



November 2020

COVID-19

Federal Efforts Accelerate Vaccine and Therapeutic Development, but More Transparency Needed on Emergency Use Authorizations

Accessible Version

GAO Highlights

Highlights of [GAO-21-207](#), a report to congressional addressees

Why GAO Did This Study

The U.S. had about 10.3 million cumulative reported cases of COVID-19 and about 224,000 reported deaths as of November 12, 2020. Given this catastrophic loss of life as well as the pandemic's effects on the U.S. economy, effective and safe vaccines and therapeutics are more important than ever.

The CARES Act includes a provision for GAO to report on its ongoing monitoring and oversight efforts related to the COVID-19 pandemic. This report examines, (1) efforts of Operation Warp Speed to accelerate COVID-19 vaccine and therapeutic development; and (2) FDA's use of EUAs for COVID-19 therapeutics and vaccines, among other objectives.

GAO reviewed federal laws and agency documents, including HHS and DOD information on vaccine and therapeutic development and EUAs as of November 2020. GAO interviewed or received written responses from HHS and DOD officials, and interviewed representatives from vaccine developers and manufacturers, as well as select public health stakeholders and provider groups covering a range of provider types.

What GAO Recommends

FDA should identify ways to uniformly disclose to the public the information from its scientific review of safety and effectiveness data when issuing EUAs for therapeutics and vaccines. HHS neither agreed nor disagreed with the recommendation, but said it shared GAO's goal of transparency and would explore approaches to achieve this goal.

View [GAO-21-207](#). For more information, contact Mary Denigan-Macauley at (202) 512-7114 or deniganmacauleym@gao.gov, or Alyssa M. Hundrup at (202) 512-7114 or hundrupa@gao.gov

November 2020

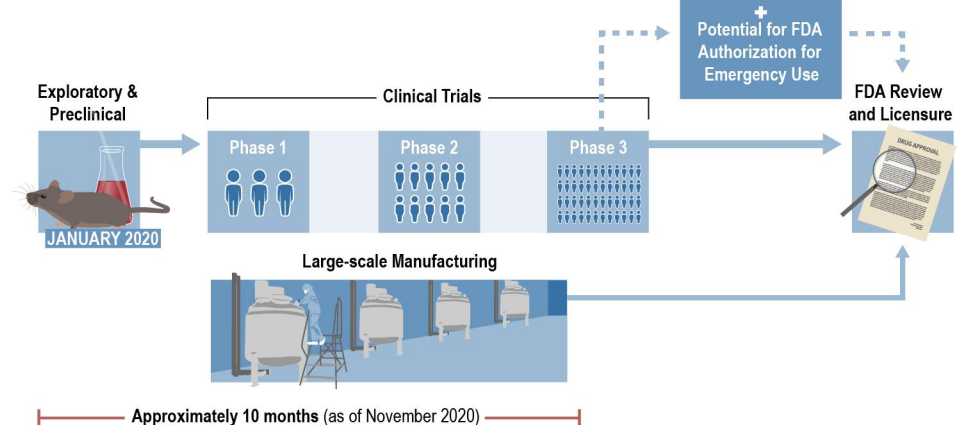
COVID-19

Federal Efforts Accelerate Vaccine and Therapeutic Development, but More Transparency Needed on Emergency Use Authorizations

What GAO Found

Through Operation Warp Speed—a partnership between the Department of Health and Human Services (HHS) and the Department of Defense (DOD)—the federal government is accelerating efforts to develop vaccines and therapeutics for COVID-19. A typical vaccine development process can take approximately 10 years or longer, but efforts under Operation Warp Speed seek to greatly accelerate this process by completing key steps simultaneously (see figure). As of October 15, 2020, Operation Warp Speed publicly announced financial support for the development or manufacturing of six COVID-19 vaccine candidates totaling more than \$10 billion in obligations. It has also announced financial support for the development of therapeutics, such as a \$450 million award to manufacture a monoclonal antibody treatment (a treatment that uses laboratory-made antibodies, which also may be able to serve as a prevention option).

Operation Warp Speed Timeline for a Potential Vaccine Candidate



Source: GAO Analysis of Food and Drug Administration (FDA), Pharmaceutical Research and Manufacturers of America, and Operation Warp Speed Information. | [GAO-21-207](#)

Note: An Emergency Use Authorization allows for emergency use of medical products without FDA approval or licensure during a declared emergency, provided certain statutory criteria are met.

The Food and Drug Administration (FDA) may temporarily allow the use of unlicensed or unapproved COVID-19 vaccines and therapeutics through emergency use authorizations (EUA), provided there is evidence that the products may be effective and that known and potential benefits outweigh known and potential risks. For vaccines, FDA issued guidance in October 2020 to provide vaccine sponsors with recommendations regarding the evidence FDA needed to support issuance of an EUA. For therapeutics, FDA has issued four EUAs as of November 9, 2020. The evidence to support FDA's COVID-19 therapeutic authorization decisions has not always been transparent, in part because FDA does not uniformly disclose its scientific review of safety and effectiveness data for EUAs, as it does for approvals for new drugs and biologics. Given the gravity of the pandemic, it is important that FDA identify ways to uniformly disclose this information to the public. By doing so, FDA could help improve the transparency of, and ensure public trust in, its EUA decisions.

Contents

Letter		1
	Background	5
	Operation Warp Speed Partnership Leads Federal Efforts to Accelerate Developing and Manufacturing COVID-19 Vaccines and Therapeutics	12
	FDA Clarified Expected Evidence for COVID-19 Vaccine EUAs, but the Evidence to Support Its COVID-19 Therapeutic EUA Decisions Is Not Always Transparent	20
	Stakeholders Indicate Initial Planning Documents Are Helpful, but Seek Additional Information on Federal Plans for Vaccine Distribution	32
	Conclusions	40
	Recommendation for Executive Action	41
	Agency Comments and Our Evaluation	41
<hr/>		
	Appendix I: Comments from the Department of Health and Human Services	45
	Appendix II: GAO Contacts and Staff Acknowledgments	48
	Appendix III: Accessible Data	49
	Agency Comment Letter	49
<hr/>		
	Related GAO Products	51
<hr/>		
Table		
	Table 1: Statutory Criteria Required for an Emergency Use Authorization (EUA)	11
<hr/>		
Figures		
	Figure 1: Traditional Vaccine Development Timeline Compared to Potential Operation Warp Speed Timeline	7
	Figure 2: Reported Operation Warp Speed Leadership Structure, as of November 2020	9

Figure 3: Overview of the Four Vaccine Platform Technologies Considered by Operation Warp Speed, as of October 2020	15
Figure 4: Timeline of Emergency Use Authorizations for COVID-19 Therapeutics, as of November 9, 2020	25
Figure 5: Data Cited to Support Issuance of Emergency Use Authorizations (EUA) for Therapeutics for COVID-19, as of November 9, 2020	28

Abbreviations

ASPR	Assistant Secretary for Preparedness and Response
BARDA	Biomedical Advanced Research and Development Authority
CDC	Centers for Disease Control and Prevention
COVID-19	Coronavirus Disease 2019
DOD	Department of Defense
EUA	Emergency Use Authorization
HHS	Department of Health and Human Services
FDA	Food and Drug Administration
NIH	National Institutes of Health
VTrckS	Vaccine Tracking System

This is a work of the U.S. government and is not subject to copyright protection in the United States. The published product may be reproduced and distributed in its entirety without further permission from GAO. However, because this work may contain copyrighted images or other material, permission from the copyright holder may be necessary if you wish to reproduce this material separately.



November 17, 2020

Congressional Addressees

The U.S. has had about 10.3 million cumulative reported cases of Coronavirus Disease 2019 (COVID-19) and about 224,000 reported deaths as of November 12, 2020. Given this catastrophic loss of life as well the pandemic's effects on the U.S. economy, safe and effective vaccines to prevent the disease and therapeutics to treat those made ill by its effects are more important than ever.

Since June 2020, we have cited the critical importance of planning for the quick and flexible development, manufacturing, distribution, and administration of COVID-19 vaccine(s) and therapeutics. In addition, we have recommended that federal plans for vaccine distribution outline how efforts will be coordinated across federal agencies and nonfederal entities. We have also noted the importance of timely, clear, and consistent communication to state and local health officials, stakeholders, and the public about vaccine and therapeutic availability, efficacy, and safety to ensure public confidence and trust, which in turn could encourage vaccine and therapeutic use.¹

Efforts to develop, manufacture, and distribute COVID-19 vaccines and therapeutics involve multiple federal agencies, the private sector, and state and local governments. These federal efforts include Operation Warp Speed, a partnership between the Department of Defense (DOD) and the Department of Health and Human Services (HHS) that aims to accelerate the development, manufacturing, and distribution of COVID-19 vaccines and therapeutics, with the goal of producing 300 million doses of a COVID-19 vaccine, with initial doses available by January 2021.

HHS's Food and Drug Administration (FDA) is responsible for licensing and approving vaccines and therapeutics. As of November 9, 2020, no vaccines were available to prevent COVID-19, though several candidates were under development. Regarding therapeutics, the agency has

¹GAO, *COVID-19: Opportunities to Improve Federal Response and Recovery Efforts*, [GAO-20-625](#) (Washington, D.C.: June. 25, 2020) and GAO, *COVID-19: Federal Efforts Could Be Strengthened by Timely and Concerted Actions*, [GAO-20-701](#) (Washington, D.C.: Sept. 21, 2020).

approved one therapeutic and made certain others available through Emergency Use Authorizations (EUA), which allows for emergency use of medical products without FDA approval or licensure, provided certain statutory criteria are met.² An FDA official has stated that the agency also likely will review COVID-19 vaccine candidates through the EUA process.³

The CARES Act includes a provision for GAO to report on its ongoing monitoring and oversight efforts related to the COVID-19 pandemic.⁴ This report is part of our body of work in response to the CARES Act and focuses on the federal government's efforts related to COVID-19 vaccines and therapeutics. Specifically, in this report, we

1. describe the efforts of Operation Warp Speed to accelerate the development and manufacturing of COVID-19 vaccines and therapeutics,⁵
2. examine FDA's potential use of EUAs for COVID-19 vaccines, as well as its use of EUAs for COVID-19 therapeutics, and
3. describe the actions the federal government has taken to plan for the distribution of any authorized or licensed COVID-19 vaccine, and initial perspectives of public health officials and providers on these efforts.

To describe the efforts of Operation Warp Speed to accelerate the development and manufacturing of COVID-19 vaccines and therapeutics, we reviewed relevant agency documents, including HHS's and DOD's Operation Warp Speed fact sheet, clinical trial protocols for Operation Warp Speed COVID-19 vaccine candidates, FDA's guidance for clinical trials, and the Operation Warp Speed memorandum of understanding between HHS and DOD. We also analyzed data on obligations for contracts and other acquisition vehicles available in the Federal

²See 21 U.S.C. § 360bbb-3.

³Vaccine sponsors may also submit biologics license applications for licensure of vaccine candidates. FDA guidance indicates that licensure is the goal for COVID-19 vaccine candidates, including those that first receive an EUA.

⁴Pub. L. No. 116-136, § 19010, 134 Stat. 281, 579-81 (2020). This report also responds, in part, to a bipartisan request from the House Select Subcommittee on the Coronavirus Crisis for GAO to examine Operation Warp Speed.

⁵In this report, we describe Operation Warp Speed's initial activities as of October 2020. We will continue to review and evaluate Operation Warp Speed's efforts to accelerate COVID-19 vaccine and therapeutic development and manufacturing in future work.

Procurement Data System-Next Generation through October 15, 2020. We assessed the reliability of this data by reviewing existing information about the system and the data it collects—specifically, the data dictionary and data validation rules—and performed electronic testing. We determined the data were sufficiently reliable for the purposes of describing agencies' reported Operation Warp Speed obligations. To help identify key challenges in scaling up manufacturing for COVID-19 vaccines and therapeutics, we conducted a literature review and reviewed reports and journal articles about vaccine and therapeutics manufacturing. We interviewed or received written responses from HHS and DOD officials, including officials working within the Operation Warp Speed partnership. We also interviewed vaccine and therapeutic manufacturing experts and representatives from vaccine developers and manufacturers working with Operation Warp Speed for additional perspectives on vaccine and therapeutic development and manufacturing activities.

To examine FDA's potential use of EUAs for COVID-19 vaccines and its use of EUAs for COVID-19 therapeutics, we reviewed relevant federal laws and agency documents, including FDA's guidance for EUAs, FDA's guidance for COVID-19 vaccines, and FDA's guidance for EUAs for COVID-19 vaccines.⁶ We also reviewed publicly available EUA documentation on FDA's website as of November 9, 2020, including authorization letters for COVID-19 therapeutics and related fact sheets to health care providers, and decision memos, as well as an EUA revocation letter and related documentation. We interviewed FDA officials, as well as received written responses to questions from FDA officials. We also interviewed a public health association and nine provider associations. We selected provider associations based on their involvement on the front lines of responding to the COVID-19 pandemic, as well as to ensure we spoke with associations covering a broad range of specialty health care providers, non-specialty health care providers, and hospitals. We also spoke with an infectious disease expert from a prominent research

⁶FDA, *Emergency Use Authorization of Medical Products and Related Authorities: Guidance for Industry and Other Stakeholders*, (January 2017); *Development and Licensure of Vaccines to Prevent COVID-19: Guidance for Industry*, (June 2020); and *Emergency Use Authorization for Vaccines to Prevent COVID-19: Guidance for Industry*, (October 2020).

institution, as well as observed presentations of FDA officials.⁷ We assessed FDA's potential use of EUAs for COVID-19 vaccines and its use of EUAs for COVID-19 therapeutics against Standards for Internal Control in the Federal Government for information and communication, as well as our past work on lessons learned during public health emergencies and the PanCAP—generally the operative plan for the federal response to COVID-19.⁸

To describe the activities the federal government has taken to plan for the distribution and administration of any authorized or licensed COVID-19 vaccine and initial perspectives on these efforts, we reviewed documents related to federal plans, including the Centers for Disease Control and Prevention's (CDC) *COVID-19 Vaccination Program Interim Playbook Jurisdiction Operations* and HHS's and DOD's *Operation Warp Strategy for Distributing a COVID-19 Vaccine*, issued in September 2020 as well as the updated interim playbook issued in October 2020.⁹ We interviewed or received written responses from HHS and DOD officials, including Operation Warp Speed officials, about federal vaccine distribution plans. We also interviewed representatives from stakeholder groups representing state and local public health officials, including the Association of Immunization Managers, Association of State and Territorial Health Officials, National Governor's Association, and provider associations for their initial perspectives on the available information on the federal government's plans for vaccine distribution and administration, including communication plans.

