREPP)** initiative in April 2020 and publicly announced it in August 2020 to identify potential forward-looking opportunities to strengthen the Agency's ongoing COVID-19 response and build the Agency's resilience to prepare for future emergencies.⁶

The PREPP initiative supports the Agency's ongoing response and resilience efforts in three practical ways: (1) Generating insights and ideas on potential improvement opportunities based on input from FDA personnel and external stakeholders and supporting facts; (2) providing direct analytical and implementation planning support to FDA leaders and subject-matter experts (SMEs) on four immediate COVID-19 response priorities to accelerate progress; and (3) creating internal transparency on response and resilience actions that cut across Centers, Office of Regulatory Affairs (ORA) and programs to strengthen the Agency's enterprise-wide COVID-19 impact.

A Core Working Team from the Office of the Commissioner led the PREPP initiative under the guidance of a Governance Committee of the Agency's executive leaders. An external third party supported the PREPP Core Working Team from July 2020 through January 2021 to conduct interviews of Agency personnel, listening sessions with external stakeholder groups and to analyze relevant facts; help Agency personnel to progress four specific immediate priorities; and help facilitate transparency on ongoing Agency response and resilience actions. The third party has prepared this objective summary report of the PREPP initiative on the basis of those activities.

The PREPP initiative identified 12 broad cross-cutting "Action Areas" that reflect ongoing and potential prospective actions to strengthen the Agency's COVID-19 response and build its resilience to respond to future emergencies. These potential Action Areas are grouped in three overarching themes based on objectives:

- **Accelerating immediate COVID-19 response:** Actions that facilitate the Agency's immediate COVID-19 response with the goals of increasing effectiveness, efficiency and transparency.
- **Selectively sustaining and scaling innovations:** Actions that build on innovations that FDA personnel are already implementing in response to COVID-19 and, in some cases, began before the pandemic.
- **Enhancing future pandemic preparedness:** Actions that could build the Agency's resilience to prepare and respond to future pandemics.

The remainder of this section elaborates on these themes, describing FDA's ongoing efforts and potential actions for the Agency to consider.

PREPP initiative report in context

This report does not offer a retrospective assessment of the Agency's COVID-19 response, which continues at the time of this writing. Rather, the PREPP initiative has focused on identifying options for, and selectively progressing, prospective enterprise-wide response and resilience actions.

The ideas presented in this report, including "actions to consider," "milestones, metrics or measures (examples)," and "considerations," are intended to serve as potential options for the Agency to consider to achieve its public health objectives. These ideas are deliberative, not exhaustive, not binding and not

⁶ [Remarks on FDA leadership to accelerate the recovery from COVID-19](#) to the Alliance for Health Policy, Aug. 10, 2020

intended to impose additional obligations on FDA. The information included in this report does not contain nor does it intend to offer policy advice.

Aspects of these potential actions may represent a continuation or progression of actions already ongoing or under consideration by FDA. Some of the facts and ideas described in this report may already be outdated, given the rapidly evolving context of the pandemic.

Agency leadership and personnel should consider these potential actions taking into account the Agency's unique and evolving context and priorities, the relevance, implementation feasibility and risks associated with specific actions, and other factors to determine appropriate courses of action, including alternative approaches to achieve the objectives described in this report. Implementation considerations for potential actions could include but are not limited to changes to the Agency's statutory authorities, increased personnel capacity, new funding, and mutual prioritization by other U.S. government agencies. The PREPP initiative has not yet assessed the practical implementation requirements associated with the potential actions described.

Accelerating immediate COVID-19 response

FDA has taken several cross-cutting actions to increase the effectiveness, efficiency and transparency of its COVID-19 response, including:

- Industry guidance to help accelerate the development of therapies, diagnostics, vaccines and other critical medical products for COVID-19, and to sustain access to those products for the duration of the PHE. Examples include the following FDA guidances: "[COVID-19: Developing Drugs and Biological products for Treatment or Prevention](#)," "[Policy for Diagnostic Tests for Coronavirus Disease-2019](#)," and "[Emergency Use Authorization for Vaccines to Prevent COVID-19](#)."
- Implementation of processes and tools to more efficiently manage the increasing review workload associated with EUA requests and investigational new drug (IND) applications submitted to the medical product Centers. Examples of such actions include the Center for Devices and Radiological Health's (CDRH) implementation of EUA request submission templates, among others. These actions have helped the Agency expedite medical product reviews while preserving the rigor of the scientific assessment of candidate products.
- Increased transparency into the Agency's scientific decision-making approach. The Agency has, for example, publicly released risk-benefit analyses associated with several EUA decisions.⁷ The Center for Biologics Evaluation and Research (CBER) has implemented broad communications to educate the public on its approach to review COVID-19 vaccine candidates, including live streaming and publicly posting the deliberations of the Vaccines and Related Biological Products Advisory Committee (VRBPAC).

As the Agency continues to respond to the pandemic, it could build on these ongoing actions, for example with four potential cross-cutting actions:

- *Continue to plan and prepare for review of COVID-19 medical products.* In the months ahead, many COVID-19 therapeutic and vaccine product developers will reach clinical development milestones that will enable relevant sponsors to request marketing approvals from the Agency. At the same time, many medical devices under EUA will seek marketing approvals. To prepare sponsors and internal review teams, the Agency could continue to communicate how it intends to approach marketing application

⁷ Example EUAs with publicly disclosed reviews: [Example 1](#); [Example 2](#); [Example 3](#); [Example 4](#)

reviews for COVID-19 products as circumstances evolve. The Agency could communicate these plans to individual sponsors on a case-by-case or product class basis and/or through policy guidances. Such communication could help sponsors plan for Agency reviews, for example, and manufacturing scale-up of COVID-19 products. The Agency could also continue to innovate operational processes and tools to manage the COVID-19 review workload efficiently and effectively.

- *Strengthen EUA processes and supporting tools.* The Agency's EUA authority and pathway could continue to be an important means to facilitate the availability and use of medical countermeasures to address COVID-19. The Agency could potentially strengthen the EUA processes and tools by modernizing and redesigning aspects of the internal and sponsor-facing processes and tools – for example by further digitizing and standardizing EUA data intake, digitally upgrading workflow management, and facilitating more streamlined cross-office collaboration – to drive efficiency while preserving the rigor of scientific reviews. The Agency could also diversify its approaches to help the public understand the EUA pathway, for example with broader and more diversified communication and selective sharing of scientific reviews.
- *Strengthen Agency COVID-19 communications.* The Agency's external communications will continue to be vital in the months to come, especially as the pandemic continues to evolve and safe and effective COVID-19 medical countermeasures become more widely available. The Agency could diversify its COVID-19 communications to reach broader and more diverse segments of the population who have been disproportionately impacted by the pandemic. FDA could do this by, for example, using more diverse communications channels, further adapting external messaging to make it more accessible to the general public, and scaling partnerships with organizations representing minority communities. The Agency could also identify and support internal leaders to act as visible “standard bearers” for FDA to cultivate stronger and more consistent engagement with the public.
- *Deepen U.S. government partnerships.* FDA has several important partnerships in place with many other U.S. government agencies, such as the U.S. Department of Agriculture (USDA) on food supply chain continuity, National Institutes of Health (NIH) on testing and clinical trials for COVID-19 therapeutic candidates, Centers for Medicare & Medicaid Services (CMS) on testing, and Centers for Disease Control and Prevention (CDC) on COVID-19 testing protocols and vaccine surveillance planning. These partnerships will continue to be important to the whole-of-government response. The Agency could deepen its partnerships that support emerging response priorities, such as the partnership with CDC on COVID-19 vaccine surveillance and adoption. In the longer term, the Agency could consider which partnerships it should deepen with other HHS Operating Divisions to build collective resilience for future emergencies. For example, it might strengthen its partnerships with NIH on master protocols, and with Biomedical Advanced Research and Development Authority (BARDA) and Office of the Assistant Secretary for Preparedness and Response (ASPR) on supply chain resilience.

Selectively sustaining and scaling innovations

The Agency has innovated in several ways throughout the COVID-19 response to date to fulfill its mission in a highly dynamic and uncertain context. These innovations include:

- Operational changes in policy guidance development and issuance processes. Centers, the Office of Regulatory Affairs (ORA) and programs are implementing several process changes, including cultivating early leadership alignment on priority guidance topics and scope, assigning lead guidance writers, and adopting more iterative, agile approaches to guidance development. These changes have accelerated the timeline from guidance inception to issuance and enabled FDA to more rapidly

progress, update and revise guidances throughout the PHE. Many Centers/ORAs and programs are also adopting Q&A and other focused guidance formats, such as bulleted, shorter guidance documents.

- Expanded use of diverse approaches to conduct inspectional work given limitations of on-site inspectional activities. The Agency has developed an approach to define “mission-critical” inspectional activities to conduct on-site and utilized other approaches such as remote records reviews and mutual recognition agreements (MRAs) with other capable national regulatory agencies globally to continue to protect public health. FDA also established the COVID-19 Advisory Rating System, which uses real-time data to assess the number of cases in local areas to inform decisions on when and where the Agency can safely conduct on-site inspections.⁸
- Participation in a variety of forums using real-world data (RWD) to progress evidence generation and safety monitoring of COVID-19 therapeutics and diagnostics. The Agency played a central role in multi-stakeholder initiatives, such as the Reagan Udall Foundation/Friends of Cancer Research *Evidence Accelerators*, to use RWD to understand COVID-19’s natural history and expedite the development of high-quality COVID-19 medical products, for example through parallel analysis of COVID-19 diagnostic testing.

The Agency could consider institutionalizing and scaling these ongoing innovations as applicable. It might also build on innovations in progress in several ways, for example, with five potential cross-cutting actions:

- *Consider how to carry forward interactive engagement with innovators and industry.* The Agency has implemented several approaches, such as webinars, individual dialogues and convenings, to work more closely with industry to address uncertainties and challenges associated with COVID-19. To further improve external engagement, the Agency could consider assessing a range of interaction models to understand their relative impact and resourcing requirements and, on the basis of that assessment, determine what if any changes to make to its external engagement model in the future. The Agency could also consider ways to strengthen its working relationships with external stakeholder groups by, for example, designating clearer points of contact to selected external stakeholders to enable more effective and efficient coordination and collaboration.
- *Create an environment conducive to sustained innovation in clinical trial conduct.* The Agency’s March 2020 [“Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency”](#) provided important clarity to the scientific community on how to adapt clinical trials to support patient safety and operational continuity. In the short term, the Agency could further clarify its plan for this guidance and the timing and scope of forthcoming guidances that would extend past the PHE. In the longer term, the Agency could use the COVID-19 experience as a catalyst to define a broader Agency-wide approach to encouraging sustained innovation in clinical trial conduct to drive efficiency and effectiveness in trial execution while improving patient experience and access.
- *Collectively strengthen policy guidance development and transition processes.* FDA’s more than 65 temporary COVID-19 guidances⁹ (unless otherwise noted) apply only through the end of the PHE. Just as these guidances have helped to create regulatory clarity and flexibility through the turbulence of the pandemic, clarity on the Agency’s plans to transition these guidances as the PHE subsides is also important. To that end, the Agency could communicate a plan to transition (e.g., continue, modify, update or retire) temporary policy guidances. This plan could share, for example, the Agency’s framework for determining policy transitions, such as assessments of the risks and benefits of

⁸ [FDA prepares for resumption of domestic inspections with new risk assessment system](#)

⁹ [FDA COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders](#)

continuing certain flexibilities, and potential timeframes for modifying and/or retiring specific guidances – recognizing that those timeframes could change based on how the PHE evolves.

- *Enhance real-world monitoring of COVID-19 products.* FDA has launched several efforts to enable effective post-authorization and post-market surveillance of safety and efficacy of COVID-19 medical products. The Agency has an opportunity to define a framework for RWD-driven surveillance and monitoring activities for COVID-19 vaccines and therapeutics. This framework could help to address questions related to real-world use of these products and/or scientific hypotheses that cannot be practically answered in clinical trials, and help to inform industry-driven post-market safety and effectiveness surveillance activities throughout and following the PHE. In the longer term, FDA could explore opportunities to broaden post-market surveillance for medical devices. The feasibility of this action could depend, however, on broader adoption of the unique device identification system for medical devices sold in the U.S.
- *Continue to evolve and optimize inspectional operations, building on the COVID-19 experience as a catalyst.* FDA could build on its experiences using diversified inspectional approaches in the pandemic to shape and pursue a longer-term, more thorough “optimization” of inspectional operations. This optimization could include expanding and scaling, as appropriate, the use of virtual tools such as read-only access to sponsor databases for the Bioresearch Monitoring program; using supportive technologies such as increased bandwidth and/or streaming capabilities for facility assessment; taking a more consistent and dynamic approach to assessing risk-based resource allocation to inspectional activities; transitioning to more continuous, stakeholder-centric engagement with regulated industry; and accelerating efforts to cultivate a convergence of approaches with other competent authorities around the world. The purposes of such an optimization could include increasing the effectiveness of inspectional operations and using the program’s resources more efficiently.

Enhancing future pandemic preparedness

The Agency is taking several actions to build longer-term pandemic preparedness and resilience, including, for example:

- Investing in enhancing data and analytical capabilities for supply chain risk surveillance. The Agency has implemented several efforts across Office of the Principal Deputy Commissioner, Center for Drugs Evaluation and Research (CDER), Office of Food Policy and Response (OFPR), and CDRH to expand data access and analytical capabilities to more rigorously monitor supply chain risks for drugs, foods, and medical devices.
- Participating in the *Accelerating COVID-19 Therapeutic Innovations and Vaccines (ACTIV)* consortia to provide industry and innovators with guidance on clinical trial designs to speed the development of promising therapeutics and vaccines. FDA, in partnership with NIH, is coordinating research strategy and encouraging broad-based adoption of master protocols, such as the Randomized Evaluation of COVID-19 Therapy – RECOVERY trial, to speed the generation of clinical evidence through this public-private partnership.

As the Agency looks to further prepare for emergencies, it could consider building on resiliency efforts with three potential cross-cutting actions:

- *Strengthen supply chain surveillance for regulated products.* COVID-19 placed unprecedented demands on many food and medical product supply chains and exposed structural vulnerabilities that could put the health and safety of the American public at risk. In light of these challenges, and building on the Agency’s active supply chain surveillance efforts, the Agency could consider enhancing its

supply chain surveillance capabilities, including those related to data and analytics. This could include, for example, developing data-sharing agreements with relevant external data providers, further integrating internal FDA data sources across office and programs where relevant, diversifying and adapting risk assessment methodologies, and strengthening cross-functional business processes to support more integrative risk assessment and mitigation planning and action.

- *Further develop the Agency's emergency management capabilities and approaches.* FDA's 2019 Emergency Operations Plan (EOP) Version 3.0¹⁰ provided the anchor for the Agency's emergency response. FDA could build on its existing emergency management practices by expanding Agency-wide scenario and strategic planning capabilities. In the immediate term, a common Agency perspective on potential COVID-19 epidemiological scenarios (aligned with prevailing U.S. government perspectives) could directly inform several of the Agency's response actions including but not limited to: operational and resource planning coordination for inspections and review activities; timing for transition of temporary guidances; communications priorities and plans; and workload and resource planning. The Agency could also consider actions to strengthen intra-Agency coordinating mechanisms and clarify emergency management roles across relevant offices.
- *Further develop regulatory frameworks to encourage broader use of adaptive trial designs and master protocols.* FDA is uniquely positioned to partner with NIH and other relevant U.S. government agencies to develop and advance an action plan that encourages broader adoption of master protocols, adaptive designs and more innovative trial execution approaches. To do so, FDA could undertake a review of potential regulatory barriers to broader adoption of master protocols and progress new guidance and industry engagement to address the identified barriers. FDA could also catalyze an industry-wide dialogue on data standards, analytical methods and clinical data exchange approaches (e.g., from electronic medical records) that facilitate consistent execution of pragmatic and adaptive designs.

1.3 Risks and implementation considerations

FDA leadership and personnel should consider these potential actions taking into account the Agency's unique and evolving context and priorities, the relevance, implementation feasibility and risks associated with specific actions, and other factors to determine appropriate courses of action, including alternative approaches to achieve the objectives described in this report. Implementation considerations and relevant risks associated with these potential actions include:

- *FDA personnel workload, well-being and resilience.* The PHE has placed exceptional demands on the FDA workforce, who continue to lead COVID-19 response activities while fulfilling many other responsibilities. For example, between March and mid-December 2020, CDRH personnel spent over 320,000 hours on activities related to COVID-19 response, equivalent to more than 150 years of full-time work.¹¹ CDER and CBER, meanwhile, have managed a 33% increase in the volume of commercial IND applications compared to last year.¹² In this context, the Agency should carefully consider the implications of any potential actions on personnel well-being, workload, and resilience. Further, to support personnel, the Agency could continue relevant policies related to telework, caregiver flexibility and time-off, and also continue to invest in recognizing personnel contributions and proactively addressing acute capacity shortages in areas facing outsized workloads, such as through temporary personnel details.

¹⁰ [FDA Emergency Operations Plan](#), version 3.0, July 2019

¹¹ Assumes 8-hour work day, 20 days of work per month, 12 months per year

¹² FDA-TRACK, Dec. 16, 2020. Includes Drugs and Biologics. January-September 2019 compared to the same period in 2020

- *Implementation feasibility.* Some of the potential actions described in this report could require additional FDA personnel capacity, new or increased funding (in some cases evergreen), changes to FDA's statutory authorities and/or rulemaking, and mutual prioritization with other U.S. government agencies, among other potential practical requirements. The PREPP initiative has not yet assessed any such requirements in relation to the potential actions described in this report. The Agency should characterize and assess implementation requirements as it contemplates pursuing any of the potential actions.
- *Continued unpredictability in how the pandemic will evolve.* These potential actions have been conceived in a context that is rapidly evolving. The Agency should therefore continue to remain agile and adaptive in its priorities and actions as the pandemic continues to evolve.

* * * *

COVID-19 has placed unprecedented challenges on American society and the Agency. FDA personnel will continue to act, adapt and innovate to meet the challenges presented by the pandemic. As the Agency looks to the remainder of its response, and to building a stronger, more resilient institution, it could consider these ideas generated through the PREPP initiative as reference points and resources.