⁷We reviewed, for example, presentations from the Journal of the American Medical Association, the Center for Infectious Disease Research and Policy at the University of Minnesota, and the Duke-Margolis Center for Health Policy.

⁸GAO, *Standards for Internal Control in the Federal Government*, [GAO-14-704G](#) (Washington, D.C.: Sept. 10, 2014). Internal control is a process effected by an entity's oversight body, management, and other personnel that provides reasonable assurance that the objective of an entity will be achieved.

⁹In this report, we are presenting initial observations about these vaccine distribution documents. We will continue to evaluate these and any additional vaccine-related planning documents, as well as federal agencies' implementation of those plans. In September 2020, we recommended that the Secretary of Health and Human Services, with support from the Secretary of Defense, establish a time frame for documenting and sharing a national plan for distributing and administering COVID-19 vaccine and that it ensure such a plan was consistent with best practices for project planning and scheduling and outlined an approach for how efforts would be coordinated across federal agencies and nonfederal entities. GAO, *COVID-19: Federal Efforts Could Be Strengthened by Timely and Concerted Actions*, [GAO-20-701](#) (Washington, D.C.: Sept. 21, 2020).

We conducted this performance audit from June 2020 to November 2020 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

FDA Approval and Licensure Process and Operation Warp Speed

Typically, before a drug, biologic, or other medical product can be marketed in the U.S., it must be approved or licensed by FDA.¹⁰ While the process varies by product type, the process for drugs and biologics—which include vaccines—generally includes FDA’s review of evidence submitted by a product’s sponsor to determine whether the new product is safe and effective for its intended use or uses, including whether the product’s known benefits outweigh the known risks. For drugs or biologics, it typically takes years of research and development to collect sufficient clinical evidence for FDA review.

Before a drug or biologic is approved or licensed, it will have gone through preclinical research, which includes in vitro and testing on animals for toxicity, and typically three phases of clinical trials to test safety and efficacy in humans.¹¹

- **Phase 1.** Clinical trials in phase 1 generally test the safety of a product with a small group of healthy volunteers (usually less than

¹⁰FDA approves chemically derived drugs through a review of new drug applications; it licenses biologically derived products, such as vaccines, through review of biologics license applications.

¹¹According to FDA officials, in some cases when a new product is being tested for a life-threatening condition, the development process may be expedited by going through only one or two phases of clinical trials before an application is submitted to FDA for marketing approval. In addition, postmarket studies are required for some products that FDA has approved for marketing. For vaccines, FDA’s Vaccine and Related Biological Products Advisory Committee reviews and evaluates data concerning the safety, effectiveness, and appropriate use of vaccines and related biological products which are intended for use in the prevention, treatment, or diagnosis of human diseases and makes appropriate recommendations to the Commissioner of Food and Drugs.

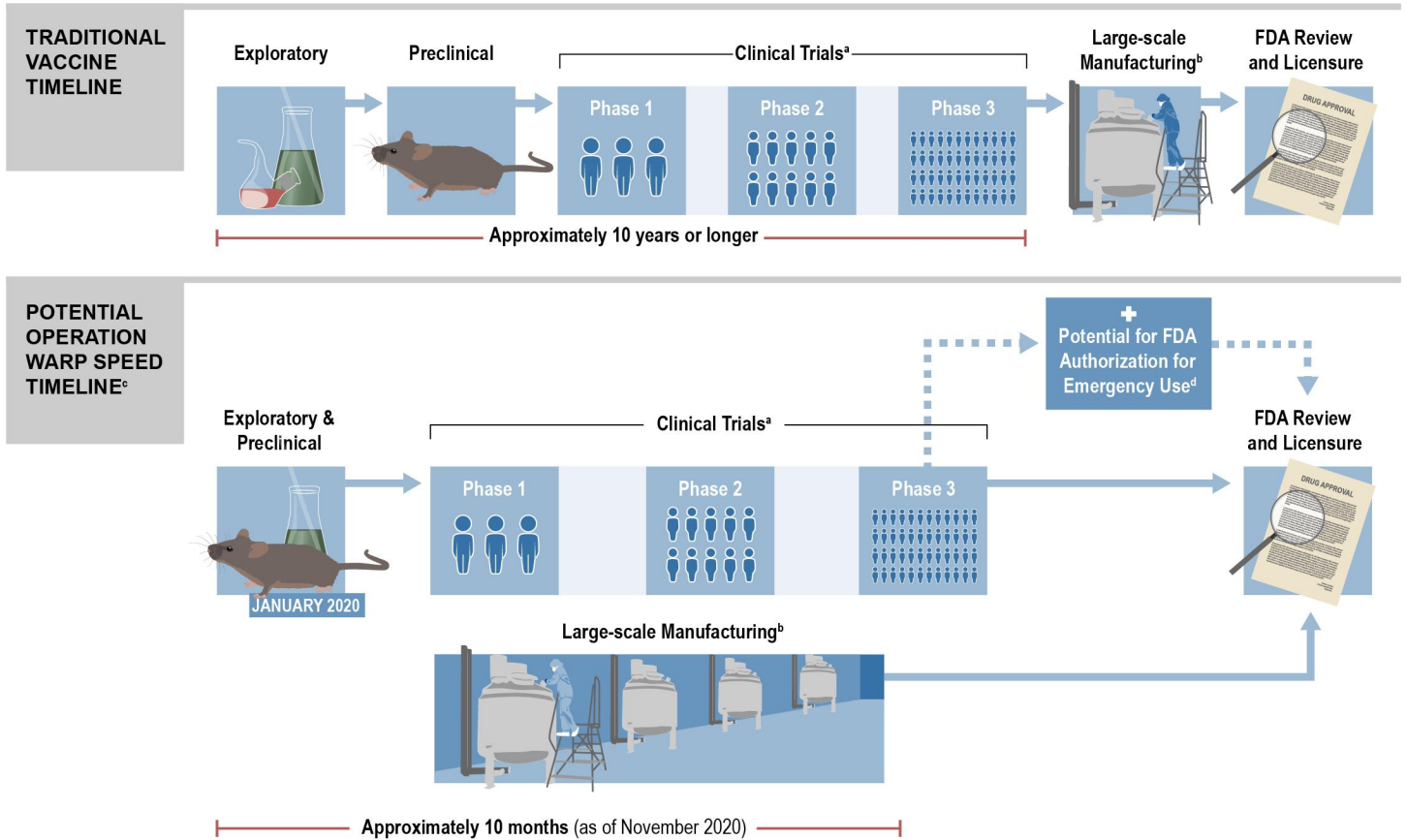
100). The goal of this phase is to determine the product's most frequent side effects and how it is metabolized and excreted.

- **Phase 2.** In phase 2, the product is given to a larger group of volunteers (usually a few dozen to hundreds) to see if it is safe and effective for a particular use. For vaccines, phase 2 trials look at questions such as the maximum tolerated dose, the optimal schedule for giving the product (how many doses and at what time intervals), and whether the immune system of a person taking the vaccine is having the desired responses.
- **Phase 3.** In phase 3, the product is given to still larger groups of volunteers (usually many thousands) than in phase 2. Researchers confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the product to be used safely. For vaccines, this phase examines things such as whether the product prevents new infections or, if people become infected, if the product helps control the infections so they do not become severe.

The vaccine development process has typically taken approximately 10 years or longer according to some studies, with many candidates failing, according to another study.¹² With Operation Warp Speed, the federal government aims to accelerate this process for the development of a COVID-19 vaccine (see fig. 1). To help accelerate the process, the federal government is taking on financial risk to develop and manufacture selected vaccines before their safety and efficacy is fully known so that any candidates receiving FDA authorization and/or licensure can be distributed as soon as possible.

¹²See for example, E.S. Pronker et al., "Risk in Vaccine Research and Development Quantified," PLOS One, vol. 8, no. 3 (2013); and Pharmaceutical Research and Manufacturers of America, "2017 State of Vaccines," (Washington, D.C. November 8, 2017). For a study on success rates for clinical trials, see A. Lo et al., "Estimation of clinical trial success rates and related parameters," Biostatistics, vol. 20, no. 2 (2019).

Figure 1: Traditional Vaccine Development Timeline Compared to Potential Operation Warp Speed Timeline



Source: GAO Analysis of Food and Drug Administration (FDA), Pharmaceutical Research and Manufacturers of America, and Operation Warp Speed Information. | GAO-21-207

Notes: The timelines for vaccine development depicted in this figure are not drawn to scale. These timelines depict examples, and the specific development steps and timelines for a given vaccine may vary from this example.

^aPhase 1 clinical trials generally test the safety of a product with a small group of healthy volunteers (usually less than 100). The goal of this phase is to determine the product’s most frequent side effects and how it is metabolized and excreted.

Phase 2 clinical trials look at questions such as the maximum tolerated dose, the optimal schedule for giving the product (how many doses and at what time intervals), and whether the immune system of a person taking the vaccine is having the desired responses. These trials are conducted with a medium-size population of volunteers (usually a few dozen to hundreds).

Phase 3 clinical trials look at things like whether the product prevents new infections or, if people become infected, if the product helps control the infections so they do not become severe. These trials involve many thousands of volunteers, usually including participants who are at increased risk for infection. According to FDA officials, these clinical trial phases may overlap.

^bAccording to FDA, manufacturing processes are reviewed as part of the vaccine licensure process. Thus, even under a traditional vaccine timeline, some initial manufacturing occurs during development, so the manufacturing processes can be adequately validated. According to an Operation Warp Speed fact sheet, the federal government is taking on the financial risk to enable large-scale manufacturing to start while clinical trials are ongoing, with the goal of having millions of doses available for distribution upon authorization or licensure of a COVID-19 vaccine.

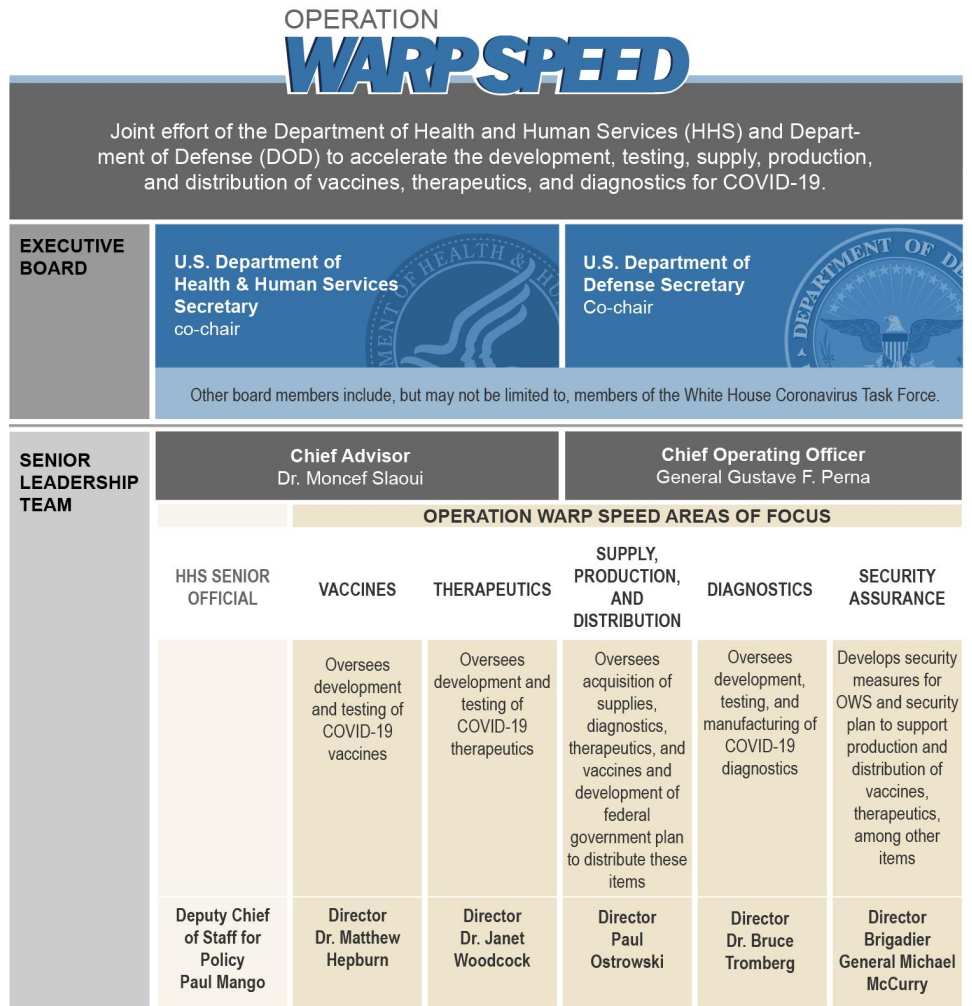
^cThe Operation Warp Speed timeline depicts an example of a potential accelerated timeline for COVID-19 vaccine development. However, the development process of any given Operation Warp Speed vaccine candidate may vary from this example. As of November 2020, approximately 10 months have elapsed since exploratory and preclinical research began in January 2020, after the first U.S. cases of COVID-19 were reported, and as of October 14, 2020, four of the six Operation Warp Speed candidates have begun phase 3 clinical trials. The timing for any remaining steps have yet to be determined as of this report. According to Operation Warp Speed documentation, certain steps may overlap or be shortened to accelerate the development of a COVID-19 vaccine.

^dDuring an emergency, as declared by the Secretary of Health and Human Services under 21 U.S.C. § 360bbb-3(b), FDA may temporarily authorize unapproved medical products or unapproved uses of approved medical products through an Emergency Use Authorization (EUA), provided certain statutory criteria are met. FDA has indicated that issuance of an EUA for a COVID-19 vaccine for which there is adequate manufacturing information would require the submission of certain clinical trial information from Phase 3 clinical trials that demonstrate the safety and effectiveness of the vaccine in a clear and compelling manner, among other things. Any COVID-19 vaccine that initially receives an EUA from FDA is expected to ultimately be reviewed and receive licensure through a biologics license application, according to FDA guidance.

The Operation Warp Speed HHS and DOD partnership also has engaged with private industry, including vaccine and therapeutic developers and manufacturers, and other federal partners, such as the Department of Veterans Affairs, to help achieve its goal of producing 300 million doses of a safe and effective COVID-19 vaccine with initial doses available by January 2021.¹³ The Secretary of Health and Human Services and the Secretary of Defense co-chair an Operation Warp Speed Executive Board, which provides guidance on initiatives and receives updates on progress toward milestones, according to Operation Warp Speed officials. See figure 2 for Operation Warp Speed's leadership structure, as outlined by officials.

¹³Multiple HHS components are involved in Operation Warp Speed, including the Biomedical Advanced Research and Development Authority (BARDA) within the Office of the Assistant Secretary for Preparedness and Response (ASPR); CDC; and the National Institutes of Health (NIH). The Department of Veterans Affairs is primarily involved in Operation Warp Speed through its participation in clinical trials for vaccine candidates supported by Operation Warp Speed. For example, as of September 2020, 19 Department of Veterans Affairs facilities were participating in clinical trials for three Operation Warp Speed supported vaccine candidates. Outside of Operation Warp Speed, DOD is also pursuing medical research and development projects for COVID-19 vaccines, therapeutics, and diagnostics as part of its efforts to protect servicemembers from COVID-19.

Figure 2: Reported Operation Warp Speed Leadership Structure, as of November 2020



Source: GAO analysis of documentation and information provided by Operation Warp Speed officials. | GAO-21-207

Operation Warp Speed has five areas of focus outlined in a memorandum of understanding between HHS and DOD: (1) vaccines; (2) therapeutics; (3) diagnostics; (4) supply, production, and distribution; and (5) security assurance. Its senior leadership team—which, according to Operation Warp Speed officials includes the directors of these five areas of focus, the Chief Advisor, the Chief Operating Officer, and an HHS senior official (the Deputy Chief of Staff for Policy)—provides information, advice, and recommendations to the Executive Board to inform the board’s decision-making.

Funding to Support the Development of COVID-19 Vaccines and Therapeutics

The CARES Act and the Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020, appropriated funding for HHS activities to support the development of vaccines and therapeutics for COVID-19. This included appropriations to FDA, the National Institutes of Health (NIH), and the Public Health and Social Services Emergency Fund for activities that include, but are not limited to, developing countermeasures and vaccines and purchasing vaccines and therapeutics.¹⁴ As of October 31, 2020, HHS reported it had obligated about \$13.3 billion and expended about \$1.3 billion for vaccines, and it obligated about \$2.8 billion and expended about \$622 million for therapeutics.

The CARES Act includes a number of provisions related to federal contracting efforts to facilitate agencies' response to the pandemic. We have reported previously that a variety of contracting flexibilities are available to agencies to facilitate contract awards and the obligation of funds in response to the pandemic including the use of "other transaction authority," which enables federal agencies to negotiate terms and conditions specific to a project without requiring them to comply with certain federal regulations.¹⁵

Emergency Use Authorization General Statutory Criteria and Guidance

The Secretary of Health and Human Services may declare that circumstances, prescribed by statute, exist justifying the emergency use of certain medical products.¹⁶ Once a declaration has been made, FDA

¹⁴See CARES Act, Pub. L. No. 116-136, div. B., tits. I, VIII, 134 Stat. 281, 509, 555-56, 560-61 (2020); Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020, Pub. L. No. 116-123, div. A., tits. I, III, 134 Stat. 146, 148, 149-50. The Public Health and Social Services Emergency Fund is an account through which funding is provided to certain HHS offices, such as ASPR.

¹⁵See GAO, *COVID-19 Contracting: Observations on Federal Contracting in Response to the Pandemic*, [GAO-20-632](#), (Washington, D.C.: July 29, 2020).

¹⁶See 21 U.S.C. § 360bbb-3(b)(1). Drugs approved by FDA for uses other than COVID-19 and without an EUA for COVID-19, such as dexamethasone, have also been used by some physicians to treat the disease as part of research studies.

may temporarily allow use of unapproved medical products or unapproved uses of approved medical products through an EUA, provided certain statutory criteria are met.¹⁷ One of these criteria—evidence that the product *may* be effective—requires less certainty of effectiveness than is required to approve therapeutics or license vaccines. For example, a request for an EUA may be submitted and FDA may authorize the product before all of the preclinical research and clinical studies that would be needed to support full approval are necessarily completed. See table 1 for a description of certain statutory criteria.¹⁸

Table 1: Statutory Criteria Required for an Emergency Use Authorization (EUA)

Criteria	Explanation
Serious or life threatening disease or condition	The chemical, biological, radiological, or nuclear threat agent referred to in the Secretary of Health and Human Services' emergency declaration must be capable of causing a serious or life-threatening disease or condition.
Evidence the product may be effective	Based on the totality of the scientific evidence available, including data from adequate and well-controlled clinical trials, if available, it must be reasonable to believe that the medical product may be effective in diagnosing, treating, or preventing the disease or condition. ^a
Risk-benefit analysis	Based on the totality of the scientific evidence available, it must be reasonable to believe that the known and potential benefits of the product, when used to diagnose, prevent, or treat the identified disease or condition, outweigh the known and potential risks of the product.
No alternatives	There must be no adequate, approved, and available alternative to the candidate product for diagnosing, preventing, or treating the disease or condition. ^b

Source: GAO summary of 21 U.S.C. § 360bbb-3(c) and FDA guidance. | GAO-21-207

Note: All criteria in this table must be met in order for a medical product to receive an EUA, in addition to further statutory criteria set forth in 21 U.S.C. § 360bbb-3(c).

^aThe “may be effective” standard for EUAs requires less certainty of effectiveness than is required to approve drugs or license biologics.

^bA potential alternative product may be considered “unavailable” if there are insufficient supplies of the approved alternative to fully meet the emergency need. A potential alternative product may be considered “inadequate” if, for example, there are contraindicating data for special circumstances of populations.

FDA may revise or revoke an EUA if the circumstances giving rise to the emergency declaration no longer exist, the above criteria for issuance are no longer met, or revocation is appropriate to protect public health or

¹⁷The FDA Commissioner may issue EUAs under delegated authority from the Secretary of Health and Human Services. See 85 Fed. Reg. 7,316 (Feb. 7, 2020).

¹⁸The law also directs FDA to impose certain required conditions in an EUA as necessary or appropriate to protect public health and allows the agency discretion to impose additional conditions. See 21 U.S.C. § 360bbb-3(e). For example, with respect to the emergency use of an unapproved product, FDA must establish appropriate conditions for the monitoring and reporting of adverse events associated with the product and for recordkeeping and reporting by the manufacturer.

safety. For example, an EUA may be revoked if new data become available indicating that the product is not effective or safe. In general, unless it is revoked, an EUA will remain in effect for the duration of the emergency declaration.

FDA issued guidance in January 2017 for industry and stakeholders regarding FDA's general recommendations and procedures applicable to all EUAs. The guidance recommends that product sponsors submit any available relevant scientific evidence regarding preclinical testing data and evidence from human experience regarding product efficacy.¹⁹ Given the variety of medical products, the guidance states that the type and amount of data needed to support an EUA may vary and does not specify the minimum number or types of studies needed to meet the statutory criteria to authorize a product. Instead, FDA states that it will assess the sufficiency of the effectiveness data and the risk-benefit profile of each candidate product on a case-by-case basis.

Operation Warp Speed Partnership Leads Federal Efforts to Accelerate Developing and Manufacturing COVID-19 Vaccines and Therapeutics

Operation Warp Speed is Accelerating the Development and Manufacturing of Six Vaccines

As of October 15, 2020, Operation Warp Speed had publicly announced financial support for the development and manufacturing of six vaccine

¹⁹FDA recommends the EUA request include any available relevant scientific evidence regarding the mechanism of action (i.e., how the medical product produces an effect in the body); preclinical research, such as in vitro and animal toxicology data; data on activity or effectiveness in animals that would contribute to understanding potential effects in humans; data on human experience such as from published case reports, uncontrolled trials, and controlled trials; and information to support dosing for the intended use. See FDA, *Emergency Use Authorization of Medical Products and Related Authorities: Guidance for Industry and Other Stakeholders*, January 2017.

candidates for COVID-19.²⁰ In selecting vaccine candidates, Operation Warp Speed officials said that they focused on candidates that had initial data on clinical safety and efficacy and the ability to enter late stage clinical trials by fall 2020, and the ability to rapidly scale up manufacturing.²¹ Through our reviews of federal procurement data and clinical trial protocols, among other information, and interviews with Operation Warp Speed officials and representatives from vaccine developers and manufacturers, we have found the following about Operation Warp Speed's support of COVID-19 vaccine development.

The federal government has announced awards for six Operation Warp Speed vaccine candidates. Through HHS and DOD, Operation Warp Speed has announced contract awards with obligations totaling at least \$10 billion and a total potential estimated value of at least \$18 billion.²² Awarded contracts for the six vaccine candidates include at least \$2 billion obligated using Federal Acquisition Regulation-based contracts and at least \$8 billion obligated using other transaction authority, which enables federal agencies to negotiate terms and conditions specific to a project without requiring them to comply with certain federal regulations. In prior work, we have noted that other transactions can enable agencies to attract companies that have not typically done business with the

²⁰The federal government has obligated funding for awards and/or modifications to each company with a product considered an Operation Warp Speed COVID-19 vaccine candidate for different types of activities. For example, for some vaccine candidates, Operation Warp Speed has publicly announced support for both clinical development and manufacturing activities; while for other candidates, it has only announced support for the manufacturing or purchase of initial vaccine doses.

²¹According to a *New England Journal of Medicine* article co-authored by Operation Warp Speed's Chief Advisor (Dr. Moncef Slaoui) and its Director of Vaccines (Dr. Matthew Hepburn), Operation Warp Speed prioritized candidates that 1) had robust preclinical data or early-stage clinical trial data supporting their potential for clinical safety and efficacy; 2) could enter phase 3 clinical trials during summer or fall 2020; and 3) were based on vaccine-platform technologies permitting fast manufacturing and had developers with the ability to produce more than 100 million doses by mid-2021. See M. Slaoui and M. Hepburn. "Developing Safe and Effective COVID Vaccines — Operation Warp Speed's Strategy and Approach," *New England Journal of Medicine*, Aug. 26, 2020. Our analysis of acquisition documents associated with Operation Warp Speed vaccine candidates remains ongoing, and the criteria that officials have outlined for selecting Operation Warp Speed candidates may differ from the source selection criteria for specific acquisitions.

²²The six vaccine candidates are considered to be part of Operation Warp Speed, but the awards to the candidates were made by offices within HHS and DOD, including BARDA and the Army Contracting Command on behalf of the Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense, respectively. Total potential estimated value is based on all contracts being definitized and options being exercised.

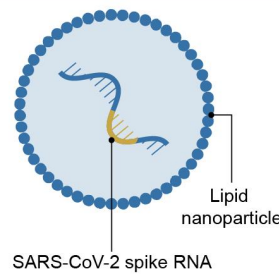
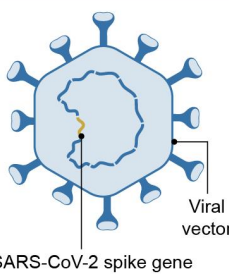
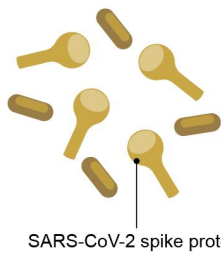
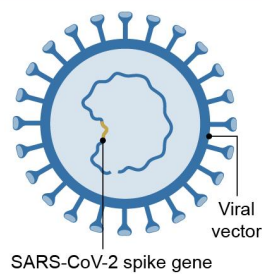





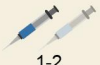


government, in part through the ability to negotiate intellectual property provisions that are tailored to each party's needs.²³ We also have noted challenges with the use of other transactions in terms of a risk of reduced accountability and transparency, in part because such transactions are exempt from the Federal Acquisition Regulation and related controls and oversight mechanisms that apply to government procurement contracts.