Section 2. Introduction and approach

2.1 Context of COVID-19 public health emergency (PHE)

The global COVID-19 pandemic continues to be a public health crisis of unprecedented scale and severity, with more than 350,000 deaths and 20 million cases in the United States as of January 5, 2021.¹³ The U.S. response to COVID-19 has been multi-faceted and involves government organizations at the federal, state and local levels. The U.S. Food and Drug Administration (FDA or the Agency) plays a critical role in the whole-of-government effort to address this pandemic on many fronts, including, for example, expediting access to COVID-19 medical countermeasures for the detection, protection against and treatment of COVID-19, supporting the stability and quality of medical product and food supply chains, and ensuring that the Agency's decisions follow an open and transparent process guided by science to promote public confidence in FDA and the appropriate use of the authorized products.

FDA's all-hazards preparedness framework¹⁴ equips the Agency with specific authorities in emergencies and provides a foundation for much of the Agency's response. FDA's COVID-19 response has drawn on its experiences responding to previous health crises, including H1N1 influenza, MERS-CoV, Zika, and Ebola. However, the novelty of the SARS-CoV-2 pathogen and the unprecedented scale and severity of this pandemic has required the Agency to act dynamically in real time while learning how the virus works and how best to detect infections, treat their effects, and contain further spread, for example.

Over the past 12 months, the Agency's far-reaching pandemic response has included a range of policy, programmatic and operational actions to carry out its public health mission. FDA has published more than 65 industry guidance documents ("guidances") related to COVID-19,¹⁵ issued over 150 warning letters,¹⁶ prevented or removed more than 1,200 fraudulent COVID-19 products from the market,¹⁷ issued over 600 emergency use authorizations (EUAs) for medical countermeasures (e.g., therapeutics, and vaccines, testing, PPE, ventilators and other devices) to combat COVID-19,¹⁸ and collaborated more closely with industry than perhaps ever before to accelerate the development, review and patient access to COVID-19 medical countermeasures.

The Agency has also engaged in inter-agency efforts across the U.S. government, including but not limited to working with the U.S. Department of Agriculture (USDA) on food supply chain continuity, National Institutes of Health (NIH) on clinical trials for COVID-19 therapeutic candidates, Centers for Medicare & Medicaid Services (CMS) on testing, and Centers for Disease Control and Prevention (CDC) on COVID-19 on testing protocols and vaccine surveillance planning. The Agency has led these COVID-19 response actions while fulfilling its user fee commitments and other non-COVID regulatory priorities.

2.2 PREPP Initiative objectives, scope and approach

FDA Commissioner Stephen M. Hahn initiated the Pandemic Recovery and Preparedness Plan (PREPP) initiative in April 2020 and publicly announced it in August 2020 to identify and pursue forward-looking opportunities to strengthen the Agency's ongoing COVID-19 response and build the Agency's resilience to

¹³ CDC [COVID-19 Data Tracker](#), accessed Jan 5, 2021

¹⁴ FDA [Pandemic and all-hazards preparedness reauthorization Act of 2013](#) (PAHPRA)

¹⁵ [COVID-19-related guidance documents for industry, FDA staff, and other stakeholders](#)

¹⁶ [FDA COVID-19 Response, At-A-Glance Summary](#) as of Dec. 21, 2020

¹⁷ [FDA COVID-19 Response, At-A-Glance Summary](#) as of Dec. 21, 2020

¹⁸ [FDA COVID-19 Response, At-A-Glance Summary](#) as of Dec. 21, 2020

prepare for future emergencies. The opportunities reflect both relevant internal innovations and ongoing actions that the Agency could scale and sustain, as well as additional actions that could strengthen FDA's COVID-19 response and future preparedness (see **Table 1**). As an Agency-wide effort, the PREPP initiative has focused on opportunities that cut across the Agency's Centers/ORAs and programs.

The PREPP initiative has directly complemented and supported ongoing Agency response and resilience efforts in three practical ways:

- Generating insights and ideas on potential improvement opportunities based on input from FDA personnel and external stakeholders and supporting facts;
- Providing direct analytical and implementation planning support to FDA leaders and subject-matter experts on four immediate COVID-19 response priorities to accelerate progress (see **Table 2**);
- Creating internal transparency on response and resilience actions that cut across Centers/ORAs and programs to strengthen the Agency's enterprise-wide COVID-19 impact.

A Core Working Team from the Office of the Commissioner led the PREPP initiative under the guidance of a Governance Committee of the Agency's executive leaders. An external third party supported the PREPP Core Working Team from July 2020 through January 2021 to conduct interviews of Agency personnel, listening sessions with external stakeholder groups and to analyze relevant facts; help Agency personnel to help progress four specific immediate priorities (see **Table 2**); and help facilitate transparency on ongoing Agency response and resilience actions. The third party has prepared this objective summary report of the PREPP initiative on the basis of those activities.

The remainder of this section describes the approach for the PREPP initiative consistent with the three actions described above.

Generating insights and ideas for improvement opportunities

The first phase of the PREPP initiative, from July through September 2020, was designed to generate ideas and hypotheses on potential areas to strengthen the Agency's responses to COVID-19 and future emergencies. This phase also characterized the Agency's ongoing activities to respond to the PHE. Activities included interviewing FDA personnel, listening to external stakeholders, analyzing relevant facts and reviewing relevant documentary materials.

More than 70 FDA leaders and personnel from across Centers, ORAs and programs participated in interviews to share facts on relevant response and resilience actions in progress and offer ideas for innovations and actions the Agency could consider.

PREPP facilitated individual virtual listening sessions with seven external stakeholder groups including the American Association of Medical Colleges (AAMC), American Clinical Laboratory Association (ACLA), Biotechnology Innovation Organization (BIO), Pharmaceutical Research and Manufacturers of America (PhRMA), Sustainable Food Policy Alliance (SFPA), Food and Beverage Issue Alliance (FBIA) and National Association of State Departments of Agriculture (NASDA). The stakeholders offered input on the aspects of the Agency's response that have been most impactful for them and suggested forward-looking ideas about how the Agency might strengthen its COVID-19 response and its resilience. External stakeholders were provided with a standard set of suggested discussion prompts in advance of the listening sessions and invited to guide the discussion on the most important topics for their organizations or constituents. The insights from the listening sessions served as one of several inputs to inform the development of the themes, potential Action Areas and immediate priorities for PREPP support.

The first phase of the PREPP initiative concluded with descriptive analyses and desk research related to themes and ideas emerging from the interviews and listening sessions. These descriptive analyses included, for example, characterization of the clinical trial pipeline for COVID-19 therapeutics and vaccines; quantification of submission volumes for COVID-19 therapeutics, vaccines and diagnostics; and high-level analysis of selected internal processes to better understand strengths and potential process improvements. This phase also involved review of publications related to COVID-19 response by leading external FDA stakeholders including AdvaMed, Duke-Margolis Center for Health Policy, Reagan Udall Foundation, and the Milken Institute FasterCures Center. Some members of the PREPP Core Working Team separately participated in informal discussions with stakeholders from Duke-Margolis Center for Health Policy, Reagan Udall Foundation and the Milken Institute FasterCures Center to discuss PREPP initiative objectives and to understand leading think tanks' perspectives on FDA's response to the ongoing pandemic.

This phase of the PREPP initiative generated 12 potential Action Areas for response and recovery, which the PREPP Governance Committee endorsed. **Table 1** provides a summary of the three overarching themes identified through the PREPP initiative, and the 12 associated potential Action Areas. The Action Areas comprise the *Agency's current and potential* response and resilience actions.

Table 1: Overarching Themes and Cross-Cutting potential Action Areas for the Agency's COVID-19 response and resilience

Overarching themes	Cross-cutting potential Action Areas
<p>Accelerating immediate COVID-19 response: Actions that facilitate the Agency's immediate COVID-19 response with the goals of increasing effectiveness, efficiency and transparency</p>	1. Continue to plan and prepare for review of COVID-19 medical products
	2. Strengthen EUA processes and supporting tools
	3. Strengthen Agency COVID-19 communications
	4. Deepen U.S. government partnerships
<p>Selectively sustaining and scaling innovations: Actions that build on innovations that FDA personnel are already implementing in response to COVID-19, and in some cases began before the pandemic</p>	5. Consider how to carry forward interactive engagement with innovators and industry
	6. Create an environment conducive to sustained innovation in clinical trial conduct
	7. Collectively strengthen policy guidance development and transition processes
	8. Enhance real-world monitoring of COVID-19 products
	9. Continue to evolve and optimize inspectional operations, building on the COVID-19 experience as a catalyst
<p>Enhancing future pandemic preparedness: Actions that could build the Agency's resilience to prepare and respond to future pandemics</p>	10. Strengthen supply chain surveillance for regulated products
	11. Further develop the Agency's emergency management capabilities and approaches
	12. Further develop regulatory frameworks to encourage broader use of adaptive trial designs and master protocols

Providing analytical and implementation planning support for select response priorities

The second phase of the PREPP initiative, from September through November 2020, involved direct analytical, design and implementation planning support to FDA leaders and SMEs on four immediate Action Areas (see **Table 2**). The PREPP Governance Committee prioritized these four Action Areas based on the following criteria: (a) relevance to current and near-term impact priorities and resulting urgency of action; (b) time to potential collective at-scale Agency impact; (c) Degree of FDA leadership support to pursue collective action in context of the PREPP initiative; and (d) current momentum and degree of existing FDA personnel ownership for specific innovations. **Section 3** of this report elaborates on the work that the relevant FDA leaders and SMEs and PREPP Core Working Team conducted in these Action Areas over the last several months.

FDA executive sponsors guided the work on each of the four priority areas, and the PREPP Core Working Team and external third party collaborated with more than 50 relevant program SMEs to conduct the relevant analyses, solution design and implementation planning. Some of the work included analyses of relevant FDA data, such as capacity requirements for COVID-19 vaccine safety surveillance, qualitative design of solutions, including standardizing process for Agency-wide COVID-19 communications roll-out support, and engagement with personnel from across programs to gather input and cultivate alignment, such as on the definition of “mission critical” inspections across programs.

Creating transparency on relevant response and resilience actions

In the third phase of the PREPP initiative in November and December 2020, the PREPP Core Working Team worked with the Governance Committee and relevant SMEs to canvass Centers/ORAs and programs to identify work underway related to the 12 potential Action Areas. The purpose of documenting the active work was to create visibility across the Agency to identify potential cross-Center/ORAs interdependencies and/or opportunities for learning across programs, and to encourage personnel to pursue such collaboration.

The PREPP Core Working Team summarized the relevant activities in a set of “charters” that described the objectives of the work underway, the outputs intended, the relevant subject-matter owners, and the timing of key milestones where applicable. The Agency’s Enterprise Risk Management (ERM) team will maintain these charters as a living summary of the relevant COVID-19 work underway. The ERM team will also help track a subset of PREPP initiative activities and assess potential risk management implications.

Table 2: Four priority Action Areas of PREPP Initiative focus

Action Area <i>(Lead Center or Office)</i>	Description of major activities supported by the PREPP initiative
Strengthen Agency COVID-19 communications <i>(Office of External Affairs)</i>	Articulate a standardized approach for OEA-supported roll-out of high priority Center/ORAs and program COVID-19 communications for external and select internal actions. Analyze existing tools and supporting processes for tracking COVID-19 communications across OEA, CDER, CDRH and CBER; analyze options for tracking tools that could simplify and streamline OEA's communications operations.
Collectively strengthen policy guidance development and transition processes <i>(Office of Policy, Legislation and International Affairs)</i>	Document relevant guidance development process innovations and best practices that Centers/ORAs and programs pursued prior to and during the COVID-19 PHE, such as the adoption of bulleted guidances, agile ways of working and concurrent reviews; develop a short summary document of those practices to serve as a reference for Center/ORAs and program personnel.
Enhance real-world monitoring of COVID-19 products <i>(Principal Deputy Commissioner, CBER)</i>	Analyze CBER's capacity to address COVID-19 vaccine adverse event reporting in the FDA-CDC Vaccine Adverse Event Reporting System (VAERS), quantify additional resourcing needs, and document options to address those capacity needs.
Continue to evolve and optimize inspectional operations, building on the COVID-19 experience as a catalyst <i>(ORA)</i>	Define a framework to conduct inspectional activities through the remainder of PHE, including: (a) a description of approaches to prioritizing work, (b) a framework outlining inspectional approaches including records reviews, mutual recognition agreements, virtual interviews, and (c) guidelines and considerations for the application of those approaches through the remainder of the PHE. Clarify the definition of "mission critical" inspectional activities in the context of the COVID-19 pandemic across programs, including guiding threshold criteria and illustrative examples; develop a plan to communicate definition and criteria internally and externally

Section 3. Insights and actions to consider

In September 2020, the PREPP Governance Committee reviewed the insights from the first phase of the PREPP initiative and validated 12 potential Action Areas structured around three themes, described in **Table 1**. The Governance Committee validated these potential Action Areas based on the degree of cross-Agency relevance and importance to the COVID-19 response and future resilience.

The remainder of this section describes each of these 12 Action Areas. For each area, the report summarizes the relevant context with key facts, highlights relevant ongoing Agency work, and offers potential actions for FDA's consideration with associated objectives and example milestones, metrics or measures. The "actions for FDA to consider" are intended to serve as ideas for FDA to contemplate as it looks to strengthen its COVID-19 response and pandemic readiness. These ideas are deliberative and pre-decisional. These potential actions may represent a continuation or progression of actions already ongoing or under consideration by FDA. The Agency should contemplate these ideas in the context of all the demands on and priorities of Agency personnel over time, as well as several risks, including:

- *FDA personnel workload, well-being and resilience.* The PHE has placed exceptional demands on the FDA workforce, who continue to lead COVID-19 response activities while fulfilling many other responsibilities. For example, between March and mid-December 2020, CDRH personnel spent over 320,000 hours on activities related to COVID-19 response, equivalent to more than 150 years of full-time work.¹⁹ CDER and CBER, meanwhile, have managed a 33% increase in the volume of commercial IND applications compared to last year.²⁰ In this context, the Agency should carefully consider the implications of any potential actions on personnel well-being, workload, and resilience. Further, to support personnel, the Agency could continue relevant policies related to telework, caregiver flexibility and time-off, and also continue to invest in recognizing personnel contributions and proactively addressing acute capacity shortages in areas facing outsized workloads, such as through temporary personnel details.
- *Implementation feasibility.* Some of the potential actions described in this report could require additional FDA personnel capacity, new or increased funding (in some cases evergreen), changes to FDA's statutory authorities and/or rulemaking, and mutual prioritization with other U.S. government agencies, among other potential practical requirements. The PREPP initiative has not yet assessed any such requirements in relation to the potential actions described in this report. The Agency should characterize and assess implementation requirements as it contemplates pursuing any of the potential actions.
- *Continued unpredictability in how the pandemic will evolve.* These potential actions have been conceived in a context that is rapidly evolving. The Agency should therefore continue to remain agile and adaptive in its priorities and actions as the pandemic continues to evolve.

¹⁹ Assumes 8-hour work day, 20 days of work per month, 12 months per year

²⁰ FDA-TRACK, Dec. 16, 2020. Includes Drugs and Biologics. January-September 2019 compared to the same period in 2020

3.1 Continue to plan and prepare for the review of COVID-19 medical products

Responding to and recovering from the COVID-19 pandemic requires the development and availability of effective and safe medical countermeasures, including therapeutics, vaccines and devices to combat the novel Coronavirus. The scientific community has put “all hands on deck” for the last 12 months to investigate, develop and scale access to a broad portfolio of countermeasures.

FDA has played a vital role in guiding industry in product innovation and clinical trial design, reviewing and regulating new medical countermeasures, and regulating products on the market to protect public health and safety. To date, FDA has reviewed more than 390 trials for COVID-19 therapeutic candidates, authorized eight COVID-19 treatments for emergency use during the PHE, and approved one drug to treat certain patients with COVID-19.²¹ FDA has also reviewed over 2,300 EUA requests and issued over 600 EUAs for medical countermeasures to combat COVID-19, as described in **Section 3.2**.²²

Given the exceptional scale and urgency of patient need for medical countermeasures, FDA has taken actions to open communication channels to provide timely guidance to product developers and accelerate the review of COVID-19 products while maintaining its scientific rigor. One such action is the Agency’s Coronavirus Treatment Acceleration Program (CTAP). FDA launched CTAP in March 2020 as a mechanism for CDER and CBER to leverage cross-Agency scientific resources and expertise to accelerate COVID-19 therapeutic development and review. CTAP has allowed relevant review divisions and SMEs to quickly triage requests and engage with sponsors intensively to provide guidance on product and trial design in pre-IND and IND discussions. External stakeholders noted in listening sessions that the increase in flexible, real-time communications on COVID-19 products across medical product Centers has helped to accelerate product development processes.

In the coming months, many of the drug and vaccine candidates in development (including those under EUA) and devices under EUA could pursue marketing approval. There are two practical implications associated with these product transitions. First, FDA has several expedited review programs (e.g., Priority, Fast-Track, Breakthrough) and review approaches (e.g., rolling, real-time) that it could potentially use for COVID-19 medical product marketing application reviews. Second, this wave of applications could increase the workload in the relevant review divisions and associated offices (e.g., pre-approval, pre-licensing and post-approval inspections for ORA and relevant programs).

Summary of relevant active efforts

FDA is taking several actions to communicate marketing application review approaches, to transition policies for products under EUA, and to make reviews more operationally efficient. The specific actions in progress include:

- *Clarifying review approaches for prospective marketing applications with sponsors.* Both CBER and CDER are working individually with sponsors to determine and communicate the appropriate review approaches for eventual marketing application submissions. CDRH is developing a guidance to clarify how devices now being used under EUA or FDA’s enforcement policy guidances will “transition” to use under full marketing approval (*“Transition Plan for Medical Devices Distributed Under Enforcement*

²¹ [2020 at FDA: A year of unparalleled contributions to public health](#), CDRH EUA data provided on Jan. 4, 2021

²² [2020 at FDA: A year of unparalleled contributions to public health](#), CDRH EUA data provided on Jan. 4, 2021

Policies or Emergency Use Authorization (EUA) During the COVID-19 Public Health Emergency)²³ that the Center plans to issue in FY21, clearance permitting.