Operation Warp Speed is supporting multiple vaccine candidates to mitigate uncertainties associated with safety or efficacy, among other factors. Regarding potential vaccines, Operation Warp Speed officials said their intent was to select vaccine candidates that utilize various technologies. Specifically, they said they identified four vaccine platform technologies that would be most likely to yield a safe and effective vaccine: the mRNA platform, the replication-defective live-vector platform, the recombinant-subunit-adjuvanted protein platform, and the attenuated replicating live-vector platform (see fig. 3).²⁴ According to Operation Warp Speed officials, their strategy includes selecting different platform technologies to mitigate the risk that any one platform or specific vaccine could fail because of problems with safety, efficacy, industrial manufacturability, or scheduling factors. As of October 2020, Operation Warp Speed has publicly announced support for vaccine candidates using three of the four vaccine platform technologies.

²³GAO, *Defense Acquisitions: DOD's Use of Other Transactions for Prototype Projects Has Increased*, [GAO-20-84](#) (Washington, D.C.: Nov. 22, 2019); and *Federal Acquisitions: Use of 'Other Transaction' Agreements Limited and Mostly for Research and Development Activities*, [GAO-16-209](#) (Washington, D.C.: Jan. 7, 2016).

²⁴When referring to vaccine platform technologies, we are referring to the underlying technology used as the basis of the vaccine.

Figure 3: Overview of the Four Vaccine Platform Technologies Considered by Operation Warp Speed, as of October 2020

	mRNA platform	Replication-defective live-vector platform	Recombinant-subunit-adjuvanted protein platform	Attenuated replicating live-vector platform
	 <p>Lipid nanoparticle SARS-CoV-2 spike RNA</p>	 <p>Viral vector SARS-CoV-2 spike gene</p>	 <p>SARS-CoV-2 spike protein</p>	 <p>Viral vector SARS-CoV-2 spike gene</p>
Description	Encapsulated genetic instructions that allow vaccinated individuals to produce spike protein of SARS-CoV-2	Non-replicating virus that delivers genetic instructions to allow vaccinated individuals to produce spike protein of SARS-CoV-2	Fully-formed spike protein of SARS-CoV-2 delivered with adjuvant, which helps to stimulate immune system of vaccinated individuals	Replicating virus that delivers genetic instructions to allow vaccinated individuals to produce spike protein of SARS-CoV-2
Technology used in prior FDA-licensed vaccine	 No vaccine using this technology has ever been licensed by FDA	 No vaccine using this technology has ever been licensed by FDA	 Example: seasonal influenza vaccine (licensed by FDA)	 Example: Ebola vaccine (licensed by FDA)
Doses required	 2	 1-2	 1-2	 1 (potentially)
Operation Warp Speed candidates (clinical trial phase)	Moderna (phase 3) Pfizer/BioNTech (phase 2/3)	Janssen (phase 3) AstraZeneca (phase 3)	Sanofi/GSK (phase 1/2) Novavax (phase 1)	None

Source: GAO (analysis); Adaptation of images depicting vaccine technologies with permission from Springer Nature: *Nature* ("The Race for Coronavirus Vaccines: A Graphical Guide," Ewen Callaway) © 2020. | GAO-21-207

Notes: In parentheses next to the name of the company are details about the most advanced clinical trial phase of that company's COVID-19 vaccine candidate, according to the Biomedical Advanced Research and Development Authority's website, [MedicalCountermeasures.gov](https://www.fda.gov/medical-products/medical-countermeasures) as of October 15, 2020.

The federal government has obligated funding for awards and/or modifications to each company with a product considered an Operation Warp Speed COVID-19 vaccine candidate for different types of activities, such as clinical development, manufacturing, or purchase of initial vaccine doses.

SARS-CoV-2 is the virus that causes COVID-19.

Phase 1 clinical trials generally test the safety of a product with a small group of healthy volunteers (usually less than 100). The goal of this phase is to determine the product's most frequent side effects and how it is metabolized and excreted.

Phase 2 clinical trials look at questions such as the maximum tolerated dose, the optimal schedule for giving the product (how many doses and at what time intervals), and whether the immune system of a person taking the vaccine is having the desired responses. These trials are conducted with a medium-size population of volunteers (usually a few dozen to hundreds).

Phase 3 clinical trials look at things like whether the product prevents new infections or, if people become infected, if the product helps control the infections so they do not become severe. These

trials involve many thousands of volunteers, usually including participants who are at increased risk for infection. According to FDA officials, these clinical trial phases may overlap.

Four vaccine candidates in phase 3 clinical trials follow typical clinical trial design by enrolling mostly healthy non-pregnant adults.

Four of the six Operation Warp Speed supported vaccine candidates had begun phase 3 clinical trials in the United States, as of October 2020.²⁵

The developers of these four vaccine candidates released their phase 3 clinical trial protocols to the public in September 2020.²⁶ These protocols explain how the developers will test each vaccine in humans for safety and effectiveness through the phase 3 trials.²⁷

Through our review of the four vaccine candidates' protocols, we found that they generally appeared to follow a typical clinical trial design by enrolling mostly healthy non-pregnant adult populations and excluding other groups such as children, pregnant women, and those with certain comorbid or unstable conditions.²⁸ Excluding these groups in the initial phase 3 trials is not unusual, but a potential consequence is that the data on vaccine safety and effectiveness may not apply to these excluded populations. Whether FDA will consider authorizing or licensing these vaccine candidates for such excluded populations, including for people with certain comorbid or unstable conditions, is currently unknown. How and when testing for vaccine safety and efficacy would be conducted for these groups also is presently unknown.

We also found that the four candidates' clinical trial protocols provide limited details on how the vaccine developers will analyze their safety and

²⁵On September 24, 2020, a fifth candidate, Novavax, announced that it had initiated phase 3 trials in the United Kingdom (U.K.). On September 9, 2020, AstraZeneca paused the phase 3 trial for its COVID-19 vaccine after a trial participant in the U.K. experienced an unexplained illness in the phase 3 trial. As of October 23, 2020, AstraZeneca's trials have resumed, including in the United States. On October 12, 2020, Janssen announced that it paused the phase 3 trial for its COVID-19 vaccine after a trial participant experienced an unexplained illness, but on October 23, 2020 Janssen announced that preparations were underway to resume the trial.

²⁶We reviewed the clinical trial protocols that AstraZeneca, Janssen, Moderna, and Pfizer released in September 2020.

²⁷On November 9, 2020, Pfizer publicly announced findings from its first interim efficacy analysis from phase 3 clinical trials of its COVID-19 vaccine candidate and stated plans to share additional data on safety and efficacy for this candidate in the coming weeks.

²⁸Three of the four companies set a minimum enrollment age of 18 years for their phase 3 clinical trials, while one company (Pfizer) planned to enroll people as young as 16 years old. In October 2020, Pfizer announced on its website that it received permission from FDA to enroll children as young as 12 years old.

efficacy data, specifically for population subgroups (e.g., the elderly, people with comorbidities, or racial/ethnic groups) or sample sizes needed for such subgroup analyses. Unless vaccine developers collect sufficient data for a subgroup analysis, it may not be possible to identify the potential for different safety or efficacy results for one or more subgroups, even if vaccine candidates are found safe and effective in the aggregate for the general population. The protocols reference separate analysis plan documents that may contain more information on their methodologies and planned analyses. We intend to request and review these plans in future work.

Operation Warp Speed documents emphasize the importance of ensuring that participation in clinical trials for COVID-19 vaccines includes those disproportionately affected by COVID-19, such as people in racial and ethnic minority groups. Moreover, FDA's June 2020 guidance on the development and licensure of COVID-19 vaccines encourages the inclusion of diverse populations in all phases of vaccine clinical development.²⁹ In this guidance, FDA strongly encourages the enrollment of populations most affected by COVID-19, specifically citing racial and ethnic minorities. Several stakeholders we interviewed noted that, at a minimum, clinical trials for COVID-19 vaccines should include the same percentage of persons from racial and ethnic minority groups as the overall population, particularly in light of the disparities found in indicators of COVID-19, including testing, cases, hospitalizations, and deaths.³⁰

Efforts to Develop COVID-19 Therapeutics through Operation Warp Speed Also Underway

To support the development of therapeutics for COVID-19, Operation Warp Speed is using criteria similar to those used to select candidate vaccines. In particular, it is focusing its funding support on candidate therapeutics that are (1) advanced enough to enter clinical trials in the short term (i.e., by early fall 2020), (2) have the potential for FDA

²⁹FDA, *Development and Licensure of Vaccines to Prevent COVID-19: Guidance for Industry*, June 2020.

³⁰See [GAO-20-701](#), 186; and the Department of Health and Human Services, Centers for Disease Control and Prevention, *Report to Congress on Paycheck Protection Program and Health Care Enhancement Act Disaggregated Data on U.S. Coronavirus Disease 2019 (COVID-19) Testing, 5th 30-Day Update & COVID-19 Diagnosis, Hospitalizations, and Deaths* (October 2020).

authorization or approval by the end of 2020, and (3) are able to be rapidly manufactured at scale, according to a journal article written by Operation Warp Speed officials.³¹

For example, in July 2020, Operation Warp Speed announced a DOD award of \$450 million to support the large-scale manufacturing of Regeneron's monoclonal antibody treatment. In October 2020, it also announced an agreement with Eli Lilly and Company for the federal government to purchase initial doses of the company's antibody therapeutic treatment subject to FDA authorization or licensure of the treatment.³² According to Operation Warp Speed officials, they are also evaluating whether to support clinical trials that would repurpose certain existing antiviral drugs for the treatment of COVID-19. Further, Operation Warp Speed is supporting clinical trials of various anticoagulation regimens for the treatment of patients with COVID-19 in various clinical settings, according to officials.³³

³¹M. Slaoui, S.E. Green and J. Woodcock. "Bridging the Gap at Warp Speed — Delivering Options for Preventing and Treating Covid-19," *New England Journal of Medicine*, Sept. 15, 2020. In this article, officials explained that the short time frame means that in certain cases, Operation Warp Speed is focusing on drugs that are already approved by FDA or in human trials for other indications because these drugs can be rapidly evaluated for use for COVID-19 and further developed if clinical activity is detected. Our analysis of acquisition documents associated with Operation Warp Speed candidate therapeutics remains ongoing, and the criteria that officials have outlined for selecting Operation Warp Speed candidates may differ from the source selection criteria for specific acquisitions.

³²Monoclonal antibodies are laboratory-made antibodies that may be able to serve as another prevention option until a vaccine becomes available. They usually only last for a few months, thus potentially requiring people to get multiple infusions or injections on a regular schedule for them to remain effective. Regeneron and Eli Lilly submitted EUA requests for their monoclonal antibody treatments in early October 2020. On November 9, 2020, FDA issued an EUA for Eli Lilly's treatment (bamlanivimab).

³³NIH announced these clinical trials on September 10, 2020. According to the NIH press release, these trials will evaluate the safety and effectiveness of varying types of blood thinners (i.e., anti-coagulants) in treating adults diagnosed with COVID-19 by preventing or reducing the formation of blood clots. These trials, which are being conducted with inpatients and outpatients and will be conducted with patients discharged from the hospital are also part of the Accelerating COVID-19 Therapeutic Interventions and Vaccines initiative.

Operation Warp Speed's Efforts to Scale Up Production May Face Challenges

There is the potential for challenges to arise in the scaled up production of COVID-19 vaccines and therapeutics through Operation Warp Speed. Such challenges include:

- **Limited manufacturing capacity.** Before the COVID-19 pandemic, most existing vaccine manufacturing capacity was already in use, according to experts we interviewed. Therefore, new capacity has had to be created, or production shifted from other products. Additionally, once bulk quantities of vaccines or therapeutics are produced, they must be sealed into sterile containers, such as vials or syringes, in a process known as fill-finish manufacturing. Experts from three pharmaceutical industry groups we interviewed said there is a shortage of facilities with capacity to handle fill-finish manufacturing, which could lead to production bottlenecks.
- **Disruptions to manufacturing supply chains.** Vaccine manufacturing supply chains may be strained by disruptions caused by the global pandemic, including changes in the labor market, increases or decreases in the demand for certain goods, or as one DOD official noted, export restrictions implemented by some countries. For example, officials at one COVID-19 vaccine manufacturing facility told us that they have experienced challenges obtaining materials, including disposable reactor bags, reagents, and certain chemicals. They also said that due to global demand, they sometimes must wait 4-12 weeks for items that before the pandemic were typically available for shipment within one week. One expert we interviewed also told us that the supply of the materials used in fill-finish manufacturing, such as glass vials and pre-filled syringes, is limited.
- **Difficult technology transfer processes.** According to literature we reviewed, scaling up manufacturing requires transferring knowledge of how to produce COVID-19 vaccines and therapeutics across multiple manufacturing sites, often involving the use of subcontractors. This knowledge transfer is a complex process, and one expert we interviewed told us that it is especially difficult for new technologies such as RNA vaccines, where there is little experience in scaling up production—going from making a small amount of vaccine in a laboratory setting to commercial scale production of hundreds of millions of vaccine doses. Additionally, there has been at least one instance in which the technology transfer process for a COVID-19

vaccine has been hampered by disagreements over ownership of intellectual property rights related to manufacturing technology.

- **Gaps in available workforce.** The ability to hire and train personnel with the specialized skills needed to run vaccine manufacturing processes may be a challenge for even experienced manufacturers. For example, we heard from representatives at a COVID-19 vaccine manufacturing facility that filling open positions for mid- to upper management positions had been a challenge. These positions are significant because manufacturing managers function as the technical points of contact for production questions and are responsible for managing safety, quality, and compliance with current good manufacturing practices.

Through Operation Warp Speed, federal agencies and vaccine manufacturers said they are working together to mitigate these challenges. For example:

- Operation Warp Speed has announced HHS and DOD awards to enhance domestic manufacturing capacity, including fill-finish manufacturing.
- Representatives from a COVID-19 vaccine manufacturing facility told us that they are in frequent communication with officials from Operation Warp Speed to coordinate and that DOD is assisting them with expediting procurement and delivery of critical manufacturing equipment.
- Officials from BARDA said that agency subject matter experts worked with each of the six Operation Warp Speed vaccine developers to create a list of critical supply needs that are common across the vaccine candidates. BARDA has been working with suppliers to increase production capacity for the materials identified as critical needs, according to officials.

We will continue to examine the federal government's efforts to develop and manufacture COVID-19 vaccines and therapeutics, including Operation Warp Speed's activities and any further actions it may take to mitigate potential challenges.

FDA Clarified Expected Evidence for COVID-19 Vaccine EUAs, but the Evidence to Support Its

COVID-19 Therapeutic EUA Decisions Is Not Always Transparent

EUAs are an important tool for quickly making vaccines and therapeutics available in time of emergency, when speed and flexibility are needed. For COVID-19 vaccines, FDA issued guidance in October 2020 to provide vaccine sponsors with recommendations regarding the evidence—that is, data and information—needed to support issuance of an EUA. For therapeutics, FDA has issued four EUAs as of November 9, 2020. However, the evidence to support FDA’s COVID-19 therapeutic EUA decisions has not always been transparent, because the agency has not uniformly disclosed information from its scientific review of the safety and effectiveness data at the time of each authorization. Further, EUAs can be beneficial in bringing vaccines and therapeutics quickly to market during an emergency, but there can be some unintended consequences to consider.

New Guidance for COVID-19 Vaccine EUAs Recommends Minimum Data and Information for Vaccine Sponsors to Submit with EUA Requests

In October 2020, FDA issued additional EUA guidance specific to COVID-19 vaccines that recommends minimum evidence for vaccine sponsors to submit with EUA requests for vaccines to FDA.³⁴ FDA has indicated through guidance that vaccine sponsors will likely submit requests for EUAs, once clinical data are ready, as a means to get any vaccine to market more quickly. Specifically, FDA’s October guidance includes recommendations regarding the manufacturing, safety, and effectiveness data and information needed to support the issuance of an EUA for a COVID-19 vaccine.

According to an FDA official, the risk-benefit analysis that it must conduct before issuing an EUA should be based on certain, minimum evidence, in part because any COVID-19 vaccine will be administered to healthy individuals, raising the standard for what it considers allowable risk. The October 2020 guidance states that FDA does not expect to be able to

³⁴FDA, *Emergency Use Authorization for Vaccines to Prevent COVID-19: Guidance for Industry*, October 2020.

issue an EUA without certain data from phase 3 clinical trials.³⁵ It also reiterates that any vaccine candidate should follow the recommendations set forth in COVID-19 vaccine guidance that the agency published in June 2020, including that any vaccine should reduce the risk of infection or of serious illness by at least 50 percent over a placebo group.³⁶

The October 2020 EUA guidance also states that, prior to authorization, FDA expects developers to have a median follow-up duration of at least 2 months after completion of the full vaccine regimen, to help provide adequate information to assess the vaccine candidate's risk-benefit profile. This is in contrast to the 6 months of safety data usually submitted for FDA licensure of a vaccine, according to an FDA official. An FDA official said the agency is working with CDC and vaccine sponsors to create plans to collect safety information from any individuals who receive a vaccine under an EUA so that they can continue to monitor these data. The October EUA guidance also states that any EUA request for COVID-19 vaccine should include a plan for active follow-up for safety.

FDA's Support for Its COVID-19 Therapeutic EUA Decisions Is Not Always Transparent

FDA has issued four EUAs for COVID-19 therapeutics as of November 9, 2020, but the evidence to support these authorization decisions has not always been transparent. Since March 24, 2020, when the Secretary of Health and Human Services declared that circumstances existed

³⁵On November 9, 2020, Pfizer announced that its first interim efficacy analysis from phase 3 clinical trials of its COVID-19 vaccine candidate had found that the vaccine was more than 90 percent effective in preventing COVID-19 in participants who did not have evidence of a prior infection. Pfizer announced that it plans to submit an EUA request for this vaccine candidate in late November 2020.

³⁶FDA, *Development and Licensure of Vaccines to Prevent COVID-19: Guidance for Industry*, June 2020. The June 2020 guidance applies to any vaccine candidate submitted to FDA, whether for an EUA or licensure, according to officials.

justifying emergency use of drugs and biologics during the COVID-19 pandemic, FDA has issued four EUAs for therapeutics:³⁷

- one for a new use for two existing drugs—chloroquine and hydroxychloroquine—on March 28, 2020,³⁸
- one for a new drug—remdesivir—on May 1, 2020,
- one for a new biologic—COVID-19 convalescent plasma—on August 23, 2020,³⁹ and
- one for another new biologic—bamlanivimab, a monoclonal antibody—on November 9, 2020.

After reviewing additional scientific evidence, about 2.5 months after its authorization (on June 15, 2020), FDA revoked the EUA for chloroquine and hydroxychloroquine. FDA’s revocation letter states that based on continued review of scientific evidence including a randomized controlled trial and adverse event reporting (including adverse cardiac events), it determined the drugs were unlikely to be effective in treating COVID-19 and that the known and potential benefits no longer outweighed the known and potential risks for the authorized use.

Additionally, FDA revised the EUA for remdesivir to broaden the scope of its authorized uses about 4 months after initial authorization (on August 28, 2020).⁴⁰ Then, on October 22, 2020, FDA approved remdesivir, through the new drug approval process, to treat COVID-19 in adult and pediatric patients (12 years of age and older weighing at least 40 kg)

³⁷See 85 Fed. Reg. 18,250 (Apr. 1, 2020). FDA also issued three EUAs for drugs and blood products that we do not consider therapeutics for the purpose of this report because they support other existing treatments—one drug for maintaining sedation and two fluids for continuous renal replacement therapy. These other products are 1) REGIOCIT replacement solution, 2) Fresenius Kabi Propoven 2%, and 3) Fresenius Medical, multiFiltrate PRO System and multiBic/multiPlus Solutions. Our review focused on the four EUAs FDA issued for drugs or biologics to treat COVID-19—hydroxychloroquine and chloroquine, remdesivir, COVID-19 convalescent plasma, and bamlanivimab.

³⁸The EUA was for oral formulations of chloroquine phosphate and hydroxychloroquine sulfate to treat adults and certain adolescents who are hospitalized with COVID-19 when participation in a clinical trial is not available or feasible. We refer to these products as chloroquine and hydroxychloroquine in this report. These products are approved for other uses, such as to treat lupus.

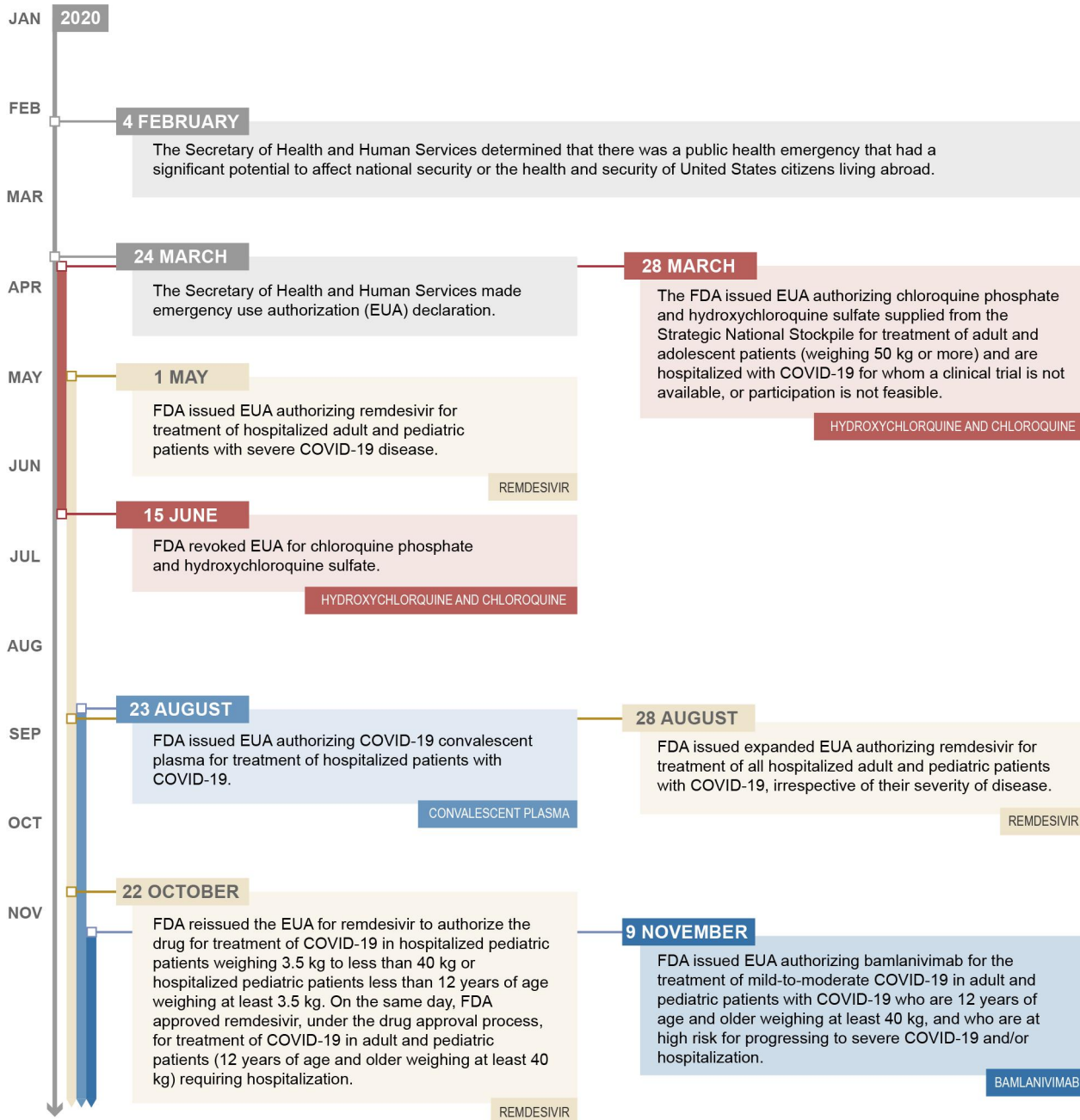
³⁹Plasma is the liquid portion of blood that contains antibodies.

⁴⁰FDA first authorized the use of remdesivir on May 1, 2020, to treat hospitalized adult and pediatric patients with severe COVID-19 disease, defined as patients with low blood oxygen levels or needing oxygen therapy or more intensive breathing support such as a mechanical ventilator.

requiring hospitalization. On the same day, the agency revised the EUA for remdesivir for use to treat COVID-19 in hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg.

As of November 9, 2020, three therapeutics—remdesivir, COVID-19 convalescent plasma, and bamlanivimab—remain authorized for emergency use for COVID-19, of the four FDA has authorized to date. See figure 4 for a timeline of EUAs for COVID-19 therapeutics.

Figure 4: Timeline of Emergency Use Authorizations for COVID-19 Therapeutics, as of November 9, 2020



Source: GAO analysis of Food and Drug Administration (FDA) information. | GAO-21-207

Although FDA’s COVID-19 therapeutic EUA decisions are articulated through authorization letters and other publicly available supporting

documents, the evidence to support FDA's authorization decisions has not always been transparent. This is because FDA has not uniformly disclosed to the public information from its scientific review of each therapeutic's safety and effectiveness data, at the time of its authorization. For example:

- For all four EUAs it has authorized so far, FDA released fact sheets for health care providers, but they contained different levels of information. For example, the fact sheets for chloroquine and hydroxychloroquine and COVID-19 convalescent plasma were silent on the evidence supporting the EUA, whereas the fact sheets for remdesivir and bamlanivimab included a section entitled, "Clinical Trial Results and Supporting Data for EUA," with detailed information on the studies, including subjects enrolled, dosing used, and end point results.
- FDA released a clinical decision memo in August 2020 along with the COVID-19 convalescent plasma authorization letter, summarizing the literature it reviewed to inform its decision that the product may be effective to treat hospitalized patients with COVID-19. Specifically, the convalescent plasma decision memo contained a detailed summary of the preclinical and clinical studies reviewed in support of the EUA, including subjects enrolled and other information, as well as FDA's summary of the evidence of effectiveness and risk-benefit analysis. In contrast, FDA did not release decision memos with the chloroquine and hydroxychloroquine, remdesivir, or bamlanivimab authorization letters.⁴¹
- It was not until the chloroquine and hydroxychloroquine EUA revocation letter was publicly released on June 15, 2020, that further details on the evidence used to support the March 28, 2020, EUA were published; these details were in a memo attached to the revocation letter.

Moreover, there has been considerable variation in the type and amount of data and information FDA cited in its authorization letters and available

⁴¹FDA released a number of additional documents for chloroquine and hydroxychloroquine and remdesivir under the Freedom of Information Act, which requires federal agencies to provide the public access to certain government records and information. See 5 U.S.C. § 552. About 3 months after its initial authorization of remdesivir and 3 months after authorization of chloroquine and hydroxychloroquine, the agency disclosed review summaries containing information about its review of the products, including detailed information about the preclinical and clinical data reviewed to support efficacy and safety.





supporting documentation, compounding the lack of transparency surrounding the evidence supporting FDA's EUA decisions. For example, stakeholders, including three of nine provider associations, a public health association, and an infectious disease expert we interviewed about EUAs, as well as several former FDA officials, have expressed concern regarding the threshold of evidence FDA cited for authorization of some COVID-19 therapeutics.⁴² FDA officials noted that the statute requires FDA to consider the totality of information available in its EUA reviews, and the evidence for each product can vary. The following are examples of variation in evidence:

- The evidence cited to support the EUAs for both remdesivir and bamlanivimab included randomized, placebo-controlled clinical trials—considered the gold standard for determining effectiveness—while the evidence cited to support the EUA for chloroquine and hydroxychloroquine included no clinical trial data.
- FDA initially authorized remdesivir to treat a limited hospitalized group though it cited more data and information about the drug's safety and effectiveness in treating COVID-19 than for other therapeutic EUAs. By comparison, it authorized chloroquine and hydroxychloroquine to treat any hospitalized patient with confirmed COVID-19 when participation in a clinical trial was not available or feasible and it authorized COVID-19 convalescent plasma for treating any hospitalized patient.