- *Implementing ongoing operational changes to drive review effectiveness.* Centers are implementing several operational adjustments to help increase efficiency of COVID-19 product reviews while preserving the same high standard of scientific review rigor. CDER has established a working group focused on review processes and approaches, for example, developed “checklists” and other tools for sponsors to indicate critical application components to prioritize for preparation, and implemented cross-functional task forces to address key review issues such as those related to technology transfers.

Actions FDA could consider

FDA could continue these ongoing actions to clarify its approach to marketing application reviews and make operational adjustments as the pandemic continues to evolve.

Objective: *Accelerate and scale patient access to safe and effective COVID-19 medical products and support workload sustainability for FDA personnel.*

Action to consider:

Continue to communicate FDA’s approach to marketing application reviews for COVID-19 medical products. The external stakeholders who participated in the PREPP listening sessions asked that the Agency continue to clarify the review approaches it intends to use for COVID-19 therapeutics, diagnostics and other devices, and vaccines. In particular, sponsors seek clarity on whether and where the Agency plans to use formal expedited review programs, rolling and real-time review approaches, and the range of potential review timelines to expect. The Agency could continue to communicate these review plans to sponsors individually on a case-by-case or product class basis and/or through policy guidances. Such dynamic and regular communication will enable sponsors to adapt their plans for their regulatory submissions and manufacturing scale-up.

Milestones, metrics or measures (example): Communication on a case-by-case basis and/or through broader communications of the Agency’s planned approach to COVID-19 medical product marketing application reviews; and analysis of associated feedback from sponsors and industry trade groups on the communication’s effectiveness in creating transparency and clarity.

Action to consider:

Continue to adapt operational plans for reviews of COVID-19 medical products. The purpose of such continued actions could be to manage workload sustainability for FDA personnel and support efficient and effective reviews. Potential actions for this purpose could include continued dynamic workload planning based on estimates of submission timelines, volumes, likelihood of progression to licensing application, and complexity of products, including novel modalities such as mRNA and DNA vaccines. FDA could also continue to make dynamic operational adjustments that drive efficiency while upholding the scientific rigor of the reviews, for example by scaling digital tools to standardize sponsor inputs, adapting triage approaches, and deploying available technology to enable more effective and efficient review team collaboration. Centers, ORA and programs might also benefit from sharing and learning more about each other’s operational innovations, to the extent that they are broadly applicable within the Agency.

²³ [CDRH Proposed Guidances for Fiscal Year 2021](#)

Milestones, metrics or measures (examples):

- Benchmarks and ranges of review timelines for COVID-19 medical products; User Fee goal dates and commitments fulfilled for COVID-19-related medical products.
- Review team feedback on sustainability of workload and effectiveness of planning and operational measures.

3.2 Strengthen EUA processes and supporting tools

Under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the FDA Commissioner may allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by chemical, biological, radiological and nuclear (CBRN) threat agents. The EUA authority enables FDA to help strengthen the nation's public health protections against CBRN threats by facilitating the availability and use of medical countermeasures (MCMs) needed during public health emergencies.

FDA considers EUA requests when (a) there are no adequate, approved, and available alternative countermeasures; (b) it is reasonable for FDA to believe that the product "may be effective" based on the totality of scientific evidence available; and (c) the product's known and potential benefits, when used to diagnose, prevent, or treat such disease or condition, outweigh known and potential risks. In situations where FDA grants emergency use of a product, the Agency continues to monitor the product's benefits and risks and, on the basis of that evolving evidence, may decide to revise or revoke authorization.

FDA has used the EUA authority to enable patient access to critical medical products to diagnose, treat and prevent COVID-19, including PPE, ventilators, antivirals, convalescent plasma, neutralizing antibody therapies, and vaccines. Prior to COVID-19, FDA has issued a total of 65 EUAs in previous public health emergencies. For COVID-19 to date, FDA has reviewed more than 2,300 EUA requests and authorized over 600 products for emergency use. FDA has also revoked several EUAs, including for some KN95 masks, serology tests, and hydroxychloroquine, based on its continuous monitoring of product risks and benefits. **Table 3** summarizes the count of EUAs by status, and **Table 4** summarizes the number of EUAs for COVID-19 by product type.

Table 3: Count of EUAs by status as of Dec. 16, 2020²⁴

Status	Count
Pre-EUA submitted	More than 2,000
EUA requests submitted	More than 3,000
EUA requests reviewed	More than 2,300 including more than 600 EUAs issued

²⁴ Estimate based on FDA Coronavirus Disease 2019 Pandemic internal daily situation report, Dec. 16, 2020, and CDRH data provided on Jan. 4, 2021. Also see [2020 at FDA: A year of unparalleled contributions to public health](#). IVD = in-vitro diagnostics. The majority of EUA volume is associated with IVD and non-IVD medical products managed by CDRH.

Table 4: Count of COVID-19 products available under EUA by product type as of Jan. 4, 2021²⁵

Product type	Count
In-vitro diagnostics (IVD)	More than 300
Non-IVD devices ²⁶	More than 300
Therapeutics and vaccines	10

CDRH has received the highest volume of pre-EUA and EUA requests – more than 3,000 since the PHE declaration. CDRH has taken a range of actions to accelerate patient access to testing, including but not limited to: issuing and regularly updating guidance on the development of in vitro diagnostic tests for COVID-19; developing and issuing templates for EUA requests to facilitate their preparation, submission, and authorization; and creating and implementing several umbrella EUAs for devices such as surgical masks and non-NIOSH-approved disposable filtering facepiece respirators to allow less complex and similar technologies meeting specified criteria to be authorized under a single EUA.

External stakeholders who participated in PREPP listening sessions noted that the EUA request templates were helpful and deployed rapidly – providing sponsors with clarity on what to submit and how. External stakeholders also observed improvements in CDRH's EUA communications early in the pandemic, and noted the utility of broader interactive forums such as the CDRH webinar series to help stakeholders understand how the Center's approach to EUA policy was evolving.

Summary of relevant active efforts

FDA is making several efforts to strengthen and adapt EUA processes while maintaining the scientific rigor of its reviews. The specific actions underway include:

- *Improving CDRH EUA processes.* The Agency's operational approach to EUAs has been governed by internal standard operating procedures (SOPs) including a cross-program procedure developed in 2010 and an industry guidance, "[Emergency Use Authorization of Medical Products and Related Authorities](#)" ("EUA Guidance"), published in 2017. CDRH has implemented modifications to its Center-specific procedures to more efficiently triage and review the pre-EUA/EUA requests received.
- *Increasing transparency on EUA processes and decision criteria.* The Agency has taken several actions over the last few months to increase transparency on how it reviews EUA requests and makes risk-benefit decisions on COVID-19 medical products. CDRH, for example, led a weekly webinar series with test innovators and sponsors to share information on the EUA pathway and regulatory considerations. For COVID-19 vaccine candidates, CBER has taken actions to increase transparency on the EUA pathway, including live-streaming and posting VRBPAC's COVID-19 meetings on YouTube and publishing in USA Today and the New England Journal of Medicine.²⁷ CBER and CDER have also

²⁵ Based on [FDA Emergency Use Authorization](#) and CDRH data provided on Jan. 4, 2021. Also see [2020 at FDA: A year of unparalleled contributions to public health](#). IVD = in-vitro diagnostics. The majority of EUA volume is associated with IVD and non-IVD medical products managed by CDRH.

²⁶ Non-IVD devices include blood purification devices, continuous renal replacement therapy and hemodialysis devices, decontamination systems for personal protective equipment (PPE), infusion pumps, PPE, remote and wearable patient monitoring devices, respiratory assist devices, ventilators and ventilator accessories. Count includes umbrella EUAs. See [Coronavirus Disease 2019 \(COVID-19\) Emergency Use Authorizations for medical devices](#).

²⁷ <https://www.youtube.com/watch?v=I4psAfbUtC0>, <https://www.usatoday.com/story/opinion/2020/10/27/fda-covid-vaccine-ensuring-safety-and-efficacy-column/6047702002/>, <https://www.nejm.org/doi/full/10.1056/NEJMp2031373>

publicly posted reviews of the scientific data to support issuance, revision or revocation of several EUAs.²⁸ These actions complement the Agency's standard practice of posting the EUA Letter of Authorization and provider and patient fact sheets, which include risk-benefit information.

Actions FDA could consider

FDA could take actions to strengthen and make more transparent the end-to-end EUA processes, from pre-EUA and EUA request to submission review to monitoring and revision.

Objective: *Increase patient access to safe and effective medical countermeasures in emergencies by strengthening EUA processes and tools and improving public understanding and transparency of the EUA pathway*

Action to consider:

Explore opportunities to modernize and enhance EUA processes and supporting tools. A diagnostic of strengths and limitations of EUA processes and tools in the COVID-19 context could potentially help the Agency to continuously improve this aspect of its response infrastructure. The objectives of such a diagnostic and associated redesign could be to make the EUA process more effective and efficient and help FDA personnel to more easily manage high volumes of EUA requests. The diagnostic could aim to generate ideas about how to accomplish these objectives, for example by digitizing more submission intake and data, simplifying cross-functional collaboration across offices and/or adapting the triage approach. As it relates to the sponsor interface, external stakeholders who participated in PREPP listening sessions expressed enthusiasm for even more direct engagement with the Agency on EUAs, for example by establishing a single point of contact at FDA dedicated to answering aggregated questions from industry groups and by increasing FDA's involvement in recurring calls with industry and other public health organizations.

Milestones, metrics or measures (example): Issuance of updated guidance to industry, internal SOPs and other critical documents that reflect the Agency's changes to the EUA processes and tools and other changes that the Agency intends to implement.

Action to consider:

Continue to diversify approaches to improving transparency and stakeholders' understanding of the EUA pathway. FDA could continue to expand and diversify how it communicates with the public about the EUA pathway and its decision-making approach.²⁹ For example, the Agency could use additional communications channels, such as talk radio, local news, and at-scale community organizations, to reach population segments who might not engage with the Agency's current communications channels. FDA could also consider opportunities to selectively expand the relevant use of advisory committees open to the public, as it has for COVID-19 vaccines, to other COVID-19 medical product reviews, while carefully considering the additional workload burden that such an action could create for Agency personnel. FDA has also already committed to having drug and biological product Centers publicly post, to the extent appropriate and permitted by law, reviews of the science data and information supporting the issuance, revision or revocation of EUAs for all drug and biological products, including vaccines, through the PHE and beyond.³⁰

²⁸ Example EUAs with publicly disclosed reviews: [Example 1](#); [Example 2](#); [Example 3](#); [Example 4](#)

²⁹ FDA statement: "[FDA's ongoing commitment to transparency for COVID-19 EUAs](#)," Nov. 17, 2020

³⁰ FDA statement: "[FDA's ongoing commitment to transparency for COVID-19 EUAs](#)," Nov. 17, 2020

Milestones, metrics or measures (example): Frequency and diversity of EUA-related external communications and communications tools, market research to gain insights into the public's knowledge of the Agency's EUA pathway and processes.

3.3 Strengthen Agency COVID-19 communications

The COVID-19 pandemic called on FDA to engage regularly and intensively with industry, healthcare providers, policy-makers and other external stakeholders, including the American public. Since the pandemic began, these external stakeholders have looked to FDA for information on everything from medical product emergency use authorization, to food and medical product supply chain adjustments in response to the pandemic, to the process and timelines associated with COVID-19 vaccine development. Indeed, in the first three months of the pandemic in the United States, FDA mentions more than tripled in online news sources and online forums.³¹

Beginning with the launch of a COVID-19 landing page on its website in January 2020, the Agency has issued a steady stream of external communications on a broad range of issues. As of late 2020, the Agency had developed and published more than 750 discrete communications pertaining to the COVID-19 PHE.³² Centers/ORAs also have many external communications and engagement efforts underway. For example, CDRH has hosted a weekly virtual town hall series to answer technical questions about the development and validation of COVID-19 tests.³³

The cross-programmatic nature of the pandemic – in that it affected regulation of nearly every product and industry within FDA's purview in some way – required more coordination among FDA Centers/ORAs and programs than is commonly the case. In this context, FDA took several actions early in the PHE to coordinate its externally-facing communications, including standing up working groups such as The Joint Information Center (JIC), an arm of the Incident Management Group (IMG). The JIC is stood up in emergencies to support creation, clearance, and documentation of communications materials and to provide an additional mechanism for communications coordination across Centers/ORAs and programs, among other responsibilities.

Adding to the complexity of the cross-programmatic communications, political dynamics raised questions about the FDA's independence. In September 2020, for example, a Kaiser Family Foundation poll found that 62% of American adults surveyed reported being "worried that the U.S. FDA will rush to approve a Coronavirus vaccine without making sure that it is safe and effective due to political pressure."³⁴

Summary of relevant active efforts

FDA is implementing several efforts to further strengthen communications with external stakeholders on COVID-19 issues, for example:

- *Increasing transparency into scientific decisions.* The Agency has taken several actions to increase public confidence in the independence of its scientific reviews and decisions by offering greater transparency into scientific decision-making processes. One such example is the Agency's issuance of the COVID-19 vaccines EUA guidance, which described specific criteria for the Agency's review of COVID-19 vaccine candidates.³⁵ Another example is the Agency's live-stream of the VRBPAC COVID-19 meetings to the public, which attracted more than 230,000 live views on Dec. 10, 2020, and about

³¹ Sampling of mentions of FDA catalogued across channels including Twitter, Facebook, YouTube, Reddit, Tumblr, news sources, forums, and blogs from January to July 2020 using a website analysis tool.

³² FDA JIC COVID-19 communications historical tracker. (Internal FDA tracker as of Dec. 30, 2020)

³³ [Virtual town hall series](#) – Coronavirus test development and validation

³⁴ Kaiser Family Foundation Health Tracking Poll: "[Top issues in 2020 Election, the Role of misinformation, and views on a potential coronavirus vaccine](#)" published Sept. 10, 2020

³⁵ <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-vaccines-prevent-covid-19>

100,000 live views on Dec. 12 across Facebook, Twitter and YouTube. Agency leaders have also diversified the channels by which they communicate to the public, for example, with opinion pieces in USA Today.³⁶

- *Coordinating and expediting communications among Office of External Affairs (OEA), Centers/ORA and Offices.* The Agency has implemented a COVID-19 communications roll-out process supported by OEA. The purpose of this roll-out process is to facilitate rapid and consistent progression of major COVID-19 communications materials and events, both internal and external. The PREPP initiative provided direct support to further standardize and strengthen this roll-out process, as described in the box that follows.

PREPP initiative-supported immediate response priority: COVID-19 communications roll-out process improvement

Agency leaders identified an opportunity to streamline internal communication processes to better coordinate and streamline communications roll-out across Centers/ORA and programs during the COVID-19 PHE. To this end, a working group led by the Office of External Affairs (OEA) was stood up to explore potential actions to better support communications prioritization, tracking, and roll-out activities.

Objectives: The effort was guided by two primary objectives:

1. Strengthen end-to-end operational processes for OEA-supported prioritization & roll-out of high-priority Center/ORA and program communications
2. Identify opportunities to improve OEA Agency-wide tracking and forecasting for communications requiring roll-out support or Agency-wide visibility

Approach: The PREPP initiative interviewed more than 10 personnel across OEA, the Office of Media Affairs (OMA), the JIC, and medical product Centers/ORA to explore communications process strengths and opportunity areas. The PREPP initiative carried out desk research which included a review of internal processes. The PREPP initiative also facilitated regular working sessions with an OEA-led core team to refine outputs and align on potential steps to implement changes.

Key insights and actions: First, OEA made revisions to strengthen roll-out processes for externally facing communications that are especially cross-functional and/or high priority for the Agency. On this front, FDA is developing guidelines for internal Center/ORA and program personnel regarding the types of communications that merit roll-out support. These guidelines also aim to clarify and streamline the roles that personnel in OEA, OMA, Centers/ORA and programs play during the roll-out process. A second internal operational improvement in progress relates to improving the tracking and transparency of communication actions within and across the Agency.

This effort resulted in the creation of an internal document to codify roll-out best practices for Centers/ORA and programs to engage OEA. It included descriptions of roll-out models, checklists and potential process steps to streamline clearance of communications. This effort also produced a summary of communications tracking tool options for OEA, including potential user requirements, pros and cons of the various solutions available, and stakeholder feedback on process improvement opportunities. OEA

³⁶ <https://www.usatoday.com/story/opinion/2020/10/27/fda-covid-vaccine-ensuring-safety-and-efficacy-column/6047702002/>, <https://www.usatoday.com/story/opinion/2020/09/10/sound-science-to-meet-covid-challenges-fda-career-officials-column/5756948002/>

will explore near-term opportunities to adopt an improved tracking tool to improve efficiency and coordination of communications.

Actions FDA could consider

Despite the Agency's actions to improve external communications, Agency personnel and external stakeholders have noted several additional improvement opportunities.³⁷ For example, external stakeholders who participated in the PREPP listening sessions noted the importance of the Agency working towards a more cohesive narrative that is accessible to the general public and consistent with other U.S. government entities. External stakeholders also expressed a desire for more forward-looking Agency communication, such as communications about the Agency's plans to transition temporary policies, as described in **Section 3.7**. Agency personnel have also noted potential improvement opportunities, in particular to strengthen and streamline internal communications processes and tools to track communications in development, and more streamlined membership and consistent levels of seniority in the representation on the JIC.

FDA could consider further building on the ongoing actions in several ways.

Objective: *Increase the scientific accuracy, timeliness, cohesion and reach of the Agency's external communications and engagement.*

Action to consider:

Diversify the Agency's COVID-19 communications approach to reach broader and more diverse audiences in more targeted ways. The Agency's external communications will continue to be vital in the months to come, especially as the pandemic continues to evolve and safe and effective COVID-19 medical countermeasures become more widely available. The Agency could diversify its COVID-19 communications to reach broader and more diverse segments of the population who have been disproportionately impacted by the pandemic. FDA could do this by, for example, using more diverse communications channels, further adapting external messaging to make it more accessible to the general public (which is particularly important given the wide variation in health literacy³⁸), and scaling partnerships with organizations representing minority communities who have been disproportionately impacted by the pandemic. In broadening its reach, the Agency could also align its messaging internally and with other U.S. government agencies to achieve greater consistency and cohesion.

Milestones, metrics or measures (example): The volume and type of communications issued through various channels, and data on uptake, such as page views and social media engagement.