It is understandable that FDA might expect different types of data and information to support issuance of EUAs for different products. For example, FDA could expect different data for an EUA for a drug that has not previously been approved for any use than it could for a drug that is already on the market, but has been approved for other uses. However, absent communication about FDA's review of evidence, the basis upon which it has issued EUAs is not transparent. See figure 5 for the evidence cited by FDA as the basis for its EUA decisions.

⁴²See Congressional Research Service, *The U.S. Blood Supply and the COVID-19 Response: In Brief* (August 2020) and Congressional Research Service, *Treatment of COVID-19: Hydroxychloroquine and Chloroquine* (May 2020).

Figure 5: Data Cited to Support Issuance of Emergency Use Authorizations (EUA) for Therapeutics for COVID-19, as of November 9, 2020

PRODUCT	Prior FDA approval ^a	Research studies ^b			
		Preclinical data	Clinical data		
			Data were not from a randomized controlled clinical study	Randomized controlled clinical trial data	Randomized placebo-controlled clinical trial data
 chloroquine phosphate and hydroxychloroquine sulfate ^c	YES	Limited studies ^e	Limited studies	No studies completed	No studies completed
 remdesivir ^d	NO	Completed studies	No studies completed	Completed studies	Completed studies
 COVID-19 convalescent plasma	NO	Completed studies	Completed studies	Limited studies ^f	No studies completed
 bamlanivimab	NO	Completed studies	No studies completed	No studies completed	Limited studies ^g

Source: GAO analysis of Food and Drug Administration (FDA) information. | GAO-21-207

Notes:

We reviewed supporting documentation made publicly available by FDA, including authorization letters, revocation letters, fact sheets for providers, and decision memos.

^aPrior to receiving an EUA for COVID-19 treatment, the product was approved for uses unrelated to COVID-19.

^bThe National Institutes of Health considers the “gold standard” for testing interventions in humans to be randomized, placebo-controlled clinical trials—meaning volunteers are randomly assigned either to a test group receiving the experimental intervention or to a control group receiving a placebo or standard care. Human testing can also involve clinical trials that do not adhere to all of these practices; for example, not using a placebo. Preclinical studies are conducted to test products in animals and in the laboratory.

^cFDA subsequently revoked the EUA for chloroquine and hydroxychloroquine. Based on continued review of scientific evidence including a randomized controlled trial and adverse event reporting (including adverse cardiac events), FDA determined that chloroquine phosphate and hydroxychloroquine sulfate were unlikely to be effective in treating COVID-19 and that the known and potential benefits no longer outweighed the known and potential risks for the authorized use. Clinical trial data were referenced in the revocation letter, but not the initial EUA authorization letter, which stated that the clinical data were anecdotal.

^dFDA first authorized the use of remdesivir on May 1, 2020, to treat hospitalized adult and pediatric patients with severe COVID-19, defined as patients with low blood oxygen levels or needing oxygen therapy or more intensive breathing support such as a mechanical ventilator. The data reported in the table reference data cited in FDA’s initial May 1 authorization letter, including a randomized, placebo-controlled clinical trial. On August 28, 2020, FDA revised the EUA for remdesivir to broaden the scope of its authorized uses to treat all hospitalized COVID-19 patients based on review of an additional randomly controlled trial without placebo. On October 22, 2020, FDA approved remdesivir, through the new drug approval process, to treat COVID-19 in adult and pediatric patients (12 years of

age and older weighing at least 40 kg) requiring hospitalization. On the same day, the agency revised the EUA for remdesivir for use to treat COVID-19 in hospitalized pediatric patients less than 12 years of age and weighing at least 3.5 kg.

^eWe refer to “limited studies” to include instances of FDA characterizing the studies as limited, studies in which the data were anecdotal only, or studies that were still ongoing at the time of authorization.

^fAccording to the FDA authorization letter for COVID-19 convalescent plasma, the EUA was issued based on review of historical evidence using convalescent plasma in prior outbreaks of respiratory viruses, certain preclinical evidence, results from small clinical trials of convalescent plasma conducted during the current outbreak, and data obtained from the ongoing National Convalescent Plasma Expanded Access Protocol, but without the presence of data from prospective, well-controlled randomized clinical trials.

^gAccording to the authorization letter, the EUA was issued based on review of the topline data from the planned interim analysis of an ongoing randomized, double-blinded, placebo-controlled, phase 2 dose finding trial of bamlanivimab in outpatients with mild to moderate COVID-19. The provider fact sheet provided additional detail on the findings from this study. There are additional clinical trials for bamlanivimab, at least one of which was for a different indication to treat hospitalized patients, but these studies were not explicitly cited by FDA as support for the EUA.

Because the type and amount of data needed to support authorization of a therapeutic can vary, it is especially important for FDA to uniformly disclose the evidence supporting its EUA decisions. Doing so would enhance transparency and be consistent with federal internal control standards for information and communication. These standards specify that agencies should obtain quality data from reliable sources and communicate quality information to external stakeholders, including the public, to achieve objectives, such as maintaining the public’s trust in agency decision-making.⁴³ Further, it would be consistent with our past work, as well as with the PanCAP—the general operative plan for the federal response to COVID-19—which both highlight the importance of clear communication during a crisis.⁴⁴ In addition, the FDA Commissioner has cited the paramount importance of ensuring public trust in FDA during this crisis.

FDA officials we spoke with agreed that improved transparency is important. These officials stated that the agency has tried to improve

⁴³According to federal internal control standards for information and communication, management should use quality information to achieve the entity’s objectives and externally communicate the necessary quality information to achieve the entity’s objectives. [GAO-14-704G](#).

⁴⁴See, for example, our June 2020 report on the federal government’s response to the pandemic, which states that in the midst of a nationwide emergency, clear and consistent communication—among all levels of government, with health care providers, and to the public—is key. GAO, *COVID-19: Opportunities to Improve Federal Response and Recovery Efforts*, [GAO-20-625](#) (Washington, D.C.: June 25, 2020). The PanCAP also stresses the importance of clear, concise, accurate, and accessible critical public health messages. See Department of Health and Human Services, *U.S. Government COVID-19 Response Plan* (Mar. 13, 2020).

transparency about their EUA decisions by publicly issuing a decision memo with each authorization, as they did with the COVID-19 convalescent plasma authorization. However, FDA officials told us that the agency may not be able to uniformly disclose the same information from its scientific review of the safety and effectiveness data for each COVID-19 therapeutic EUA because of federal laws protecting certain information from public disclosure without the sponsor's consent—such as confidential commercial information and trade secrets.⁴⁵ Officials noted that for new drugs and biologics, the agency publishes drug approval packages. These packages include summary review memos that contain detailed information about the preclinical and clinical data reviewed to support effectiveness and safety for each product, including clinical statistical efficacy trials as well as conclusions about those trials.⁴⁶ Officials indicated that consistently publishing this information for EUA decisions would be beneficial.

We understand FDA's reported constraints. However, in light of the gravity of the pandemic and the need for a high degree of public confidence in FDA's decisions, the agency should identify ways to uniformly disclose the information from its scientific review of safety and effectiveness data when issuing EUAs for therapeutics and vaccines, and, if necessary, seek the authority to publicly disclose such information. This could be achieved, for example, by seeking authority to more uniformly disclose information from its clinical review memorandum supporting the issuance of an EUA for a therapeutic or vaccine product, similar to the summary of safety and effectiveness data that FDA discloses from approval packages for new drugs and biologics. Improving the transparency of its therapeutic decisions could, in turn, bolster public trust in those decisions.

⁴⁵See 21 U.S.C. § 360bbb-3(h)(2) (referring to 18 U.S.C. § 1905 and 5 U.S.C. § 552(b)(4)).

⁴⁶FDA is required to publish the approval package for new drugs and biologics on FDA's website. Among other things, each package is to include a summary review that documents conclusions from all reviewing disciplines about the approved product, noting any critical issues and disagreements with the applicant and within the review team and how they were resolved, recommendations for action, and an explanation of any nonconcurrency with review conclusions. 21 U.S.C. § 355(l). FDA officials noted that the documents in these packages may also be redacted for certain information such as trade secrets.

EUAs Can Result in Unintended Consequences

While EUAs can be beneficial in bringing medical products quickly to market during an emergency, there can be some unintended consequences, according to FDA officials and stakeholder groups we interviewed.

Potential decrease in clinical trial participation. A therapeutic or vaccine made widely available to the public under an EUA can affect the ability of product sponsors to enroll participants in clinical trials and may even incentivize clinical trial participants to withdraw from the trial, according to an FDA official and two stakeholder groups we interviewed. Three stakeholder groups told us the public seems to interpret an EUA for a COVID-19 therapeutic to be the “standard of care” recommended for treatment, even though that is not the intent of an EUA. Such interpretations may decrease public willingness to enroll in clinical trials for other therapeutics that may have more efficacy potential, according to one of the stakeholder groups. For example, the EUA for COVID-19 convalescent plasma has generated concern about the ability to stand up clinical trials for potentially more promising, specific therapies, such as monoclonal antibodies, according to one of the stakeholder groups.

FDA officials have stated that this unintended consequence is especially important to consider for vaccines, since the first authorized or licensed vaccine may not be as effective as candidates still in development, for example. FDA’s October 2020 EUA guidance specifies that FDA expects a vaccine sponsor to continue to collect placebo-controlled data to work toward submission of a biologics license application. Specifically, the guidance states that an EUA request for COVID-19 vaccine should include strategies that will be implemented to ensure that ongoing clinical trials of the vaccine are able to assess long-term safety and efficacy in sufficient numbers of subjects to support vaccine licensure through a biologics license application. Further, the Director of the Office of Vaccines Research and Review at FDA’s Center for Biologics Evaluation and Research stated that FDA is actively holding internal discussions about ways to address this trial participation challenge. According to this official, when an EUA is first issued, the vaccine may not be widely deployable so phase 3 clinical trials may be able to continue with participants receiving vaccine or a placebo.

Vaccine hesitancy. FDA officials and stakeholder groups have noted that, if there is public concern that an EUA will be issued for a vaccine

with less certainty of effectiveness than is required to license a vaccine, it may result in the public being hesitant about getting the vaccine, affecting vaccine uptake. FDA's October 2020 EUA guidance is one effort to combat this risk and help the public feel confident about an EUA decision. Further, FDA officials have stated, and the agency's October EUA guidance reiterates, that any vaccine under consideration for an EUA will go to a public meeting of its Vaccines and Related Biological Products Advisory Committee. The public will be able to view the briefing package, the committee discussion and deliberations, and FDA's recommendation, according to FDA officials.⁴⁷

Drug shortages. An EUA for additional uses of existing therapeutics can increase demand for a drug, which can in turn create shortages of that drug. Such shortages occurred when hydroxychloroquine and chloroquine were authorized for emergency use for COVID-19. Several versions of hydroxychloroquine and chloroquine are approved by FDA for other uses, such as prophylaxis and treatment of malaria. After the EUA for chloroquine and hydroxychloroquine was issued in March 2020, FDA reported shortages of these drugs, limiting their availability for individuals who use the drugs for these approved conditions.

Stakeholders Indicate Initial Planning Documents Are Helpful, but Seek Additional Information on Federal Plans for Vaccine Distribution

In September 2020, we recommended that the Secretary of Health and Human Services with support from the Secretary of Defense, establish a time frame for documenting and sharing a national plan for distributing and administering COVID-19 vaccine; ensure that such a plan is consistent with best practices for project planning and scheduling; and that it outlines an approach for how efforts would be coordinated across federal agencies and nonfederal entities. As discussed below, HHS and DOD have released initial planning documents for the distribution and administration of potential COVID-19 vaccines. Stakeholders we interviewed said these documents were helpful, but would like to see

⁴⁷According to FDA officials, the Vaccines and Related Biological Products Advisory Committee will make a recommendation to FDA and FDA will consider that recommendation in deciding whether to issue an EUA.

additional information as planning for vaccine distribution continues. We will continue to examine the federal government's vaccine distribution planning efforts in future work.

Federal Government Released Interim Planning Documents for the Distribution of Potential COVID-19 Vaccines and Plans to Identify Priority Groups for Initial Allocation

HHS with support from DOD has begun to develop plans for how any authorized or licensed COVID-19 vaccine will be distributed, including which groups may have priority and how it might be allocated and administered. On September 16, 2020, HHS and DOD released two documents—CDC's *COVID-19 Vaccination Program Interim Playbook for Jurisdiction Operations* and HHS's and DOD's *From the Factory to the Frontlines: The Operation Warp Speed Strategy for Distributing a COVID-19 Vaccine*—outlining a strategy for the distribution and administration of any COVID-19 vaccine.⁴⁸ HHS and DOD subsequently released an updated version of CDC's *COVID-19 Vaccination Program Interim Playbook for Jurisdiction Operations* on October 29, 2020.⁴⁹

CDC's *COVID-19 Vaccination Program Interim Playbook for Jurisdiction Operations* is intended to assist state, territorial, and local public health programs and their partners plan and operationalize local vaccination response to COVID-19.⁵⁰ The interim playbook notes that it is not yet known which vaccines may be available, in what volumes, at what time, with what efficacy, and with what storage and handling requirements, all of which could impact the distribution and administration of a vaccine.