Action to consider:

Identify and activate key leaders across the Agency to act as "standard bearers." The Agency has an opportunity to make its leaders more widely seen, heard, and trusted by the public – during the pandemic and beyond. To pursue this goal, FDA could identify a cadre of leaders who are senior enough to speak from a position of authority but close enough to the science that they are credible experts in a given area. Doing this well could require increased coordination within the Agency and across Centers/ORAs to maintain the consistency of key messages, and when appropriate, coordinate with U.S. government partners such

³⁷ External stakeholder listening sessions

³⁸ National Center for Education Statistics, "[The Health Literacy of America's Adults](#)"

as the CDC on the safety, efficacy and distribution of vaccines, or USDA on issues relevant to the food supply chain.

Milestones, metrics or measures (example): Number and type of engagements, publications, or news or social media posts by FDA leaders and staff – “standard bearers.”

Action to consider:

Use more technology that is already available to support internal FDA communications workflows and communications development. FDA could evaluate and adopt technologies that better support internal processes for reporting, tracking and managing work associated with communications. Such technology adoption could help to reduce rework and improve staff productivity, and provide Center/ORA and program personnel with more consistent, real-time insights into important communications activities, including those requiring roll-out support from OEA. Beyond tracking solutions, FDA could assess collaboration and productivity tools related to communication content management, knowledge-sharing and document retention. These tools could, for example, enable subject-matter experts to submit facts and insights via a user-friendly platform to support consistent Agency messaging, and workflow management to facilitate cross-functional work, including hand-offs based on defined processes.

Milestones, metrics or measures (examples):

- Implementation of new processes, tracking systems, or other enabling tools for supporting external communications.
- “Customer satisfaction” scores and feedback based on surveys of FDA personnel on topics such as the perceived quality of roll-out support, ease of use, and availability and accuracy of communications tracking data.

3.4 Deepen U.S. government partnerships

COVID-19 has called on U.S. government agencies to rapidly coordinate their actions and decisions on a broad range of issues. FDA plays a critical role in the U.S. whole-of-government response, for example, by providing guidance and technical assistance and sharing data as appropriate with U.S. government partners to address immediate and emerging health issues (see **Exhibit 1**).

Among many such examples, FDA has harnessed partnerships with USDA, CDC, the Occupational Safety and Health Administration and numerous state and local agencies to support supply chain stability and the safety of foods and food workers. FDA has also coordinated agencies including NIH, Biomedical Advanced Research and Development Authority (BARDA), CDC and CMS to support COVID-19 medical product innovation and access. **Exhibit 1** summarizes a few of the FDA's partnerships with other U.S. Government agencies.

Exhibit 1: FDA's active COVID-19 partnerships with other U.S. government agencies³⁹

Program name	Partners (all include FDA)	Program objectives
RADx	 National Institutes of Health	To speed innovation in the development, commercialization, and implementation of technologies for COVID-19 testing
ACTIV	 National Institutes of Health	To develop a coordinated research strategy for prioritizing and speeding development of the most promising treatments and vaccines through public-private partnerships
Operation Quack Hack		To protect consumers from fraudulent medical products by leveraging Agency expertise and advanced analytics
MOU on food supply		To establish a process by which determinations will be made about circumstances in which USDA could exercise its authority under the DPA over certain FDA-regulated entities to help prevent interruptions at food facilities
Collaboration on antibody tests	  	To establish a capability at NIH to evaluate serological tests for developers (including tests already available for use, as well as tests not yet on the market where additional validation data is needed to support an EUA)
Serology studies workshop	     	To explore strategies to address key scientific opportunities for serology testing to address COVID-19
MOU on advanced manufacturing	 National Institutes of Health 	To facilitate information-sharing regarding the use of 3D printing and other advanced manufacturing technologies in the context of personal protective equipment (PPE) and other medical device parts.
Vaccine safety monitoring		To expand safety systems including CDC's V-safe and National Healthcare Safety Network (NHSN)

³⁹ Sources: FDA, NIH, HHS websites, press search

Summary of relevant active efforts

FDA is implementing ongoing activities to further clarify and coordinate its role in whole-of-government COVID-19 response:

- *Continuing to engage key U.S. government partners on opportunities to align major response priorities, more clearly align on key messages, and develop a plan to sustain and coordinate shared messaging.* Relevant ongoing efforts to further strengthen FDA's U.S. government partnerships include (a) joint FDA-CDC-USDA coordination to align on the potential prioritization of essential food workers to receive early access to COVID-19 vaccines; (b) collaboration with BARDA and the Office of the Assistant Secretary for Preparedness and Response (ASPR) and the Federal Emergency Management Agency (FEMA) to align objectives and approaches to strengthen the supply chains for COVID-19 medical products, including, where relevant, coordination with manufacturers to help address capacity constraints and/or scale production; and, (c) further development of FDA-CMS processes to coordinate on coverage, coding, payment of COVID-19 medical products as relevant and clinical laboratory improvement amendments (CLIA) laboratory considerations as required.

Actions FDA could consider

Given the continued evolution of the PHE and the many interdependencies between the U.S. government agencies leading response activities, FDA could continue to adapt and deepen its partnerships with other agencies.

Objective: *Advance FDA's public health mission and goals related to the COVID-19 response through strategic, targeted collaborations with U.S. government partners.*

Action to consider:

Partner with U.S. government agencies on flagship initiatives to address COVID-19 recovery needs. FDA could dynamically determine which U.S. government partnerships are most critical to evolving response priorities as the PHE evolves. For these partnerships, FDA could consider establishing clearer joint objectives, milestones, and establishing even closer working relationships across the relevant Agencies. Closer partnerships could also help FDA and its U.S. government partners to more closely align external messaging and potentially also extend joint reach externally. In the near term, for example, FDA could further formalize and invest in its partnership with CDC to jointly engage the general public and health care professionals about COVID-19 vaccines and therapeutics. FDA could also help to provide targeted messaging to at-risk subpopulations and minorities regarding recent EUAs for COVID-19 vaccines. Another potential area of focus could include coordinating with CDC on post-authorization monitoring of diagnostic testing, particularly with the recent authorization of at-home tests and other types of rapid diagnostics.

Milestones, metrics or measures (examples):

- Formalization and potentially additional funding to support flagship U.S. government partnerships related to the COVID-19 response.
- External public perception scores related to FDA's openness and transparency of immediate and emerging public health issues on topics requiring cooperation with other U.S. government partners.

Action to consider:

Pursue targeted collaboration with other HHS Operating Divisions to improve pandemic preparedness. FDA could play a catalytic and leading role with other HHS Operating Divisions to define specific actions

that the agencies can take collectively to improve their readiness for future crises. Three examples of such pandemic preparedness inter-agency partnerships could include: (a) partnering with CDC to contemplate approaches to accelerating patient access to testing in future pandemics and coordinating more closely with commercial manufacturers and laboratories, similar to the actions taken by the South Korean government early in the pandemic;⁴⁰ (b) collaborating with NIH to advance strategy and planning in relation to master protocols (as discussed in **Section 3.12**); (c) working with ASPR/BARDA to improve the security of supply chains of essential medicines and other essential medical products, such as through the Strategic National Stockpile 2.0⁴¹ and existing advanced manufacturing initiatives. Such partnerships could put HHS, the U.S. government, and the American people on stronger footing to respond more effectively to future emergencies.

Milestones, metrics or measures (example): Further formalization of U.S. government partnerships, including defining and progressing mutual milestones related to pandemic preparedness activities.

⁴⁰ BioWorld online article. [“South Korea approves first four COVID-19 test kits under urgent use license”](#) March 17, 2020

⁴¹ U.S. Department of HHS, [Strategic national stockpile 2.0: The Next Generation](#)

3.5 Consider how to carry forward interactive engagement with innovators and industry

FDA has played a central role throughout the PHE in coordinating with external innovators and industry, providing input on COVID-19 medical product development and clinical trial conduct, and offering guidance on maintaining the continuity of supply chains for food and medical products, among many other public health and safety priorities. FDA adopted a more agile engagement model from the start of the PHE, emphasizing high-touch, high-frequency interactions, particularly as these types of interactions provided ongoing input to accelerate the development of medical products. The direct, bidirectional communication also provided the Agency with valuable input that helped inform the development of industry guidances and external stakeholder communications.

External food industry groups noted FDA's critical role early in the PHE in providing credible, accessible information to stakeholders on COVID-19-related food and workplace safety, including factsheets and visuals. For example, the Center for Food Safety and Applied Nutrition (CFSAN) and OFPR proactively communicated to food industry stakeholders and the general public that there is no evidence that food or food packaging is associated with transmission of COVID-19. CFSAN and OFPR also took actions to be accessible to external stakeholders by, for example, responding to thousands of direct inquiries to the CFSAN Food and Cosmetic Information Center, and triaging incoming comments and flagging common incoming requests for clarification in outgoing Agency communications. In this capacity, FDA continues to work with industry leaders and state government partners to troubleshoot Foods program-related issues quickly and provide relevant guidance when warranted.

External stakeholders who participated in the PREPP listening sessions noted that, since early March, FDA has communicated using a more interactive approach. They cited this interactive engagement model as an important factor in allowing industry to accelerate product development timelines and improve clarity, for example, about the process for medical device EUAs and developing COVID-19 therapeutics and vaccines. External stakeholders also noted that new direct, virtual communication venues with Centers helped to improve the overall EUA pre-submission process. These virtual venues included weekly public town halls, 37 virtual webinars on testing and 14 on PPE, respirators and 3D printed swabs hosted by CDRH.⁴²

Such interactive engagement models have demanded significant time from FDA personnel. Combined with the finite Agency resources, this model has placed strains on the Agency. For medical product Centers in particular, the intensity of such interactive models may not be sustainable.

Summary of relevant active efforts

FDA Centers/ORAs and programs continue to engage directly with stakeholders to accelerate the development of promising medical products to diagnose, prevent and treat COVID-19, and to support supply chain stability for foods, drugs and devices. These interactive approaches build on existing models that many Centers/ORAs and programs have been implementing for some time, such as [CBER's Interact program](#) and [CDRH Breakthrough Devices program](#). FDA's ongoing engagement activities include:

- *Engaging directly with manufacturers regarding drug and device supply shortages.* In CDER, the Drug Safety Staff (DSS) have maintained direct contact with more than 180 drug manufacturers to jointly assess and mitigate drug shortage risks. These actions have enabled industry to mitigate supply chain risks to reduce the probability, duration and magnitude of critical drug shortages. CDRH has engaged with non-traditional manufacturers, including those in the textile, automotive, aeronautics industries

⁴² [FDA medical device webinars and stakeholder calls](#)

who are new to the medical product space, to help them mitigate and address shortages of certain key products such as PPE.

- *Providing frequent, informal feedback early in the COVID-19 product development and review processes to solve challenges quickly.* CDRH hosts regular webinars, uses manufacturer hotlines and monitors dedicated inboxes for manufacturers to speed development of diagnostics, PPE and other devices relevant for COVID-19 response. This has enabled CDRH to help sponsors accelerate specific submissions, including rapid point-of-care testing,⁴³ quickly address questions, and enable a more efficient review of EUA requests for COVID-19 medical devices.
- *Engaging with importers to solve real-time issues surrounding COVID-19 products.* FDA import staff have increased their outreach to importer groups, hosted webinars, made ongoing updates to FDA websites including relevant contact information, and have worked to promptly resolve questions posed by importers throughout the PHE.
- *Continuing to engage with food suppliers, helping to solve issues for the industry promptly while maintaining food safety and supply chain continuity.* CFSAN and OFPR maintain interactive engagement through direct two-way communication, often via phone, on issues requiring greater regulatory clarity. For example, early in the PHE, FDA granted food suppliers more labeling flexibility with temporary policy guidance to help minimize the impact of supply chain disruption.⁴⁴

Actions the FDA could consider

FDA could examine how it engages with industry in ways that are practical, timely and productively interactive, both in the context of the PHE and on a steady-state basis. This could help FDA make external engagement more efficient and impactful, taking into consideration the many demands on FDA personnel time.

Objective: *Advance FDA's patient and consumer health mission by creating greater and more timely regulatory clarity for external stakeholders while creating opportunities to jointly address regulatory challenges or provide direction to support innovation for regulated products.*

Action to consider:

Assess interactive interaction models with industry and innovators to understand relative impact and resourcing requirements and identify opportunities to strengthen two-way communication with key external stakeholder groups. FDA could take stock of its interactions with innovators and external stakeholder groups. This could start with assessing engagement approaches and tools that the Agency implemented during COVID-19 to understand strengths and limitations, and their applicability through and following the PHE. Such an analysis could account for the fact that the requirements and context for interactions in a PHE vastly differ from those in a non-emergency setting. The assessment could also characterize key enablers to provide more interactive exchanges between FDA and external groups, such as the use of more effective virtual collaboration tools or platforms. Overall, the findings of this assessment could help if, when and how to continue to adapt its engagement model with external stakeholders.

⁴³ Coronavirus (COVID-19) update: [FDA authorizes first point-of-care antibody test for COVID-19](#). Sept. 23, 2020

⁴⁴ [Temporary policy regarding certain food labeling requirements during the COVID-19 public health emergency](#): Minor formulation changes and vending machines. Guidance for Industry, May 2020

Milestones, metrics or measures (examples):

- Improvements in qualitative feedback from external stakeholders on their engagement experiences with FDA in terms of quality, timeliness, frequency, etc.
- Concrete examples of achievements driven by external stakeholder interactions.

Action to consider:

Where applicable, strengthen direct ties with external stakeholder groups and designate FDA points of contact (POCs) to improve rapid two-way coordination and build pandemic preparedness. This action could build on existing examples of designated POCs, such as in OFPR and CFSA's Communications and Public Engagement Staff for FBIA, SFPA and NASDA. First, the Agency could prepare a short list of prioritized stakeholder groups. Individual POCs or teams could be selected based on experience and expertise, capacity and endorsement by Center/ORA or program leadership. POCs could coordinate interactions with SMEs across a variety of topics, and enable more rapid feedback during crises. A CDRH point person could be assigned to ACLA, for example, to maintain ongoing dialogue related to diagnostics product development. Similarly, the Foods program could expand use of the Food and Cosmetic Info Center⁴⁵ to triage and assign FDA staff to incoming email requests. The assessment described above may also highlight key activities for the POC, such as participation in regular stakeholder townhalls to maintain dialogue and transparency for priority issues or to provide a venue to field questions from organizations.

Milestones, metrics or measures (example): Frequency, type and quality of external stakeholder interactions, especially through defined POCs.

⁴⁵ [FDA's Food and Cosmetic Information Center answers your questions](#)

3.6 Create an environment conducive to sustained innovation in clinical trial conduct

The COVID-19 pandemic significantly disrupted many clinical trials as public health measures restricted in-person interaction. In the pandemic's first three months alone, more than 1,200 trials reported a suspension of operations to the NIH (via clinicaltrials.gov).⁴⁶

Recognizing the imperative to support clinical trial continuity, FDA worked quickly to guide sponsors on approaches to conduct trials in the pandemic context, providing flexibility where appropriate but guided by the requirement to ensure the safety of trial participants and the integrity of the clinical data obtained. In March 2020, within weeks of initial lockdowns in the U.S., FDA issued "Guidance on Conduct of Clinical Trials of Medical Products during the COVID-19 Public Health Emergency,"⁴⁷ covering topics related to general process and trial management, use of remote and digital tools, and flexible trial logistics, such as changing sites for high-risk products and shipping investigational product to participants' homes. FDA built this guidance largely on approaches it had already worked with sponsors to validate, but provided a measure of clarity at a highly uncertain time.

Overall, external stakeholder feedback on the impact of the guidance has been positive. Industry groups noted that the guidance helped to minimize pandemic-related disruptions, especially as the guidance was developed and released in a span of weeks – in time to affect newly disrupted trials – and that clarification could be obtained directly from the Agency and in virtual town halls and forums. Since June, there has been a trend toward trial resumptions. In June, the number of monthly trial resumptions overtook the number of suspensions, and as of Dec 1, 2020, more than 950 trials have reportedly resumed. Overall, trials unrelated to COVID-19 have returned to pre-COVID-19 levels; with the addition of trials for COVID-19, the total number of trials now exceeds pre-pandemic levels.⁴⁸

Beyond the positive reception from industry and impact on the clinical trial landscape, many stakeholders expect a number of innovations to become routine. In a recent global survey of 245 trial principal investigators, about 75% expect to use more telemedicine and remote patient monitoring in their trial practices after the crisis; 50-60% expect wider use of eConsent, eSource, electronic Patient Reported Outcomes (ePRO) and electronic Clinical Outcome Assessment (eCOA), while about 40% expect to use more in-home nurse visits, direct sponsor- and site-to patient clinical supply.⁴⁹ Given this largely positive experience, stakeholders across the clinical development ecosystem are eager to understand post-emergency status of issued guidance and approaches FDA might take to encourage sustained innovations in clinical trial conduct.

Summary of relevant active efforts

In addition to an increase in dialogue with industry sponsors over the course of the pandemic, including the express use of a dedicated mailbox for queries related to the implementation of new guidance, FDA has taken two primary actions to support clinical trial continuity and innovation:

- *Routinely updating relevant COVID-19 guidances and supplementing updates with "Q&A" appendices.* FDA has responded to specific external stakeholder challenges and questions to keep policy guidance

⁴⁶ [Clinical trial recovery from COVID-19 disruption](#). Nature Reviews Drug Discovery. 19, 662-663 (2020)

⁴⁷ [FDA guidance on conduct of clinical trials of medical products during COVID-19 public health emergency](#), Guidance for industry, investigators, and Institutional Review Boards, Dec. 2020

⁴⁸ [ClinicalTrials.gov](https://clinicaltrials.gov) as of Dec 1, 2020; WHO International Clinical Trials Registry Platform (ICTRP)

⁴⁹ [Clinical trial recovery from COVID-19 disruption](#). Nature reviews drug discovery. 19, 662-663 (2020)

current, for example by issuing several updates to the guidance on conduct of clinical trials⁵⁰ and providing additional information on approaches for obtaining informed consent. The specific updates described methods to obtain informed consent under routine scenarios for COVID-19 patients, given limitations on in-person interactions. In a similar vein, FDA intends to update draft guidance issued in March 2019 related to risk-based approaches to monitoring clinical trials⁵¹, which is in an environment where site access restrictions for non-essential personnel remain in place.

- *Initiating a process to assess which interventions could be sustained through careful evaluation of potential benefits beyond the current pandemic, and the potential new risks these interventions could entail.* FDA is creating a framework for how industry could scale and sustain decentralized clinical trials and digital monitoring tools post-PHE, including issuance of three primary guidances: (a) guidance on the use of decentralized clinical trial tools and methods beyond the PHE; (b) guidance on the use of digital health technologies to capture study-related data directly from patients; and (c) guidance on data integrity issues arising from trial disruption.

Actions for FDA to further consider

In addition to supporting trial continuity during the pandemic, decentralized and digitally-enabled clinical trials are proving to be feasible and resource-efficient in several trial types and therapeutic areas. And, while definitive research is ongoing, several stakeholders suggest that innovative approaches to clinical trials are critical to achieving other aims, such as including more diverse and representative populations, and an enhanced patient experience that improves protocol adherence and patient retention. Against this backdrop, FDA could take several actions to create an environment more conducive to sustained innovation in clinical trial conduct.

Objective: *Clarify the plan for clinical trial-related immediately-in-effect guidance beyond the current pandemic and continue to prioritize sustained innovation in clinical trial conduct over the long term.*

Action to consider:

Clarify the plan for existing guidance and publication timing for forthcoming guidances. Trial sponsors are eager to understand how FDA will guide clinical trial conduct through the remainder of the pandemic and beyond. As a first step, FDA could communicate expectations regarding what elements of the current guidance on clinical trial conduct will remain in effect following the PHE. Continuing to add to the Q&A section content that clarifies how FDA will treat data that suffered a measure of “interruption” during the pandemic would also provide welcome clarity while sponsors await publication of formal guidance on the topic. Firm knowledge of when foundational guidance related to clinical trial conduct will be published will help sponsors plan upcoming clinical trials. Alerting sponsors when to expect draft guidance will allow them to plan to introduce and embed innovative trial conduct approaches.

Milestones, metrics or measures (example): Issuing an externally facing communication, complemented by relevant mechanisms for sponsor engagement, clarifying (a) the plan for existing guidance related to clinical trial conduct and (b) specifying publication timing for relevant COVID-19-related forthcoming guidances now under development, such as [CDRH proposed guidances for fiscal year 2021](#).

⁵⁰ [FDA guidance on conduct of clinical trials of medical products during COVID-19 public health emergency](#), Guidance for industry, investigators, and Institutional Review Boards, December 2020

⁵¹ [A risk-based approach to monitoring of clinical investigations](#), Questions and Answers. Draft Guidance for Industry, March 2019

Action to consider:

As a longer-term priority, FDA could use the COVID-19 experience as a catalyst to define a broader Agency-wide approach to encouraging sustained innovation in clinical trial conduct. Providing external stakeholders with greater clarity, such as through guidance, could be an important initial step toward encouraging broader adoption of innovations in clinical trial conduct. To achieve this, FDA could focus sponsor engagement activities (either through public meetings or a dedicated consortium-driven approach) to better understand barriers to adoption of innovative trial approaches and identify “next-horizon” innovations, some of which will likely be therapeutic area-specific. This situational intelligence could inform incremental guidance or clarify existing guidance and position FDA to work with sponsors or other industry stakeholders to test and learn about additional innovations. To have the greatest benefit, FDA would pursue a common approach to evaluating and supporting appropriate innovations across medical product Centers, especially CDER and CBER given shared regulatory pathways, and selectively coordinate with international health authorities to anticipate implementation considerations given the global footprint of most clinical trials.

Milestones, metrics or measures (examples):

- Conducting a survey of trial investigators and participants on the effectiveness of COVID-19 related flexibilities.
- Developing and publishing a specific plan that covers a range of activities FDA will undertake following the end of the PHE, to foster continued innovation in clinical trial conduct and specifying a measure that captures the extent of adoption of new trial execution approaches, such as by assessing the percentage of protocols that incorporate novel elements.
- Conducting a pilot study after the end of the PHE to measure whether innovations and flexibilities used during the pandemic increased patient enrollment, increased diversity of patient populations (e.g., geographically), increased patient retention and/or accelerated development such as patient recruitment; and to measure any positive or negative impacts on data integrity.

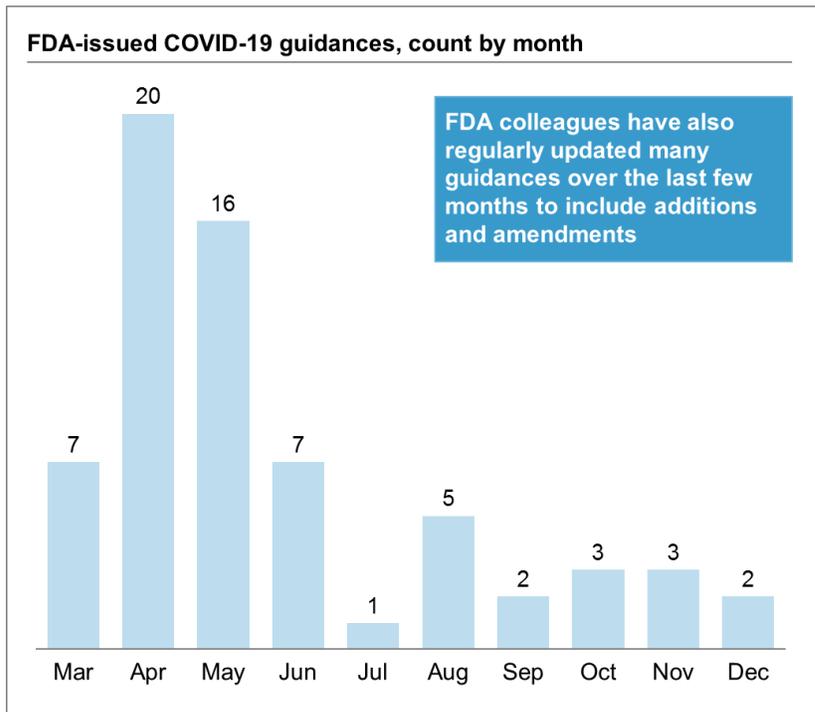
3.7 Collectively strengthen policy guidance development and transition processes

The COVID-19 pandemic has presented unique challenges in the regulation of food and medical products. Examples include: (a) pandemic-related shut downs led to clinical trials being put on hold to avoid putting patients and investigators at risk; (b) novel products were rapidly developed for the testing, prevention, and treatment needs associated with the novel coronavirus; and (c) inspections were delayed due to transmission risk in COVID-19 hot spots. While numerous innovations were made in the substance of policies FDA put forth as a result of the COVID-19 pandemic, these factors also required FDA to drastically accelerate the pace and volume of guidance issuance, as a way to provide clarity to industry, physicians, patients, and other key stakeholders on important issues. This section focuses on the process by which the Agency develops and issues guidances, other policy documents, and associated communications content including press releases, FDA.gov, etc.

In the months preceding the COVID-19 crisis, many Centers/ORAs and programs already had efforts underway to streamline and modernize policy guidance development processes. During the crisis, these efforts became even more important, and expanded, as the Agency issued a record number of guidance documents in response to stakeholder needs. The Agency issued more than 65 COVID-19-related guidance documents, with many addressing cross-cutting topics requiring significant inter- and intra-Agency coordination (see **Exhibit 2**).⁵² Under normal circumstances, guidance documents often take months to develop and advance through clearance. Several COVID-19-related guidances were developed, cleared and published in a few days or a few weeks, given the urgency of the context, and FDA's ability to issue IIE guidances. FDA personnel also generally wrote the COVID-19 guidances in more concise a manner than pre-pandemic guidance documents: on average, they had about two thirds as many pages – an average of 12 for COVID-19-related guidances vs. 19 for guidances issued before the pandemic.

Process innovations used during the COVID-19 pandemic for policy and guidance development included (a) streamlining by encouraging early senior leadership alignment on topic selection and scope; (b) clarifying roles in the guidance development process; (c) using enabling tools and processes; and (d) adopting more agile approaches, such as parallel processing and accelerating clearance activities. The Agency will benefit from codifying and scaling true process improvements.

⁵² See [COVID-19-related guidance documents for Industry, FDA staff, and other stakeholders](#)

Exhibit 2: Number of new COVID-19 related guidances⁵³**Summary of relevant active efforts**

FDA has issued COVID-19-related guidances at an unprecedented pace and volume since the start of the PHE. Across the Centers/ORAs and the Office of the Commissioner, personnel adopted a variety of innovative approaches to accelerate and improve guidance development and issuance to get clear and timely guidances to external stakeholders. FDA has taken two primary actions to make progress in this area:

- *Aligning on more effective and efficient processes for developing, drafting, clearing and finalizing guidance documents within individual Centers/ORAs.* Prior to and during the COVID-19 pandemic, several Centers/ORAs already had efforts underway to improve guidance development and harmonize internal processes. In November 2020, for example, CDER launched a process to increase consistency, reduce development time, reduce iterations and clearance time, and provide more consistent guidances to industry and other stakeholders. In addition to making processes consistent across Offices within CDER, this Center-wide effort aims to leverage new guidance development tools and templates, and provides staff with a common set of training materials. Similarly, CDRH continues to make progress on streamlining policy- and guidance-related processes. As other Centers/ORAs and programs make efforts to refine guidance development, there may be an opportunity to share process optimization learnings across FDA and otherwise enable horizontal alignment across FDA Centers/ORAs and programs.
- *Identifying actions taken in Centers/ORAs and OPLIA to streamline guidance development during COVID-19 to improve efficiency, cross-functional collaboration and stakeholder clarity through discrete*

⁵³ [COVID-19-related guidance documents for Industry, FDA staff, and other stakeholders](#). Based on initial posted date from FDA guidance database. Amendments not counted

process changes. The PREPP Governance Committee prioritized this initiative as an area for focused analytical and design support (see inset).

PREPP initiative-supported immediate response priority: Policy guidance process innovation

Policy personnel from across the Agency participated in an effort to institutionalize process innovations in guidance and policy development arising from the COVID-19 health crisis. This involved understanding each Center/ORAs or programs unique process improvements implemented during the PHE and extracting specific improvements that could be scaled across the Agency.

Objectives: Overall, the effort was guided by three primary aims:

1. Identify process improvement opportunities to reduce the time or resources required to develop guidance, while maintaining or enhancing quality and scientific rigor
2. Improve cross-functional collaboration across Centers/ORAs and Offices by identifying innovations that enable work on cross-cutting issues through shared tools or resources
3. Identify opportunities to improve stakeholder clarity and experience, and increase external stakeholders' ability to interpret and engage with guidance documents

Approach: The PREPP initiative interviewed personnel across all Centers/ORAs and OPLIA involved in driving policy guidance activities and reviewed documents related to internal guidance development processes and templates. SMEs characterized a set of innovative practices that were codified and distilled into a collection of best practices for FDA staff.

Key insights and actions: Potential process improvements were identified that could be broadly applicable across the Agency, including in the Centers/ORAs and programs, such as: (a) Aligning on topic, scope, and key elements to address at the beginning of the guidance development process to ensure that the work being done aligns with what Center/ORAs or program leadership sees as the important, strategic issues; (b) establishing clear roles early, including using designated "writers" who are (often) distinct from the regulatory subject matter experts to free up expert time for other tasks and improve overall writing quality in guidance documents; (c) adopting an iterative and more agile approach to enable an early version to be shared sooner (e.g., providing monthly updates to Q&A sections); and (d) implementing other types of process enablers or accelerators to shorten the timeline from inception to issuance.

The main output of this effort was a short document to catalogue process innovations as a reference guide for personnel across the Agency. Each Center/ORAs or Office will decide which process innovations are more relevant in the context of a PHE and which could be applied on a more steady-state basis, broadly or selectively, and how these practices might fit into the context of existing policy development frameworks.

Actions for FDA to further consider

FDA's efforts to quickly issue guidance to industry have been instrumental in enabling the pandemic response. FDA could take additional action to continue to streamline and increase the transparency of the development and use of guidance throughout the remainder of the PHE and beyond, where relevant.

Objective: *Create greater regulatory clarity to enable industry to plan through and beyond the PHE, to enable continuity of scientific and manufacturing operations for regulated products.*

Action to consider:

Collectively strengthen policy guidance development and transition processes. FDA's more than 65 temporary COVID-19 guidances⁵⁴ (unless otherwise noted) apply only through the end of the PHE. Just as these guidances have helped provide industry with regulatory clarity and flexibility through the turbulence of the pandemic, clarity on the Agency's plans to transition these guidances as the PHE subsides is also important. To that end, the Agency could communicate a plan to transition (e.g., continue, modify, update or retire) temporary policy guidances. This plan could share, for example, the Agency's framework for determining policy transitions, such as assessments of the risks and benefits of continuing certain flexibilities, and potential timeframes for modifying and/or retiring specific guidances – recognizing that those timeframes could change based on how the PHE evolves.

Milestones, metrics or measures (example): Implementation of a framework and process for transition of temporary policies and guidances.

Action to consider:

Establish and implement an integrative and dynamic approach to communicate transition plans to external stakeholders. The Agency could continuously monitor the evolving PHE to provide updates on transition planning and whether to continue, modify, update or retire policies for individual guidances. The external stakeholder groups who engaged in PREPP listening sessions expressed a desire for such communication and transition plan clarity from the Agency, which they said would help their constituents plan ahead.⁵⁵ The Agency could also consider engaging with more detailed external stakeholder feedback on the policy guidance transitions received through the HHS's Request for Information (RFI), which was issued on November 25. The RFI seeks "feedback and relevant evidence" from stakeholders related to temporary regulatory flexibilities in various COVID-19 related guidances.

Milestones, metrics or measures (example): Qualitative assessment of comments received on guidances relating to the transition out of the PHE for types of questions asked, nature of feedback, and quantitative assessment of engagement with guidance, such as usage, views and downloads.

⁵⁴ [FDA COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders](#)

⁵⁵ PREPP Initiative external stakeholder listening sessions

3.8 Enhance real-world monitoring of COVID-19 products

The global pandemic has significantly accelerated timelines for development programs associated with COVID-19 medical products. Sponsors have embraced new technologies to respond rapidly to changing development paradigms, clinical trial conduct and evidence generation approaches. This has enabled new methods for collecting RWD to help address challenges with data continuity during development, and in certain post-authorization settings.

Two major forces have made RWD an important topic for the Agency throughout the PHE. First, FDA has encouraged sponsors to use RWD-based approaches to accelerate investigation of COVID-19 therapeutics and vaccines. These approaches are also valuable in setting post-marketing surveillance given the prevalence of EUAs. Second, sponsors can capitalize on what they have learned in the PHE to take advance the prevailing paradigm for use of RWD and generation RWE.

FDA engages with a broad array of external stakeholders including sponsors, investigators and academics focused on the generation of RWD and RWE, such as in the Duke Margolis Center for Health Policy, FasterCures and others venues. FDA has also participated in the broader RWD community throughout the PHE through the CDER Sentinel,⁵⁶ CBER Biological Effectiveness and Safety (BEST) and CDRH National Evaluation System for health Technology (NEST) initiatives – which focus largely on the use of RWD in post-market safety monitoring.

The Agency continuously looks to enhance its capabilities related to real-time safety and surveillance, which are even more critical in an environment attenuated by therapeutics and vaccine EUAs. The importance of “traditional” RWD sources, including the anticipated surge in vaccine-related adverse event reports, underscores the need for FDA to use RWD efficiently in day-to-day operations in a resource-limited environment through the remainder of the PHE.

Summary of relevant active efforts

FDA is pursuing several efforts to enable effective post-authorization and post-market surveillance of the efficacy and safety of COVID-19 medical products, including these three examples:

- *Playing a central role in the Reagan Udall Foundation/Friends of Cancer Research Evidence Accelerators (EAs) for therapeutics and diagnostics.* Overall, the EAs⁵⁷ are working to define: (a) a prioritized list of research questions about COVID-19’s natural history, treatment patterns and medication use, etc., to direct application of RWD for COVID-19 treatment and product development; (b) common data elements relevant for COVID-19 such as case definitions of disease severity and intubation status, use of algorithms, and translation tables for common data models to drive a more consistent approach to data availability and interpretation; and (c) common protocols for repeated analysis and development of analytic plans and methodology to conduct “parallel analyses” of priority research questions across data partners to enable comparisons of real-world product performance versus RWD-driven observational data.
- *In CDRH, optimizing the balance of RWD generated in pre-market and post-market settings to expedite the development of high-quality medical devices in response to the pandemic.* For example, CDRH has participated in the Diagnostics EA⁵⁸ and helped to establish methods for parallel analysis of

⁵⁶ [FDA Sentinel System’s Coronavirus \(COVID-19\) activities](#)

⁵⁷ Reagan Udall Foundation/ Friends of Cancer Research [COVID-19 Evidence Accelerator](#)

⁵⁸ Reagan Udall Foundation/ Friends of Cancer Research [COVID-19 Diagnostics Evidence Accelerator](#)

COVID-19 diagnostic testing. CDRH has also participated in national real-time COVID-19 surveillance using RWD with external partners including NIH (Rapid Acceleration of Diagnostics – RADx)⁵⁹ and Medical Device Innovation Consortium⁶⁰ (harmonized coding for authorized COVID-19 diagnostics).

- *In CDER, supporting the generation of safety and efficacy data related to COVID-19 through RWD-related initiatives.* FDA’s Sentinel initiative, for example, has carried out 20 discrete COVID-19 studies to date,⁶¹ including an analysis of the disease’s natural history. It also aims to address the critical evidence gap in the use of anti-coagulant therapy during in-patient treatment of COVID-19.¹³ The results of this work and other comparable studies could inform clinical treatment, protocol design and RWD-driven descriptive or inferential analyses.
- *Confirming the adequacy of plans and resourcing for forward-looking RWD-driven post-authorization and post-market surveillance activities.* The PREPP Initiative provided direct analytical support to CBER to define work plans and estimate workloads related to projected increases in safety monitoring activities (see below).

PREPP initiative-supported immediate response priority: Post-EUA monitoring of COVID-19 vaccines

CBER is augmenting its post-market surveillance capabilities in anticipation of COVID-19 vaccine approvals, including through the Biologics Effectiveness and Safety (BEST) initiative and the Vaccine Adverse Event Reporting System (VAERS), both of which depend on RWD. From an operational perspective, CBER identified VAERS work planning as a high-priority area for PREPP initiative analytical support, given potential workload increases related to an anticipated surge in adverse event (AE) reporting for authorized COVID-19 vaccines.