⁴⁸Department of Health and Human Services, Centers for Disease Control and Prevention, *COVID-19 Vaccination Program Interim Playbook for Jurisdiction Operations* (Washington, D.C.: Sept. 16, 2020) and Department of Defense and Department of Health and Human Services, *From the Factory to the Frontlines: The Operation Warp Speed Strategy for Distributing a COVID-19 Vaccine* (Washington, D.C.: Sept. 16, 2020).

⁴⁹Department of Health and Human Services, Centers for Disease Control and Prevention, *COVID-19 Vaccination Program Interim Playbook for Jurisdiction Operations, version 2.0* (Washington, D.C.: Oct. 29, 2020).

⁵⁰According to the interim playbook, jurisdictions may include state, local, territorial, and tribal governments. The interim playbook notes that CDC is working directly with the Indian Health Service at the federal level.

CDC stated that it intends to update its interim playbook over time as more information about any COVID-19 vaccines becomes available.⁵¹

The September release of the interim playbook set a deadline of October 16, 2020, for 64 jurisdictions to submit interim COVID-19 vaccination plans that address requirements outlined in the playbook.⁵² All 64 jurisdictions submitted their interim COVID-19 vaccination plans to CDC, according to the updated interim playbook released in late October. CDC provided feedback to the jurisdictions on their plans in late October, and posted executive summaries of each jurisdiction's interim plan on the CDC website.⁵³

CDC's Advisory Committee on Immunization Practices established a COVID-19 vaccine work group to consider options for priority groups for vaccination.⁵⁴ This work group intends to collect, analyze, and prepare information related to COVID-19 vaccines for presentation, discussion, deliberation, and vote by the advisory committee.⁵⁵ According to CDC, the

⁵¹The October 29, 2020, updated interim playbook provides new details on distribution, storage, and handling of any COVID-19 vaccine, such as which federal entities CDC will coordinate with in allocating available vaccine and updated hypothetical vaccination scenarios for planning purposes. Such scenarios contain more details on potential vaccine storage and handling requirements.

⁵²The 64 jurisdictions include the 50 states, the District of Columbia, American Samoa, Guam, Republic of the Marshall Islands, Federated States of Micronesia, Commonwealth of the Northern Mariana Islands, Republic of Palau, Puerto Rico, the U.S. Virgin Islands, Chicago, Houston, New York City, Philadelphia, and San Antonio. These jurisdictions are CDC Immunization and Vaccines for Children Cooperative Agreement funding recipients.

⁵³See Department of Health and Human Services, Centers for Disease Control and Prevention, *COVID-19 Vaccination Program Operational Guidance: The COVID-19 Vaccination Program Interim Operational Guidance for Jurisdictions Playbook*, <https://www.cdc.gov/vaccines/covid-19/covid-19-vaccination-guidance.html> for the posted executive summaries, updated as of Nov. 5, 2020.

⁵⁴The Advisory Committee on Immunization Practices is comprised of medical and public health experts who make recommendations on the use of vaccines in the civilian population of the United States. Its recommendations serve as public health guidance for safe use of vaccines and other related products. Advisory Committee on Immunization Practices work groups are subgroups of the larger advisory committee that review relevant information and develop recommendations for presentation to the advisory committee.

⁵⁵According to CDC, the COVID-19 vaccine work group has 41 members, including advisory committee voting members, liaisons, ex-officios, and consultants with expertise in epidemiology, vaccine safety, vaccinology, immunology, general medicine, geriatrics, pediatrics, obstetrics and gynecology, immunocompromised hosts, vaccine administration and delivery, public health and surveillance, ethics, health equity, communications, and emergency preparedness.

advisory committee, including its COVID-19 vaccine work group, will review evidence on COVID-19 epidemiology and burden, vaccine safety, vaccine efficacy, evidence quality, and implementation issues to inform recommendations for COVID-19 vaccine policy, including priority groups for vaccination. The Advisory Committee on Immunization Practices met at the end of October 2020 and discussed an ethical framework for early COVID-19 vaccine allocation, among other things. The advisory committee has not made recommendations on priority groups for any COVID-19 vaccine, as of November 10, 2020.

Vaccine prioritization policies are formulated by recommendations from the advisory committee and approved by the CDC Director. The Director's recommendations are then shared with the Secretary of Health and Human Services, according to CDC officials. The officials said the recommendations will also be provided to the National Security Council for interagency staffing for executive decision-making, and Operation Warp Speed is to distribute available vaccine in accordance with these recommendations and decisions.

In addition, CDC and NIH sponsored an expert committee that the National Academies of Sciences, Engineering, and Medicine convened to make recommendations about the allocation of any COVID-19 vaccine. On October 2, 2020, the expert committee issued its final report, *Framework for Equitable Allocation of a COVID-19 Vaccine*.⁵⁶ In the report, the committee recommended that any vaccine for COVID-19 be allocated under a phased approach. The first phase would prioritize health care personnel and first responders, people at significantly higher risk for severe illness based on comorbid or underlying conditions, and older adults living in congregate settings. The committee noted that its report can inform the recommendations of CDC's Advisory Committee on Immunization Practices and also includes additional recommendations for HHS, such as to create and appropriately fund a COVID-19 vaccination risk communication and community engagement program to support state, tribal, local and territorial authorities in its engaging with community-based organizations and communicating about any COVID-19 vaccine.

⁵⁶See National Academies of Sciences, Engineering, and Medicine 2020. *Framework for Equitable Allocation of COVID-19 Vaccine*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/25917> (accessed Oct. 13, 2020).

State and Local Public Health Officials and Providers Seek Additional Information about Vaccine IT Systems, Allocation Plans, Handling and Storage, and Communication Efforts

Representatives of state and local public health officials and health care providers said that the federal government’s planning efforts to date have been helpful, and they have heard that additional information is forthcoming. They also noted several areas where additional information and assistance may be necessary. For example, in an October 2020 public letter to the administration, the National Governors Association noted that additional guidance and clarification is needed on the roles and expectations of states in distributing any COVID-19 vaccine. In another letter, the association had questions about funding for vaccine administration, the formula for allocation of vaccine, and what information would be shared publicly on each vaccine.⁵⁷ Associations representing state and territorial health officials, including immunization managers, stated the need for \$8.4 billion in additional resources to support COVID-

⁵⁷National Governors Association, “NGA Leadership Letter Requesting White House Meeting on Vaccine Distribution,” October 15, 2020, accessed on Oct. 19, 2020, <https://www.nga.org/advocacy-communications/letters-nga/executive-committee/nga-leadership-letter-requesting-white-house-meeting-on-vaccine-distribution/> and National Governor’s Association, “Working Together For Vaccine Distribution”, October 19, 2020, accessed Oct. 23, 2020 <https://www.nga.org/advocacy-communications/working-together-vaccine-distribution/>. HHS responded to the questions from the October 19, 2020 letter from the National Governors Association, stating that CDC intends to award an additional \$140 million for COVID-19 vaccine readiness by December 15, 2020, but stated that states should recognize that most of the major costs of a vaccine campaign are already being covered by the federal government. HHS’s response also provided additional details on distribution plans, initial allocation of the COVID-19 vaccine, and public messaging, among other topics. Department of Health and Human Services, “Readout from the Trump Administration’s 40th Governors Briefing on COVID-19 Response and Vaccine Distribution Best Practices,” October 30, 2020, accessed on November 6, 2020. <https://www.hhs.gov/about/news/2020/10/30/readout-from-trump-administrations-40th-governors-briefing-covid-19-response-vaccine-distribution-best-practices.html>.

19 vaccine distribution activities, including workforce recruitment and training, and communication outreach.⁵⁸

Representatives of state and local public health officials and health care providers we interviewed identified the following examples of additional information they are seeking:

Specific information on IT systems and reporting requirements.

Additional information is needed on the IT systems providers will be required to use and how they will be required to track and report certain information. Providers will be required to record and report information within 24 hours of administration in their jurisdiction's current Immunization Information System or an alternative federal system if their current system does not meet CDC's data reporting requirements, according to the updated interim playbook.⁵⁹ The updated interim playbook also stated that additional information on these data requirements is forthcoming. Representatives from one provider group and one group representing state officials we spoke with stated that some providers are not adequately prepared for any new IT systems.

Providers enrolled in the federal COVID-19 Vaccination Program will order and monitor vaccines and ancillary supplies at no cost through new and existing IT systems, according to the interim playbook.⁶⁰ Specifically, CDC recommended jurisdictions use its existing Vaccine Tracking System (VTrckS) for this purpose, but indicated that it may also develop a

⁵⁸Association of State and Territorial Health Officials and Association of Immunization Managers, "ASTHO and AIM Letter to Congressional Leadership Requesting Funds for COVID-19 Vaccination Distribution and Seasonal Influenza," October 15, 2020, accessed on Oct. 20, 2020, <https://www.astho.org/Federal-Government-Relations/Correspondence/ASTHO-AIM-Funds-for-Vaccination-Distribution-Letter/>

⁵⁹Immunization Information Systems, sometimes known as "vaccine registries," are confidential, population-based, computerized databases that record all immunization doses administered by participating providers to persons residing within a given jurisdiction. According to the interim playbook, required data elements may include the type of vaccine administered, administration date, and administration location.

⁶⁰According to the interim playbook, the COVID-19 Vaccination Program encompasses all plans for the allocation and deployment of COVID-19 vaccines to state, local, territorial, and tribal governments, as well as any communication plans. Providers must enroll in the COVID-19 Vaccination Program to administer the vaccine to patients, which will be coordinated by their local governments.

new IT system to supplement VTrckS.⁶¹ The updated interim playbook also specifies that providers will be required to update their vaccine inventory daily in VaccineFinder, which the public can check online to find COVID-19 vaccination clinics.⁶² Several provider groups supported the use of existing IT infrastructure rather than the implementation of a new system to reduce any potential reporting or ordering problems that may come with learning and using a new system.

Method for allocating available vaccine to jurisdictions. As noted above, CDC is working to identify groups to have priority for receiving initial COVID-19 vaccine doses, but HHS has not specified how it will allocate available vaccines to individual jurisdictions, which will be important to ensure that all individuals in identified priority groups are reached. In the interim playbook, CDC states that early in the vaccination program, there is likely to be a limited supply of any available vaccine, and it provides hypothetical scenarios for state and local jurisdictions to use to develop operational plans for early COVID-19 vaccination while supplies are limited. Also, knowing how allocation decisions will be made will allow public health officials to plan for vaccine distribution and administration, as well as prepare public messaging for patients, according to representatives from two stakeholder groups we interviewed.

Guidance on handling and storing any ultra-cold or large lots of vaccine. Some COVID-19 vaccines under development may require storage at ultra-cold temperatures.⁶³ CDC has indicated that it will use a current centralized distribution contract with a private distributor to fulfill orders for most COVID-19 vaccine products. However, any vaccines that require ultra-cold temperatures will be shipped directly from the vaccine manufacturer instead of the distributor, according to the interim playbook.

Additionally, ultra-cold vaccines could have specific handling requirements. For example, according to a presentation at an August 2020 CDC Advisory Committee on Immunization Practices meeting, the thermal shipping container for one Operation Warp Speed vaccine

⁶¹VTrckS is CDC's information management system that allows providers and public health departments to order and manage publicly funded vaccines.

⁶²VaccineFinder is a public website at which patients can search for locations and/or providers that have vaccinations by location. See <https://vaccinefinder.org/>.

⁶³According to CDC's interim playbook, storage and handling requirements for each COVID-19 vaccine product will vary from refrigerated (2°C to 8°C) to frozen (-15°C to -25°C) to ultra-cold (-60°C to -80°C) temperatures. According to CDC, vaccines must be stored properly from the time they are manufactured until they are administered otherwise they may be less effective or unusable.

candidate should not be opened more than twice a day and should be closed within one minute or less after opening.⁶⁴ Two provider groups said that many providers and their offices do not have freezers that can store an ultra-cold vaccine, and another indicated in a letter that they may need additional funds from the federal government to procure supplies, such as the necessary equipment to store any ultra-cold vaccine, to safely and efficiently administer COVID-19 vaccines.

The updated interim playbook also notes that any ultra-cold vaccine would likely be shipped in 975 dose increments, which is larger than the 100 dose orders used for other COVID-19 vaccines. Our prior work on distribution of the H1N1 vaccine found that receiving vaccine lots in 100 dose minimum amounts was a challenge for states because those 100-dose lots had to be broken down further before being sent to providers, leading to delays in some providers receiving the vaccines.⁶⁵ Two stakeholders expressed concern that vaccine doses could be wasted if vaccine that requires ultra-cold storage is mishandled or if the large number of doses in one shipment are thawed, but are not administered within the time frame that they would be usable.

In an October 2020 letter, the National Governor's Association stated that if ultra-cold storage vaccines come in shipments with a large number of doses as indicated by the federal government, states will likely need to distribute them further in rural areas, and asked for guidance on redistribution of ultra-cold storage vaccines without compromising the vaccine. In response, HHS indicated that it plans to issue further guidance on ultra-cold vaccines as plans are developed and that there is ongoing work to develop smaller package sizes for ultra-cold vaccine shipments.

Additional information on public messaging. Representatives from three groups representing providers and state and local public health officials told us that public messaging and clear communications are key to effective deployment of COVID-19 vaccines, and one said that they would like to see a federal communication plan or strategy. CDC has noted the importance of clear and effective communication to promote public uptake of any COVID-19 vaccine, and that messaging should be tailored for each audience to ensure communication is effective. CDC

⁶⁴Brian Gleeson, "BNT162b2: Storage, handling and administration" (presentation shown at the August 2020 CDC Advisory Committee on Immunization Practices meeting, Atlanta, Ga., August 2020).