Objectives: CBER sought to document planned and existing efforts in OBE related to VAERS/AE reporting for COVID-19 vaccines including:

1. Outlining major categories of work on AE reporting for COVID-19 vaccine, including ownership and division of work across CDC and FDA
2. Defining how COVID-19 VAERS work will differ from traditional vaccine surveillance, such as in terms of increased volume and new signal pathways including V-Safe
3. Outlining current OBE resource and capacity plans for VAERS work, and potential strain related to a “surge” scenario in AE reporting

Approach: The PREPP Core Working Team worked closely with the Office of Biostatistics and Epidemiology to interview ten key staff members from the Division of Epidemiology, and conducted a desk review of relevant documents and data to inform the VAERS workplan and suggest specific adjustments to maximize DE resourcing and capacity.

Key insights and actions: The Division of Epidemiology is preparing for an anticipated COVID-19 VAERS volume surge. Major efforts include standing up a COVID-19-specific “SWAT” team, updating IT and building automation tools, and expanding team capacity. Staffing levels remain a tangible opportunity for DE COVID-19 work; by Jan. 2021, DE expects vacancies due to unfilled positions, retirements and departures, with three new hires. Efforts are ongoing to expand capacity through personnel details. Even with these efforts, DE capacity is likely to remain strained or exceeded. This work also characterized

⁵⁹ [NIH Rapid Acceleration of Diagnostics \(RADx\)](#)

⁶⁰ [Medical Device Innovation Consortium \(MDIC\)](#)

⁶¹ [FDA Sentinel System’s Coronavirus \(COVID-19\) activities](#)

planned interventions to maximize staff capacity, including expanding support for automation tool development and other review-related optimization approaches.

The main output of this work was a detailed plan to manage increases in VAERS work under different scenarios and immediate steps that CBER has taken to augment staff capacity. Additional work planning or resource forecasting for other types of post-market monitoring activities, including for rapid cycle surveillance for rare adverse events, may also be carried out.

Actions FDA could consider

FDA could pursue a number of actions to accelerate the use of RWD for real-world monitoring of COVID-19 medical products.

Objective: *Supplement understanding of COVID-19 medical product benefits and risks, and generate insights into efficacy and safety by expanding the use of RWD in product review and post-authorization and post-market surveillance activities.*

Action to consider:

Define a framework for post-authorization and post-market surveillance and monitoring for COVID-19 vaccines and therapeutics to articulate specific use cases for application of RWD in assessing questions related to the real-world use, safety and efficacy of these products. This could inform, for example, the prioritization of analyses for rapid RWD/E studies, tool development and standards required to assess priority post-market safety or efficacy questions. The framework could also define opportunities to incorporate extramural research, possibly in coordination with other agencies, to study the long-term health effects of COVID-19. From a sponsor perspective, communicating such a framework could inform planning for industry-driven post-market safety surveillance activities. Defining a surveillance and monitoring framework could serve as a reference point to enhance FDA's resource planning for its monitoring efforts. Given the potential cross-Center/ORA implications, such an effort could benefit from a cross-Agency working group, for example, using an existing internal venue such as the COVID-19 multi-disciplinary analysis group (CMAG). Such a framework could guide the use of RWD for medical product review with the ultimate goal of gaining insights to inform regulatory decision-making.

Milestones, metrics or measures (example): Documentation of use cases, such as the number of examples in a use case "library," to serve as an internal resource for FDA reviewers on the historical application of RWD in regulatory decision-making during the PHE or establishment of novel RWD data and analytics capabilities to strengthen proactive surveillance activities.

Action to consider:

Build internal resources linked to the utilization of RWD during the PHE to provide reference points for reviewers and staff on the appropriate application, interpretation and insight-generation from the use of RWD in evaluating COVID-19 medical products or real-world surveillance. FDA could document findings from rapid RWD/E studies to provide reviewers with generalizable use cases in the COVID-19 context, and derive a broader set of guidelines for cross-pollination across FDA medical product Centers. This could extend to creating internal reviewer tools or templates to enable more consistent approaches to analyzing and interpreting submissions that use RWD sources or are supplemented with RWE.

Milestones, metrics or measures (example): Development and active use of internal FDA tools, such as reviews that use RWD templates, and training, including the number and breadth of FDA

personnel trained, to improve consistency and efficiency in reviewing COVID-19 medical product submissions incorporating elements of RWD and RWE.

Action to consider:

Develop an Agency-level roadmap for continued expansion of RWD capabilities to strengthen post-market surveillance and promote resilience during any future PHEs. FDA could begin by characterizing potential technical capabilities to broaden its ability to carry out post-authorization and post-market monitoring activities, such as rapid cycle analysis. These could include efforts to link and enrich EHR-based datasets to other relevant sources of RWD. FDA could also evaluate engagement strategies, building on the Evidence Accelerator model, to establish or maintain data and analytics access arrangements that enable at-scale RWD-driven approaches. Based on these activities, the Agency could define priority-level initiatives. For example, it could assess the benefits and feasibility of longitudinal patient linkage across datasets, data enrichment and other potential actions.

Milestones, metrics or measures (example): Creation of an Agency-level roadmap to help guide investment in RWD capabilities.

3.9 Continue to evolve and optimize inspectional operations, building on the COVID-19 experience as a catalyst

To help reduce the spread of COVID-19 and due to travel restrictions, FDA suspended domestic and foreign onsite surveillance inspectional activities in March 2020, while continuing on-site “mission-critical” activities.⁶² Since July, on-site prioritized domestic inspectional activities resumed in domestic regions with lower COVID-19 risk based on data from the COVID-19 Advisory Rating system.⁶³ Mission-critical inspectional activities have continued domestically and in foreign countries throughout the pandemic.

Given that a large majority of the country has been impacted by the COVID-19 pandemic, FDA’s ability to safely conduct on-site surveillance inspectional activities has been significantly reduced. As infection rates continue to worsen and the pandemic is expected to continue for some time, the Agency’s ability to conduct onsite surveillance inspectional activities will continue to be limited.

FDA has therefore increased its use of certain inspectional activities and tools not requiring on-site presence to maintain flow of information and dialogue with regulated industry, as well as continued surveillance and oversight in service of its mission. For example, the Agency has used its authorities to make more than 400 record requests since January 2020 “in advance or in lieu of an inspection” through section 704(a)(4) of the FD&C Act for certain types of regulated products. FDA started conducting remote records requests of food importers while also exploring the use of remote regulatory assessments in other aspects of the Foods program.⁶⁴ It also used mutual recognition agreements (MRAs) to complete inspectional activities and help advance certain medical product applications through the review process, and to help mitigate potential drug shortages. The use of MRAs with the European Union increased by about 35% between March 18 and October 18, 2020, compared to the same period in 2019.⁶⁵

FDA also issued a guidance known as “[Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency: Questions and Answers](#)” in August 2020 to clarify which types of inspections have been suspended during the pandemic, address questions about manufacturing changes due to disruptions, and describe what types of inspections might be considered mission-critical. External stakeholders noted that while this was a helpful “starting point,” they seek clarification on the definition of mission-critical inspections, the process FDA uses to make these determinations, and how inspections will be conducted in the context of the public health emergency.

External stakeholders expressed enthusiasm for FDA’s efforts to evolve and optimize inspectional approaches, including its increased use of risk-based, continuous monitoring and further adoption of “virtual” approaches where appropriate, including virtual meetings to facilitate transfer of records before onsite inspections, to deploy FDA resources to sites with the greatest needs, while also developing capabilities to improve resilience and adaptability in future emergencies.

⁶² Mission-critical inspections are those with the highest priority based on public health benefits or where the risk of not conducting the inspection outweighed the risk of investigators’ potential exposure to COVID-19. (Definition provided by FDA ORA personnel during PREPP Initiative working sessions)

⁶³ Coronavirus Update: [FDA prepares for resumption of domestic inspections with new risk assessment system](#). July 10, 2020

⁶⁴ ORA-provided data from March 18 to Oct. 18, 2020, vs. March 18, 2019, to Oct. 18, 2020. Data accessed Oct. 28, 2020

⁶⁵ ORA-provided data from March 18 to Oct. 18, 2020, vs. March 18, 2019, to Oct. 18, 2020. Data accessed Oct. 28, 2020 and Dec. 1, 2020. Count of activities completed using MRA is based on the date an inspection or investigation conducted by a foreign regulatory partner was endorsed by FDA.

Summary of relevant active efforts

FDA has efforts underway to clarify and expand the use of alternative inspectional approaches implemented during the pandemic, and to consider how to refine inspectional processes beyond the PHE:

- *Expanding the use of record requests through section 704(a)(4) and remote regulatory assessments.* FDA is reviewing its authorities to determine whether additional legislation could help better prepare the Agency to operate during future pandemic environments. This includes a review of authority to request records and other information in advance or in lieu of inspections under section 704(a)(4), and to use remote regulatory assessments across all FDA-regulated commodities, including bioresearch monitoring inspections. FDA is also exploring expanded use of record requests for programs where section 704(a)(4) records requests does not explicitly apply.
- *Optimizing inspectional operations.* FDA is assessing its inspectional operations, including all program commodity areas and domestic and foreign inspections. This assessment goes beyond the PHE to take into account risks and benefits of preannouncing inspections, risks and benefits of records review and remote assessments performed in advance or in lieu of inspections, and feedback from internal and external stakeholders including Centers, industry and trade organizations. By the end of 2021, the assessment will provide FDA with a set of recommended solutions to further optimize its inspectional work.
- *Establishing the Intra-Agency Inspectional Affairs Council (IIAC).* FDA is establishing a governance body for tactical planning and coordination related to its inspectional approaches to discuss and coordinate important enterprise-wide considerations.

PREPP initiative-supported immediate response priority: Inspections go-forward plan for the PHE and mission critical definition

FDA has adapted its approach to inspectional activities to continue providing regulatory oversight during the PHE while also protecting the health of investigators, site employees and local communities. ORA identified the clarification and codification of this approach as a high priority for PREPP analytical support, given stakeholders' requests for additional specificity and detail.

Objectives: ORA sought to clarify how it will conduct inspections throughout the remainder of the COVID-19 PHE, including:

1. FDA's plan to continue ongoing inspectional activities
2. Criteria to designate inspectional activities as mission-critical

Approach: The PREPP initiative interviewed stakeholders and integrated written feedback from SMEs across ORA and all Centers to develop high-level criteria and a decision tree outlining when and how to apply various inspectional approaches. The team also conducted external listening sessions and reviewed written feedback to understand concerns relating to these topics.

Key insights and actions: FDA outlined criteria for what inspectional work is considered mission-critical based on its public health benefits and risks. While these align to a consistent set of categories across programs, FDA tailored criteria where appropriate based on the unique contexts of each program. FDA has codified its approach for how it will continue to apply these criteria on an ongoing basis. ORA has outlined the major inspectional approaches it will continue to use during the PHE, including onsite visits, remote reviews of records, virtual interviews, use of MRA and state contracts, and how they will be

applied based on considerations including the criticality of the inspection, epidemiological risk and investigator safety, and other factors.

The output of this work included internal documentation of the criteria, a decision tree and related materials, and a plan to share top-line messages about the criteria and plan developed with internal and external stakeholders. ORA will continue to implement the communications plan while continuously updating the criteria and plan to conduct mission-critical inspections as the context of the COVID-19 PHE evolves. ORA may also consider how these guidelines can be adapted for use in future emergencies.

Actions for FDA to further consider

FDA has a near-term opportunity to communicate with external stakeholders about its inspectional activities plan. It could alleviate industry uncertainty by setting expectations about how and in what circumstances it will conduct inspectional activities, which could help sites prepare for more productive regulatory interactions, including remote approaches. FDA also has a longer-term opportunity to further evaluate the benefits, risks and effectiveness of alternative inspectional approaches beyond the pandemic as part of a strategic modernization. Such an optimization effort could increase the effectiveness of the inspections process, direct ORA's resources more efficiently, and increase resilience for future emergencies.

Objective: *Strengthen the Agency's ability to protect public health by evaluating opportunities to optimize its inspectional approach and provide clarity to external stakeholders.*

Action to consider:

Communicate FDA's approach to inspectional activities during the COVID-19 PHE, including guidelines to designate work as mission-critical externally. In the near term, FDA could share timely and relevant guidelines internally and externally. It could begin by finalizing the codification of criteria and plans and then tailoring content based on what is most relevant to each audience. The Agency could communicate the guidelines using a variety of media, potentially as a guidance, in industry webinars that would include Q&A, and updates to the FDA website.

Milestones, metrics or measures (example): Internal and external launch of communications to clarify plans to conduct inspections through the remainder of the PHE, and provide guidelines for designating inspections as mission-critical.

Action to consider:

Develop a comprehensive optimization roadmap. FDA could build on its efforts to strengthen inspectional processes through a comprehensive, strategic "optimization" program that could include: scaling the use of virtual tools, as appropriate, such as read-only access to sponsor databases; increased bandwidth and streaming capabilities in facility assessments; a more consistent and advanced approach to assess risk-based resource allocation to inspectional activities; a transition to a more continuous, stakeholder-centric engagement model with regulated industry; and accelerated efforts to align approaches with competent authorities globally. Such a modernization could enhance the effectiveness of the inspections program and direct the program's resources more efficiently. The Agency could evaluate which approaches are more appropriate for use on an ongoing basis and which are appropriate only for emergencies. Based on that assessment, FDA could develop capabilities that would allow it to "convert" to emergency approaches more quickly.

Milestones, metrics or measures (example): Develop, communicate and advance an inspection optimization strategy.

Action to consider:

Create a framework to define and measure the effectiveness of inspectional approaches. As FDA defines its strategic optimization roadmap, it could systematically evaluate proposals for optimizing inspectional operations and related activities. Such a systematic approach could help to ensure that modifications to inspectional processes are approved for implementation only when changes would be feasible, advisable, defensible, and sustainable. For example, the framework could help define the relative effectiveness of novel and traditional inspectional approaches across programs. Any potential changes would need to be evaluated to make sure they achieve their intended outcomes and do not have unintended consequences.

Milestones, metrics or measures (example): Codification of a framework to define and measure the effectiveness of alternative inspectional approaches such as MRA and RRA, and implementation of that framework, such as in pilot studies on subsets of inspections for certain products, to determine how FDA might apply alternative approaches.

3.10 Strengthen supply chain surveillance for regulated products

COVID-19 has put unprecedented pressures on medical product and food supply chains. Demand has surged for certain medical products, putting them at risk of or into shortage. These products range from ventilators and critical care drugs such as Propofol, midazolam and azithromycin to hand sanitizer, PPE and testing supplies, including swabs, culture transport media, and general-purpose reagents. Food consumption patterns shifted considerably, which required the maintenance of the supply chain. For example, sanitizing supplies and disinfectants are vitally important for food manufacturers, grocery stores and restaurants, so any shortage could disrupt food supplies. Spikes in demand were sometimes exacerbated by hoarding or “stockpiling” in the wake of news stories about shortages, according to some research.⁶⁶

Workforce protections have been critical to keep workers safe in FDA-regulated manufacturing sectors. To keep workers socially distanced and reduce transmission risks, for example, many suppliers have reorganized shop floors and installed physical barriers. Most suppliers have preserved the continuity of operations, but some manufacturing operations have been temporarily slowed or discontinued. Several product supply chains have been disrupted in the Foods Program, for example, including canneries due to COVID-19 outbreak risk, eggs, and CO₂ as ethanol plants shut down due to lack of demand.

FDA is taking action to mitigate and address shortages for medical products and foods, including the following examples:

- Granting individual and umbrella emergency use authorizations (EUAs) and issuing guidance to provide recommendations and help expand the availability of various diagnostic, therapeutic, and protective medical devices in high demand.
- Helping industry speed the development of product and process innovations such as decontamination systems for PPE and 3D printing of swabs.
- Publishing guidance to allow temporary flexibility on nutrition labels and packaging so food suppliers can sell excess foods typically supplied to commercial establishments such as restaurants directly to consumers, easing supply and demand imbalances as Americans dine more often at home.

Summary of relevant active efforts

Several Centers/ORAs and programs have acted in recent months to strengthen their supply chain surveillance and risk-mitigation capabilities. Examples of this work include:

- *Creating and implementing CDER’s integrative supply chain surveillance model and cross-functional supply task force.* CDER created and implemented a cross-functional Supply Chain Surveillance Task Force with personnel from relevant offices. This cross-functional CDER team reviewed supply chain and shortage risks and associated data and planned and monitored mitigation measures. The Task Force also designed and is implementing an integrative supply chain surveillance data analytics platform. This cross-functional effort complemented CDER’s program to mitigate and address specific drug shortages.
- *Expanding the use of FDA’s Food Program real-time supply chain risk monitoring tool.* FDA’s food supply chain monitoring tool uses COVID-19 epidemiological forecasts overlaid with locations of FDA-regulated food establishments to forecast how outbreaks could impact food suppliers. FDA is using the

⁶⁶ [News Coverage and Drug Shortages during the COVID-19 Pandemic](#). Maryaline Catillon, Maimuna S. Majumder, Shannon F. Manzi, Kenneth D. Mandl, medRxiv, Oct. 14, 2020

tool to engage on workplace employee safety at food supply sites where disruptions would have a high impact on the supply chain, prioritizing sites in COVID-19 hotspots. The reach of this tool has begun to extend beyond FDA's food program. For example, FDA has engaged Operation Warp Speed (OWS) to discuss how the tool could help inform planning for vaccine distribution beyond the food and agriculture sectors, such as to make vaccines available to essential FDA staff.

- *Monitoring the supply chain for medical devices under the Coronavirus Aid, Relief, and Economic Security (CARES) Act.* The CARES Act, put in place on March 27, 2020, in response to the COVID-19 crisis, gave FDA the authority to help prevent or mitigate medical devices shortages in advance of or during a public health emergency. The CARES Act also requires manufacturers of certain devices to notify FDA of any permanent discontinuance or interruption in manufacturing that is likely to meaningfully disrupt supplies during a declared PHE. CDRH now maintains and publishes a devices shortages list based on evaluation of section 506J(a)(1) notifications.⁶⁷ This information and evaluation informs the use of EUAs and other tools to help mitigate shortages.
- *Cultivating partnerships to support advanced manufacturing.* FDA has taken several actions to strengthen manufacturing capacity for public health preparedness. For example, OCS and CDRH helped develop a Memorandum of Understanding between FDA, NIH, and the Department of Veterans Affairs to share information on 3D printing to support the manufacture of personal protective equipment, medical device parts and other essential supplies.
- *Developing FDA's Essential Medicine's List.*⁶⁸ In response to Executive Order 13944,⁶⁹ FDA worked in consultation with federal partners to develop a list of 227 essential drugs and biological products and medical countermeasures. The list includes 96 medical device countermeasures such as diagnostic testing kits and supplies for rapid test development and processing, ventilators, personal protective equipment, and devices for monitoring vital signs, vaccine delivery and the management of acute illnesses.