⁶⁵GAO, *Influenza Pandemic: Lessons from the H1N1 Pandemic Should Be Incorporated into Future Planning*, [GAO-11-632](#) (Washington, D.C.: June 27, 2011).

shared its COVID-19 vaccination communication objectives, such as ensuring public confidence in the safety and efficacy of COVID-19 vaccines, in the interim playbook.⁶⁶ Agency officials said they plan to develop additional communication resources for jurisdictions and tribal organizations to use so that entities can tailor messages for special populations in their communities. The interim playbook indicated this information will be available on a website that is under development, but did not provide a planned date for its completion and availability.

Conclusions

The Operation Warp Speed partnership has enabled the federal government—in concert with private industry—to move at an unusually fast pace to address the complex challenge of developing COVID-19 vaccine and therapeutic candidates, while at the same time ramping up manufacturing so that once such vaccines and therapeutics are authorized, licensed, or approved, they can be mass-produced. We are continuing to conduct work examining Operation Warp Speed’s efforts to support COVID-19 vaccine and therapeutic development and manufacturing, including steps it has taken to address challenges in achieving its goal of quickly developing safe and effective vaccines and therapeutics.

FDA has issued EUAs for four therapeutics, but the evidence to support its authorization decisions was not always transparent. As more potential COVID-19 therapeutics are developed through Operation Warp Speed and through other efforts, FDA has an opportunity to improve transparency. It can do this by identifying ways to uniformly disclose information from its scientific review of safety and effectiveness data—similar to the agency’s public disclosure of such data supporting the approval of new drugs and biologics—when it issues an EUA for a therapeutic or vaccine. FDA officials agreed that more transparency in these decisions is needed, but noted that federal law may restrict the type of information the agency can disclose for EUAs absent the sponsor’s consent. If needed, FDA could seek authority to make such information

⁶⁶COVID-19 vaccine communication objectives included in the interim playbook include educating the public about the development, authorization, distribution, and execution of COVID-19 vaccines, ensuring public confidence in the safety and efficacy of COVID-19 vaccines, helping the public to understand key differences between EUAs and vaccine licensure, and tracking and monitoring public receptiveness to COVID-19 vaccination messaging, among other objectives.

available. Doing so could help increase the public's confidence in FDA's EUA decisions.

Recommendation for Executive Action

We are making the following recommendation to FDA:

The Secretary of Health and Human Services should direct the FDA Commissioner to identify ways to uniformly disclose to the public the information from FDA's scientific review of safety and effectiveness data—similar to the public disclosure of the summary safety and effectiveness data supporting the approval of new drugs and biologics—when issuing EUAs for therapeutics and vaccines, and, if necessary, seek the authority to publicly disclose such information. (Recommendation 1)

Agency Comments and Our Evaluation

We provided a draft of this report to HHS and DOD for review and comment. HHS provided general comments, which are reproduced in appendix I. HHS neither agreed nor disagreed with our recommendation; however, in commenting on the draft, FDA stated that the agency shared GAO's goal of transparency, believed that disclosing information from its review of safety and effectiveness data would contribute to public confidence in the agency's reviews, and that it will explore approaches for greater transparency in this area, including considering whether additional authorities are needed. Both departments also provided technical comments, which we incorporated as appropriate.

We are sending copies of this report to the appropriate congressional committees, the Secretary of Health and Human Services, the Acting Secretary of Defense, and other interested parties. In addition, the report is available at no charge on the GAO website at <http://www.gao.gov>.

If you or your staff have any questions about this report, please contact Mary Denigan-Macauley at 202-512-7114 or deniganmacauleym@gao.gov or Alyssa M. Hundrup at (202) 512-7114 or hundrupa@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made major contributions to this report are listed in appendix II.

A handwritten signature in black ink that reads "Mary Denigan-Macauley". The signature is written in a cursive style with a long horizontal flourish at the end.

Mary Denigan-Macauley
Director, Health Care

A handwritten signature in black ink that reads "Alyssa M. Hundrup". The signature is written in a cursive style with a long horizontal flourish at the end.

Alyssa M. Hundrup
Acting Director, Health Care

List of Addressees

The Honorable Richard C. Shelby
Chairman

The Honorable Patrick J. Leahy
Vice Chairman
Committee on Appropriations
United States Senate

The Honorable Lamar Alexander
Chairman

The Honorable Patty Murray
Ranking Member
Committee on Health, Education, Labor, and Pensions
United States Senate

The Honorable Ron Johnson
Chairman

The Honorable Gary C. Peters
Ranking Member
Committee on Homeland Security and Governmental Affairs
United States Senate

The Honorable Nita M. Lowey
Chairwoman

The Honorable Kay Granger
Ranking Member
Committee on Appropriations
House of Representatives

The Honorable Frank Pallone, Jr.
Chairman

The Honorable Greg Walden
Republican Leader
Committee on Energy and Commerce
House of Representatives

The Honorable Bennie Thompson
Chairman

The Honorable Mike D. Rogers
Ranking Member
Committee on Homeland Security
House of Representatives

The Honorable Carolyn B. Maloney
Chairwoman

The Honorable James R. Comer
Ranking Member
Committee on Oversight and Reform
House of Representatives

The Honorable James E. Clyburn
Chairman
Select Subcommittee on the Coronavirus Crisis
Committee on Oversight and Reform
House of Representatives

The Honorable Bill Foster
House of Representatives
The Honorable Mark E. Green, MD
House of Representatives

Appendix I: Comments from the Department of Health and Human Services

**Appendix I: Comments from the Department of
Health and Human Services**



DEPARTMENT OF HEALTH & HUMAN SERVICES

OFFICE OF THE SECRETARY

Assistant Secretary for Legislation
Washington, DC 20201

November 4, 2020

A. Nicole Clowers
Managing Director, Health Care
U.S. Government Accountability Office
441 G Street NW
Washington, DC 20548

Dear Ms. Clowers:

Attached are comments on the U.S. Government Accountability Office's (GAO) report entitled, "*COVID-19: Federal Efforts Accelerate Vaccine and Therapeutic Development but More Clarity Needed on Emergency Use Authorizations*" (Job code 104575/ GAO-21-207).

The Department appreciates the opportunity to review this report prior to publication.

Sincerely,

A handwritten signature in black ink, appearing to read "S. Arbes".

Sarah C. Arbes
Assistant Secretary for Legislation

Attachment

**Appendix I: Comments from the Department of
Health and Human Services**

**GENERAL COMMENTS FROM THE DEPARTMENT OF HEALTH & HUMAN
SERVICES ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S DRAFT
REPORT ENTITLED — COVID-19: FEDERAL EFFORTS ACCELERATE VACCINE
AND THERAPEUTIC DEVELOPMENT BUT MORE CLARITY NEEDED ON
EMERGENCY USE AUTHORIZATIONS (GAO-21-207)**

GAO RECOMMENDATION

The Secretary of Health and Human Services should direct the FDA Commissioner to identify ways to consistently communicate the information from FDA's scientific review of safety and effectiveness data—similar to the summary review memo for new drugs—when issuing EUAs for therapeutics and vaccines, and if necessary, seek authority to publicly disclose such information.

FDA Response

FDA shares GAO's goal of being as transparent as possible with the public about the Agency's review of the safety and effectiveness data that supports the issuance of an EUA for a drug or biological product. FDA believes that disclosing such information from its clinical review memoranda supporting the issuance of EUAs for therapeutics and vaccines, similar to what FDA discloses from its approval packages for new drugs and biologics, will contribute to the public's confidence in the Agency's rigorous, independent review of the scientific data available and will help the Agency achieve its transparency goal. To that end, FDA will explore approaches for greater transparency in this area, including considering whether additional authorities are needed.

Appendix II: GAO Contacts and Staff Acknowledgments

GAO Contacts

Mary Denigan-Macauley, 202-512-7114 deniganmacauleym@gao.gov;
Alyssa M. Hundrup, (202) 512-7114, hundrupa@gao.gov

Staff Acknowledgments

In addition to the contacts named above Deirdre Brown (Assistant Director), Kelly DeMots (Assistant Director), Rebecca Abela (Analyst-in-Charge), Alison Goetsch (Analyst-in-Charge), Jennie Apter, Justin Cubilo, Kaitlin Farquharson, Sandra George, Haden Huang, and Ethiene Salgado-Rodriguez made key contributions to this report. Other staff contributing include, Nora Adkins, Darnita Akers, Mariel Alper, Mike Dickens, Maya Dru, Lorraine Ettaro, Cory Gerlach, Ryan Han, Nicolaus Heun, Laura Holliday, Katheryn Hubbell, Anna Irvine, Julia Kennon, Gay Hee Lee, Christopher Murray, Angie Nichols-Friedman, John Ortiz, Miranda Riemer, Meghan Shrewsbury, Amber Sinclair, and Sirin Yaemsiri.

Appendix III: Accessible Data

Agency Comment Letter

Accessible Text for Appendix I Comments from the
Department of Health and Human Services

Page 1

November 4, 2020

A. Nicole Clowers

Managing Director, Health Care

U.S. Government Accountability Office

441 G Street NW

Washington, DC 20548

Dear Ms. Clowers:

Attached are comments on the U.S. Government Accountability Office's (GAO) report entitled, " COVID-19: Federal Efforts Accelerate Vaccine and Therapeutic Development but More Clarity Needed on Emergency Use Authorizations" (Job code I04575/ GAO-21-207).

The Department appreciates the opportunity to review this report prior to publication.

Sincerely,

Sarah C. Arbes

Assistant Secretary for Legislation

Attachment

Page 2

GAO RECOMMENDATION

The Secretary of Health and Human Services should direct the FDA Commissioner to identify ways to consistently communicate the information from FDA’s scientific review of safety and effectiveness data—similar to the summary review memo for new drugs—when issuing EUAs for therapeutics and vaccines, and if necessary, seek authority to publicly disclose such information.

FDA Response

FDA shares GAO’s goal of being as transparent as possible with the public about the Agency’s review of the safety and effectiveness data that supports the issuance of an EUA for a drug or biological product. FDA believes that disclosing such information from its clinical review memoranda supporting the issuance of EUAs for therapeutics and vaccines, similar to what FDA discloses from its approval packages for new drugs and biologics, will contribute to the public’s confidence in the Agency’s rigorous, independent review of the scientific data available and will help the Agency achieve its transparency goal. To that end, FDA will explore approaches for greater transparency in this area, including considering whether additional authorities are needed.

Related GAO Products

COVID-19: Federal Efforts Could Be Strengthened by Timely and Concerted Actions. [GAO-20-701](#). Washington, D.C.: September 21, 2020.

COVID-19 Contracting: Observations on Federal Contracting in Response to the Pandemic. [GAO-20-632](#). Washington, D.C.: July 29, 2020.

COVID-19: Opportunities to Improve Federal Response and Recovery Efforts. [GAO-20-625](#). Washington, D.C.: June 25, 2020.

Defense Acquisitions: DOD's Use of Other Transactions for Prototype Projects Has Increased. [GAO-20-84](#). Washington, D.C.: November 22, 2019.

Federal Acquisitions: Use of 'Other Transaction' Agreements Limited and Mostly for Research and Development Activities. [GAO-16-209](#). Washington, D.C.: January 7, 2016.

Influenza Pandemic: Lessons from the H1N1 Pandemic Should Be Incorporated into Future Planning. [GAO-11-632](#). Washington, D.C.: June 27, 2011.

GAO's Mission

The Government Accountability Office, the audit, evaluation, and investigative arm of Congress, exists to support Congress in meeting its constitutional responsibilities and to help improve the performance and accountability of the federal government for the American people. GAO examines the use of public funds; evaluates federal programs and policies; and provides analyses, recommendations, and other assistance to help Congress make informed oversight, policy, and funding decisions. GAO's commitment to good government is reflected in its core values of accountability, integrity, and reliability.

Obtaining Copies of GAO Reports and Testimony

The fastest and easiest way to obtain copies of GAO documents at no cost is through our website. Each weekday afternoon, GAO posts on its [website](#) newly released reports, testimony, and correspondence. You can also [subscribe](#) to GAO's email updates to receive notification of newly posted products.

Order by Phone

The price of each GAO publication reflects GAO's actual cost of production and distribution and depends on the number of pages in the publication and whether the publication is printed in color or black and white. Pricing and ordering information is posted on GAO's website, <https://www.gao.gov/ordering.htm>.

Place orders by calling (202) 512-6000, toll free (866) 801-7077, or TDD (202) 512-2537.

Orders may be paid for using American Express, Discover Card, MasterCard, Visa, check, or money order. Call for additional information.

Connect with GAO

Connect with GAO on [Facebook](#), [Flickr](#), [Twitter](#), and [YouTube](#).
Subscribe to our [RSS Feeds](#) or [Email Updates](#). Listen to our [Podcasts](#).
Visit GAO on the web at <https://www.gao.gov>.

To Report Fraud, Waste, and Abuse in Federal Programs

Contact FraudNet:

Website: <https://www.gao.gov/fraudnet/fraudnet.htm>

Automated answering system: (800) 424-5454 or (202) 512-7700

Congressional Relations

Orice Williams Brown, Managing Director, WilliamsO@gao.gov, (202) 512-4400,
U.S. Government Accountability Office, 441 G Street NW, Room 7125,
Washington, DC 20548

Public Affairs

Chuck Young, Managing Director, youngc1@gao.gov, (202) 512-4800
U.S. Government Accountability Office, 441 G Street NW, Room 7149
Washington, DC 20548

Strategic Planning and External Liaison

Stephen J. Sanford, Acting Managing Director, spel@gao.gov, (202) 512-4707
U.S. Government Accountability Office, 441 G Street NW, Room 7814,
Washington, DC 20548



Please Print on Recycled Paper.