Actions for FDA to further consider

COVID-19 has spurred FDA to strengthen its role and capabilities in mitigating supply chain risk. Building on the work of several Centers/ORAs, the Agency might consider additional priorities to strengthen its capabilities.

Objective: *Improve the continuity, sufficiency and quality of medical product, food and veterinary supply chains by strengthening FDA's capabilities in supply chain surveillance.*

Action to consider:

Further develop data-analytics capabilities and approaches to risk surveillance and mitigation across programs. The Agency could build on active supply chain surveillance and consider enhancing its supply chain surveillance capabilities, including those related to data and analytics. Although each FDA program is distinct, the Agency could still potentially benefit from common data and analytical capabilities and a governing approach to supply chain risk management that programs could adapt as needed. Advances could include, for example, data-sharing agreements with external data providers, further integrating internal data sources, diversifying and adapting risk assessment methodologies, and strengthening cross-

⁶⁷ Based on Section 506J(a)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). Also see "[Medical device shortages during the COVID-19 public health emergency](#)"

⁶⁸ [Executive Order 13944 List of Essential Medicines, Medical Countermeasures, and Critical Inputs](#)

⁶⁹ Federal Register. EO 13944, Aug. 14, 2020. "[Combating Public Health Emergencies and Strengthening National Security by Ensuring Essential Medicines, Medical Countermeasures, and Critical Inputs Are Made in the United States](#)"

functional business processes to support more integrative risk assessment and mitigation planning and action. The Agency could also develop common approaches to end-to-end supply chain risk mitigation, e.g., from risk surveillance and validation to mitigation, measurement and refinement of actions. Finally, the Agency could continue to develop cross-functional business processes to support these more developed supply chain surveillance and risk mitigation capabilities

Milestones, metrics or measures (example): Further development of data and analytical tools to surveil supply chains at scale, such as new version releases and utilization and integration in cross-functional business processes.

Action to consider:

Continue to facilitate adoption and scaling of new manufacturing technologies and the use of digital and advanced analytics to improve supply chain resilience. New tools include process technology innovations such as continuous manufacturing and improved automation, digital technologies and advanced analytics such as machine learning, digital twin, and AI for operations management and delivering quality controls, assurance and compliance. The Agency plays an important role in clarifying regulatory paradigms for these innovations, and could build on existing CDER, CDRH and CBER programs to further define and adapt regulatory frameworks and accepted practices. For example, the Agency could provide industry guidance on how to (a) develop, validate and maintain tools and processes that harness artificial intelligence and machine learning in the Good Manufacturing Practice (GMP) environment; and (b) manage, share and submit digitally derived data to prove the effectiveness of analytical models for operations and quality, such as using data and analytics for automatic or even faster deviation closure.

Milestones, metrics or measures (example): Creation and publication of an Agency white paper, followed by draft guidance, on the use of advanced modeling in advanced or continuous pharmaceutical manufacturing to facilitate the adoption of model-based approaches.

3.11 Further develop the Agency's emergency management capabilities and approaches

FDA's emergency management approach includes the operational practices, organizational set-up and capabilities that enable the business continuity of core regulatory operations in ways that safeguard the workforce and coordinate the Agency's response to the COVID-19 PHE.

The declaration of the PHE in March 2020 triggered the implementation of FDA's Emergency Operations Plan (EOP), a comprehensive framework governing FDA's management of incidents.⁷⁰ The EOP includes measures, operating structures, roles and responsibilities, and mechanisms for direction and coordination of FDA resources before, during and after disease outbreaks and other crises. The Agency also developed and implemented more detailed supplemental guidance to the EOP: the COVID-19 Outbreak Concept of Operations Plan (CONPLAN). The CONPLAN defines the COVID-19 emergency operating structure and essential tasks of all organizational components involved in the prevention, protection, response and recovery effort.

On Feb. 3, 2020, FDA also activated the Incident Management Group (IMG). In accordance with the FDA EOP, the COVID-19 IMG was established to: (a) facilitate internal coordination and support for overall Agency activities; (b) facilitate external coordination with U.S. government partners and other stakeholders; (c) promote situational awareness across the Agency; (d) identify policy and resource issues for considerations by the Agency Executive Group (AEG); and (e) facilitate timely communications.

FDA staff noted that adjustments could increase resilience for future crises: increasing crisis expertise across all Centers/ORAs; holding more frequent IMG-related exercises to increase readiness; increasing the user-friendliness and comprehensiveness of playbooks to enhance operational decision-making; holding more cross-Agency tabletop simulations; and increasing the consistency of Agency surveillance and detection systems to trigger emergency structures. FDA staff also shared insights on opportunities to strengthen the organizational structure and intra-Agency coordination with respect to emergency roles and responsibilities.

Summary of relevant active efforts

FDA has launched several initiatives to advance emergency management capabilities and approaches, including these examples:

- *Preserving business continuity.* The Office of Operations (OO) is taking several actions to protect business continuity. For example, the Agency relaxed policies to enable telework flexibility for child and elder care, and authorized supervisors to approve up to 20 hours of administrative leave-excused absence per pay period for employees struggling to work a full workday while providing care for dependents. OO/OIMT also rapidly adapted the network infrastructure to accommodate more than 22,000 personnel to work on a virtual private network, provided fully remote customer service on the FDA help line (FDA's help desk received 2,159 calls on March 17 compared to a normal volume of 500 calls), and established a remote shipping model to deliver hardware to staff who needed it, helping people be productive at home.⁷¹ OO and Centers/ORAs have also maintained consistent bi-weekly dialogues to make decisions jointly and maintain programmatic continuity through the crisis.
- *Continuing to implement the Emergency Operations Plan.* Most aspects of this plan are being implemented as intended, including coordinating venues such as IMG, AEG and JIC, as OCS and OO

⁷⁰ [FDA Emergency Operations Plan](#), version 3.0, July 2019

⁷¹ U.S. FDA COVID-19 Pandemic Preparedness & Response, (Sept. 29, 2020); developed by the Office of Operations

leaders make adjustments and modifications based on the evolving situation. The AEG, for example, is serving as a forum for regular updates and dialogue among the Agency's Center/ORAs and program Directors, while the JIC serves a similar function to provide transparency and communicate with one voice on major communications. In general, these venues are facilitating important cross-programmatic transparency and dialogue. The reporting infrastructure allows regular and detailed information-sharing across programs to keep Agency personnel up to date on the activities underway across programs.

- *Utilizing agile resourcing models.* Some Centers/ORAs have developed agile working models and contributed personnel to other Centers/ORAs or Offices where workloads are surging. Examples include CFSAN's contribution of personnel to CBER, CDER, CDRH and JIC, CBER's redeployment of personnel from IOD to CBER, and CDER-OND's flexible resourcing model that shifted personnel from the policy office into review divisions. These "agile redeployments" have helped the Agency staff effectively resource important regulatory programs.
- *Planning for and executing an after-action review.* OEM's Emergency Planning, Exercise and Evaluation Staff (EPEES) is collecting observations and feedback from FDA personnel about the Agency's response to COVID-19 to inform an after-action review. This exercise will help determine how well the Agency implemented the OEM and generate ideas to improve its emergency management approach.

Actions for FDA to further consider

FDA could also consider actions in three areas to strengthen its emergency management approach:

Objective: *Strengthen the emergency management framework and internal capabilities to accelerate and improve response effectiveness in the near term, and to improve its agility and responsiveness in emergencies in the long term.*

Action to consider:

Expand capabilities related to Agency-wide scenario and strategic planning. The unprecedented velocity and complexity of the COVID-19 pandemic merit a dynamic and practical scenario planning approach to inform strategic planning and action. FDA could develop an Agency-wide scenario planning approach that (a) regularly updates scenarios based on evolving events and new information; (b) gives all FDA personnel a common view, such as through Agency-wide sharing and engagement on the scenarios and drivers; and (c) uses those scenarios to inform strategic decisions and actions. Analyzing potential COVID-19 epidemiological scenario planning, for example, could inform operational and resource planning for inspections. It could help staff estimate the number of inspectional activities that will be postponed during the crisis, for example, and the availability of tests for investigators. It could help them plan when and how postponed inspections will eventually be addressed, when personnel can return to work in FDA offices in person, inform communications planning, estimate when products used under EUAs will need to transition to full marketing approval, and estimate when COVID-19 policy guidance, such as for clinical trial conduct, will need to be transitioned. Implementing such an approach could be immediately relevant to the continued COVID-19 response and serve the Agency well in future crises.

Milestones, metrics or measures (examples):

- Development and active use of Agency-wide scenario models; frequency of refresh; ease of use and user satisfaction and feedback, and improved awareness among FDA leadership and key personnel.

- Degree of scenario planning pull-through as the model informs decision-making for a discrete set of use cases, potentially defined in an integrated action plan.

Action to consider:

Identify specific opportunities to enhance coordinating mechanisms and roles across critical emergency management bodies to inform an updated EOP. FDA could explore adjusting emergency management roles and coordinating mechanisms to improve strategic focus and decision-making rigor and speed, especially on matters that require collaboration across programs. For example, the Agency could work to clarify critical roles and responsibilities, including identifying potential sources of overlap or gaps in emergency management across relevant offices to ensure a robust end-to-end EOP. Teams could support emergency management from the Office of the Chief Scientist (OCS)/Office of Counterterrorism and Emerging Threats (OCET), Office of Operations (OO), Office of Emergency Management (OEM), and other central teams, such as the vacant role of Counsellor to the Commissioner, and Center/ORAs-level teams including CDER Counter-Terrorism and Emergency Coordination Staff (CTECS). The Agency could also set a concrete strategic agenda for the AEG, defining the three to five most important and timely Agency-wide strategic priorities that require members to work together to design, execute and adopt. Based on those priorities, the Agency could set out a comprehensive and clear set of roles and responsibilities, such as the DARE framework⁷² – decision-makers, advisers, recommenders, executors – to empower decision-owners with the authority to decide and execute.

Milestones, metrics or measures (example): Implementation of updates to the EOP, potentially including clarification of roles and responsibilities, subject-matter expertise, improved two-way communication channels, and awareness of data input from intra-Agency and inter-agency partners, as applicable.

Action to consider:

Continue to invest in and expand training and simulation exercises. The Agency has established training programs for emergency management. Many programs conduct episodic emergency simulation exercises, which help personnel understand general requirements, frameworks and practices for emergency response. The Agency could strengthen these highly practical emergency management capabilities across the organization, informed by the planned after-action review described above. For example, the Agency could standardize and scale emergency simulations and table-top exercises across programs, adopting an independent simulation or periodic review program, independent from HHS-led exercises. FDA could design a tailored simulation program and provide it on a regular basis. It could be designed to reflect the latest thinking on a wide array of emergencies and response archetypes, and “pulled through” into practical actions and tools that personnel find easy to use in a crisis.

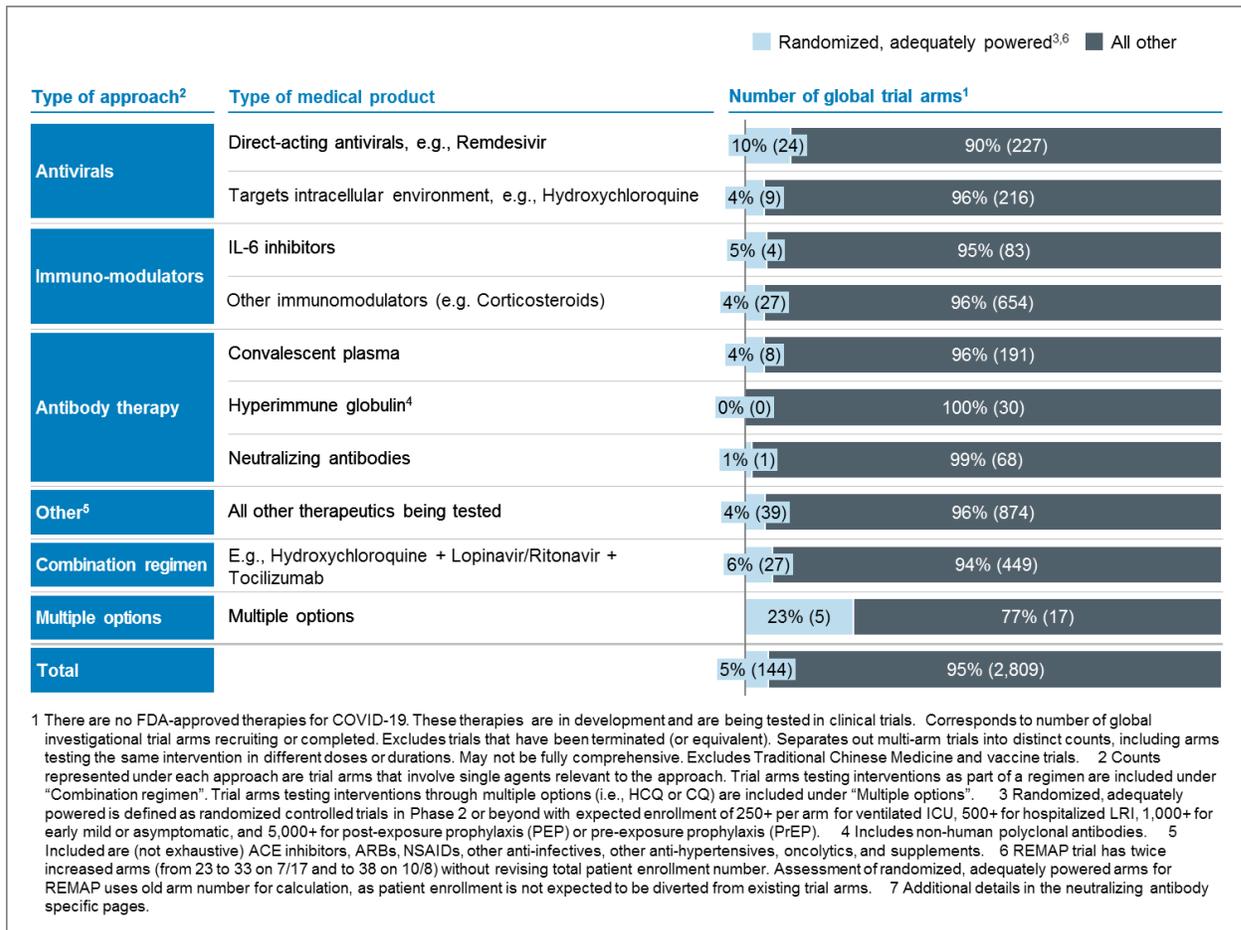
Milestones, metrics or measures (example): Frequency of staff training and simulation exercises, number of participants and level of engagement, coverage across FDA Centers/ORAs and programs, participation by other U.S. government partners or external groups, where appropriate.

⁷² [Increasing decision-making velocity: Five steps for government leaders](#). C. Griggs, S. Kleinman, JR Maxwell, K. Rieckhoff, Nov. 12, 2020

3.12 Further develop regulatory frameworks to encourage broader use of adaptive trial designs and use of master protocols

The PHE sparked an unprecedented amount of clinical trial activity investigating potential therapies across the COVID-19 patient spectrum and vaccines to prevent further spread. Yet, for therapeutics alone, only about 5% of trial arms worldwide could be considered “randomized and adequately powered,” defined as meeting a minimum patient enrollment to achieve statistical significance despite an abundance of patients infected with COVID-19 (see **Exhibit 3**).⁷³ FDA leaders have echoed this challenge in public settings, calling it “starvation in the midst of plenty.”⁷⁴

Exhibit 3: Number of randomized, adequately powered COVID-19 trials as of Nov. 27, 2020⁷⁵



While there are many plausible explanations for this observation, master protocol-based trial designs, which test multiple potential therapies in parallel, and adaptive designs, which allow for dynamic adjustments in trial conduct as data accrues, represent promising approaches to develop regulatory-grade evidence

⁷³ Woodcock, J. *Manuscript in preparation*

⁷⁴ FOIC meeting Sept 2020 – video: [“Dr. Woodcock, Dr. Marks, and Dr. McClellan at the Friends 24th annual cancer leadership reception”](#) Sept. 29, 2020

⁷⁵ Clinicaltrials.gov accessed 11/27/2020 and WHO clinical trial registry accessed 11/27/2020, Pink Sheet and BioCentury accessed Nov. 12, 2020

rapidly. The limited penetration of master protocol designs in the context of the COVID-19 PHE has translated to competition for patients, minimal coordination across sponsors, and exhaustion of site-level resources to support clinical investigation.

Master protocols have been part of the public discussion on clinical trials for some time, with well-documented benefits for clinical researchers and patients alike.⁷⁶ In fact, during the COVID-19 PHE, master protocols have been uniquely successful in generating data that have changed clinical practice, even though overall adoption has remained low; among the small fraction of trials considered randomized and adequately powered, 44% are master protocol-based designs. Adaptive designs are already common in oncology and other selected therapeutic areas where increasing specificity of therapeutics has reduced addressable patient populations, yet broad-based adoption has not occurred.

Summary of relevant active efforts

- *Heightening intensity of industry engagement through the Coronavirus Treatment Acceleration Program (CTAP) and beyond:* Early in the PHE, FDA established CTAP, a special emergency coordination mechanism designed to marshal the full breadth of FDA's resources to support investigation of coronavirus treatments. FDA engaged with industry consortia, including the COVID-19 Research & Development Alliance, to provide scientific advice and input to industry-sponsored master protocols.⁷⁷ FDA also accelerated publication of industry guidance and increased public visibility of resources for industry sponsors considering novel trial designs, including adaptive or master protocol-based designs.
- *Collaborating across government agencies to support launch of the Accelerating COVID-19 Therapeutic Innovations and Vaccines (ACTIV) partnership:* ACTIV is a whole-of-government partnership, coordinated through Friends of NIH (FNIH) and supported by OWS, to "prioritize vaccine and therapeutic candidates, streamline clinical trials, and rapidly expand the clinical research resources focused on developing therapies for the COVID-19 pandemic."⁷⁸ FDA has played an important role in providing subject-matter expertise to facilitate entry of promising candidates into master protocol-based clinical trials, four of which are underway.

Actions for FDA to further consider

FDA and other public health stakeholders have a strong interest in the broader use of novel trial designs that reduce the time, cost and risk of generating evidence that can inform clinical care.

Objective: *Encourage broader adoption of master protocol and adaptive-based trial designs, in the context of investigating COVID-19 therapeutics and beyond.*

Action to consider:

Review applicable regulatory frameworks and engage further with industry to understand regulatory enablers and challenges associated with integrating adaptive designs into future trials. FDA has a number of tools at its disposal for spurring the adoption of innovations in clinical trial design, including the issuance of new guidance, external engagement, rule-making and consortium participation, to name a few. Medical policy groups and review divisions across FDA Centers are well positioned to pair expertise in clinical

⁷⁶ Woodcock, J. and LaVange, L. M., et al. [Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both](#). *New England Journal of Medicine* 2017; 377; 62-70

⁷⁷ COVID-19 Alliance [press release](#), Nov. 30, 2020

⁷⁸ FDA [Coronavirus Treatment Acceleration Program](#) (CTAP)

design with a deeper understanding of barriers to adoption garnered from more intensive external dialogue and engagement. This process is occurring in pockets, including in CDER's Office of New Drugs, which is prioritizing the development of scientific strategies in 2021, which could provide a model to scale across FDA medical product Centers.

Milestones, metrics or measures (example): Proportion of total completed clinical trials that incorporate master protocol and adaptive design features.

Action to consider:

Partner with relevant U.S. government agencies such as NIH to develop and advance a plan to address specific therapeutic areas and relevant use cases, and promote the use of master protocols for clinical trial design and execution. Driving broad-based adoption of master protocols will, in many cases, require leadership by public health agencies and organizations, as the experience with ACTIV in the U.S. and the Randomized Evaluation of COVID-19 Therapy (RECOVERY) and the Solidarity trial in Europe has shown. FDA has a concrete opportunity to partner with other HHS Operating Divisions – particularly NIH, given its capacity to act as a study sponsor – to identify the contexts where master protocol-driven designs would be optimal, such as where multiple therapeutic agents are likely to provide complementary benefits, and for diseases with rapidly shifting clinical guidelines. FDA and partner agencies can gather and share the knowledge they gain in this effort and publicize an experience set around the utility and executability of these approaches.

Milestones, metrics or measures (example): Quantification of the pace of change in standard of care for a range of prioritized diseases aligned to the use cases mentioned above.

Action to consider:

Continue to play a leadership role in developing common data standards, clinical trial infrastructure (especially data-collection architecture) and analytical methods underpinning novel protocols and execution approaches. Master protocols and adaptive designs allow investigators to add or modify clinical trial arms based on pre-specified criteria. Central to supporting that capability for large-scale trials is greater consistency of the data captured in clinical trial management systems (CTMS) and the biostatistical methods used to assess the performance of investigational agents. Pragmatic trial designs also require the ability to extract verifiable trial data directly from electronic medical records. FDA could play a meaningful role catalyzing industry-wide dialogue on data standards, such as by participating and leading international, multi-stakeholder forums, that work toward changing clinical trial infrastructure and common methodologies in trial designs to improve comparability across time, reducing overall clinical development timelines and cost, and supporting more consistent trial execution.

Milestones, metrics or measures (example): Reduction in the time and cost required to bring new medical products to market.

Conclusion

FDA has played a vital role in the COVID-19 response. The scale and urgency of the pandemic has brought out many of the Agency's strengths, including its commitment to science-based decision-making and a willingness to innovate in service of public health. The pandemic also illuminated opportunities for the Agency to strengthen its ongoing response and improve its readiness for future emergencies.

Throughout the PREPP initiative, FDA personnel expressed their pride in the Agency's work and a desire to continue improving and innovating to meet the mission – even in the continued uncertainty and challenges of a worsening pandemic. As the Agency continues to respond, this initiative and summary report are intended to serve as a source of ideas for the Agency to consider in due course as resources may permit. Since the continually evolving nature of the PHE will warrant continued real-time adjustments, the Agency will need to continue to dynamically evaluate and identify opportunities and maintain an active dialogue across relevant FDA leaders and stakeholders.

Acronyms

AAMC - Association of Medical Colleges

AAR - After-action review

ACLA - American Clinical Laboratory Association

ACTIV - Accelerating COVID-19 Therapeutic Innovations and Vaccines

AE - Adverse event

AEG - Agency Executive Group

ASPR - Assistant Secretary for Preparedness and Response

BARDA - Biomedical Advanced Research and Development Authority

BEST - Biologics Effectiveness and Safety

BIO - Biotechnology Innovation Organization

CARES Act - Coronavirus Aid, Relief, and Economic Security Act.

CBER – Center for Biologics Evaluation and Research

CDRH – Center for Devices and Radiological Health

CDC - Centers for Disease Control and Prevention

CDER – Center for Drug Evaluation and Research

CFSAN – Center for Food Safety and Applied Nutrition

CLIA - Clinical Laboratory Improvement Amendments

CMS - Centers for Medicare & Medicaid Services

CONPLAN - Concept of Operations Plan

CTAP - Coronavirus Treatment Acceleration Program

CTMS - Clinical trial management systems

CVM – Center for Veterinary Medicine

DSS - Drug Safety Staff

EA - Evidence Accelerator

eCOA - Electronic Clinical Outcome Assessment

EOP - Emergency Operations Plan

EPEES - Emergency Planning, Exercise and Evaluation Staff

ePro - Electronic patient-reported outcome

EUA - Emergency Use Authorization

FBIA - Food and Beverage Issues Alliance

FD&C Act - Federal Food, Drug, and Cosmetic Act

FDA - Food and Drug Administration

FDASIA - Food and Drug Administration Safety and Innovation Act

FEMA - Federal Emergency Management Agency.

FNIH - Friends of NIH

GMP - Good manufacturing practice

GPO - Group Purchasing Organization

HHS - Health and Human Services

IAAC - Inspectional Approach Advisory Council

IIE - Immediately in Effect (guidances)

IMG - Incident Management Group

IND - Investigational New Drug

IVD - In vitro diagnostics

JIC - Joint Information Center

LTC - Long-term care

MDIC - Medical Device Innovation Consortium

MDUFA - Medical Device User Fee Amendments

MOU - Memorandum of Understanding

MRA - Mutual Recognition Agreement

NASDA - National Association of State Departments of Agriculture

NEST - National Evaluation System for Health Technology

NIH - National Institutes of Health

NIOSH - National Institute for Occupational Safety and Health

ORA – Office of Regulatory Affairs

OSHA - Occupational Safety and Health Administration

OWS - Operation Warp Speed

PHE - Public health emergency

PhRMA - Pharmaceutical Research and Manufacturers of America

PPE - Personal protective equipment

PREPP Initiative - Pandemic Recovery and Preparedness Plan Initiative

RADx - Rapid Acceleration of Diagnostics

RCT - Randomized clinical trial

RECOVERY - Randomized Evaluation of COVID-19 Therapy

RFI - Request for information

RRA - Remote Regulatory Assessment

RWD - Real-world data

RWE - Real-world evidence

SFPA - Sustainable Food Policy Alliance

SME – Subject-matter expert

SOP - Standard operating procedure

TA - Therapeutic area

USDA - United States Department of Agriculture

VAERS - Vaccine Adverse Event Reporting System

VRBPAC - Vaccines and Related Biological Products Advisory Committee

Appendix

Table 5: PREPP Governance Committee Members

Name	Title
Amy Abernethy	Principal Deputy Commissioner
Anna Abram	Deputy Commissioner for Policy, Legislation, and International Affairs
Stacy Amin	Chief Counsel
Jodi Black	Director, Office of Clinical Policy
Patrizia Cavazzoni	Acting Director, CDER
Stephen Hahn	FDA Commissioner
RADM Denise Hinton	Chief Scientist
Keagan Lenihan	Chief of Staff
Peter Marks	Director, CBER
Susan Mayne	Director, CFSAN
Judy McMeekin	Associate Commissioner for Regulatory Affairs
Chaitali Patel	Senior Advisor, Office of the Commissioner
Richard Pazdur	Director, Oncology Center of Excellence
Heidi Rebello	Acting Associate Commissioner for External Affairs
Anand Shah	Deputy Commissioner Medical and Scientific Affairs
Jeff Shuren	Director, CDRH
Jim Sigg	Deputy Commissioner for Operations and Chief Operating Officer
Steven Solomon	Director, CVM
Janet Woodcock	Director, CDER and Principal Medical Advisor to the Commissioner
Frank Yiannas	Deputy Commissioner for Food Policy and Response
Mitch Zeller	Director, CTP
Lowell Zeta	Senior Counselor to the Commissioner

Table 6: Summary of PREPP Initiative Action Areas and potential actions to consider

Action Areas	Actions to consider	Metrics and measures (examples)
Continue to plan and prepare for review of COVID-19 medical products	<p>Continue to communicate FDA’s approach to marketing application reviews for COVID-19 medical products.</p> <p>Continue to adapt operational plans for reviews of COVID-19 medical products.</p>	<p>Communication on a case-by-case basis and/or through broader communications of the Agency’s planned approach to COVID-19 medical product marketing application reviews; and analysis of associated feedback from sponsors and industry trade groups on the communication’s effectiveness in creating transparency and clarity.</p> <p>Benchmarks and ranges of review timelines for COVID-19 medical products; User Fee goal dates and commitments fulfilled for COVID-19-related medical products.</p> <p>Review team feedback on sustainability of workload and effectiveness of planning and operational measures.</p>
Strengthen EUA processes and supporting tools	<p>Explore opportunities to modernize and enhance EUA processes and supporting tools.</p> <p>Continue to diversify approaches to improving transparency and stakeholders’ understanding of the EUA pathway</p>	<p>Issuance of updated guidance to industry, internal SOPs and other critical documents that reflect the Agency’s changes to the EUA processes and tools and other changes that the Agency intends to implement.</p> <p>Frequency and diversity of EUA-related external communications and communications tools, market research to gain insights into the public’s knowledge of the Agency’s EUA pathway and processes.</p>
Strengthen Agency COVID-19 communications	<p>Diversify the Agency’s COVID-19 communications approach to reach broader and more diverse audiences in a more targeted way.</p> <p>Identify and activate key leaders across the Agency to act as “standard bearers.”</p> <p>Use more technology that is already available to support internal FDA communications workflows and communications development.</p>	<p>The volume and type of communications issued through various channels, and data on uptake, such as page views and social media engagement.</p> <p>Number and type of engagements, publications, or news or social media posts by FDA leaders and staff – “standard bearers.”</p> <p>Implementation of new processes, tracking systems, or other enabling tools for supporting external communications.</p> <p>“Customer satisfaction” scores and feedback based on surveys of FDA personnel on topics such as the perceived quality of roll-out support, ease of use, and availability and accuracy of communications tracking data.</p>
Deepen U.S. government partnerships	<p>Partner with U.S. government agencies on flagship initiatives to address COVID-19 recovery needs.</p>	<p>Formalization and potentially additional funding to support flagship U.S. government partnerships related to the COVID-19 response.</p>

	Pursue targeted collaboration with other HHS Operating Divisions to improve pandemic preparedness.	External public perception scores related to FDA's openness and transparency of immediate and emerging public health issues on topics requiring cooperation with other U.S. government partners. Further formalization of U.S. government partnerships, including defining and progressing mutual milestones related to pandemic preparedness activities.
Consider how to carry forward interactive engagement models with innovators and industry	Assess interactive interaction models with industry and innovators to understand relative impact and resourcing requirements and identify opportunities to strengthen two-way communication with key external stakeholder groups. Where applicable, strengthen direct ties with external stakeholder groups and designate FDA points of contact (POCs) to improve rapid two-way coordination and build pandemic preparedness.	Improvements in qualitative feedback from external stakeholders on their engagement experiences with FDA in terms of quality, timeliness, frequency, etc. Concrete examples of achievements driven by external stakeholder interactions. Frequency, type and quality of external stakeholder interactions, especially through defined POCs.
Create an environment conducive to sustained innovation in clinical trial conduct	Clarify the plan for existing guidance and publication timing for forthcoming guidances. As a longer-term priority, FDA could use the COVID-19 experience as a catalyst to define a broader Agency-wide approach to encouraging sustained innovation in clinical trial conduct.	Issuing an externally facing communication, complemented by relevant mechanisms for sponsor engagement, clarifying (a) the plan for existing guidance related to clinical trial conduct and (b) specifying publication timing for relevant COVID-19-related forthcoming guidances now under development, such as CDRH proposed guidances for fiscal year 2021. Conducting a survey of trial investigators and participants on the effectiveness of COVID-19 related flexibilities. Developing and publishing a specific plan that covers a range of activities FDA will undertake following the end of the PHE, to foster continued innovation in clinical trial conduct and specifying a measure that captures the extent of adoption of new trial execution approaches, such as by assessing the percentage of protocols that incorporate novel elements. Conducting a pilot study after the end of the PHE to measure whether innovations and flexibilities used during the pandemic increased patient enrollment, increased diversity of patient populations (e.g., geographically), increased patient retention and/or accelerated development such as patient recruitment; and to measure any positive or negative impacts on data integrity.
Collectively strengthen policy guidance development and	Collectively strengthen policy guidance development and transition processes.	Implementation of a framework and process for transition of temporary policies and guidances.

transition processes	Establish and implement an integrative and dynamic approach to communicate transition plans to external stakeholders.	Qualitative assessment of comments received on guidances relating to the transition out of the PHE for types of questions asked, nature of feedback, and quantitative assessment of engagement with guidance, such as usage, views and downloads.
Enhance real-world monitoring of COVID-19 products	<p>Define a framework for post-authorization and post-market surveillance and monitoring for COVID-19 vaccines and therapeutics to articulate specific use cases for application of RWD in assessing questions related to the real-world use, safety and efficacy of these products.</p> <p>Build internal resources linked to the utilization of RWD during the PHE to provide reference points for reviewers and staff on the appropriate application, interpretation and insight-generation from the use of RWD in evaluating COVID-19 medical products or real-world surveillance.</p> <p>Develop an Agency-level roadmap for continued expansion of RWD capabilities to strengthen post-market surveillance and promote resilience during any future PHEs.</p>	<p>Documentation of use cases, such as the number of examples in a use case “library,” to serve as an internal resource for FDA reviewers on the historical application of RWD in regulatory decision-making during the PHE or establishment of novel RWD data and analytics capabilities to strengthen proactive surveillance activities.</p> <p>Development and active use of internal FDA tools, such as reviews that use RWD templates, and training, including the number and breadth of FDA personnel trained, to improve consistency and efficiency in reviewing COVID-19 medical product submissions incorporating elements of RWD and RWE.</p> <p>Creation of an Agency-level roadmap to help guide investment in RWD capabilities.</p>
Continue to evolve and optimize inspectional operations, building on the COVID-19 experience as a catalyst	<p>Communicate FDA’s approach to inspectional activities during the COVID-19 PHE, including guidelines to designate work as mission-critical externally.</p> <p>Develop a comprehensive optimization roadmap.</p> <p>Create a framework to define and measure the effectiveness of inspectional approaches.</p>	<p>Internal and external launch of communications to clarify plans to conduct inspections through the remainder of the PHE, and provide guidelines for designating inspections as mission-critical.</p> <p>Develop, communicate and advance an inspection optimization strategy.</p> <p>Codification of a framework to define and measure the effectiveness of alternative inspectional approaches such as MRA and RRA, and implementation of that framework, such as in pilot studies on subsets of inspections for certain products, to determine how FDA might apply alternative approaches.</p>
Strengthen supply chain surveillance for regulated products	<p>Further develop data-analytics capabilities and approaches to risk surveillance and mitigation across programs.</p> <p>Continue to facilitate adoption and scaling of new manufacturing technologies and the use of digital and</p>	<p>Further development of data and analytical tools to surveil supply chains at scale (e.g., new version releases, utilization and integration in cross-functional business processes).</p> <p>Creation and publication of an Agency white paper, followed by draft guidance, on the use of advanced modeling in advanced or continuous pharmaceutical manufacturing to facilitate the adoption of model-based approaches.</p>

	advanced analytics to improve supply chain resilience.	
Further develop the Agency's emergency management capabilities and approaches	<p>Expand capabilities related to Agency-wide scenario and strategic planning.</p> <p>Identify specific opportunities to enhance coordinating mechanisms and roles across critical emergency management bodies to inform an updated EOP.</p> <p>Continue to invest in and expand training and simulation exercises.</p>	<p>Development and active use of Agency-wide scenario models; frequency of refresh; ease of use and user satisfaction and feedback, and improved awareness among FDA leadership and key personnel.</p> <p>Degree of scenario planning pull-through as the model informs decision-making for a discrete set of use cases, potentially defined in an integrated action plan.</p> <p>Implementation of updates to the EOP, potentially including clarification of roles and responsibilities, subject-matter expertise, improved two-way communication channels, and awareness of data input from intra-Agency and inter-agency partners, as applicable.</p> <p>Frequency of staff training and simulation exercises, number of participants and level of engagement, coverage across FDA Centers/ORAs and programs, participation by other U.S. government partners or external groups, where appropriate.</p>
Further develop regulatory frameworks to encourage broader use of adaptive trial designs and master protocols	<p>Review applicable regulatory frameworks and engage further with industry to understand regulatory enablers and challenges associated with integrating adaptive designs into future trials</p> <p>Partner with relevant U.S. government agencies such as NIH to develop and advance a plan to address specific therapeutic areas and relevant use cases, and promote the use of master protocols for clinical trial design and execution.</p> <p>Continue to play a leadership role in developing common data standards, clinical trial infrastructure (especially data-collection architecture) and analytical methods underpinning novel protocols and execution approaches.</p>	<p>Proportion of total completed clinical trials that incorporate master protocol and adaptive design features.</p> <p>Quantification of the pace of change in standard of care for a range of prioritized diseases aligned to the use cases mentioned above.</p> <p>Reduction in the time and cost required to bring new medical products to market.</p>