GAO@100 Highlights

Highlights of GAO-21-319, a report to congressional addressees

February 2021

OPERATION WARP SPEED

Accelerated COVID-19 Vaccine Development Status and Efforts to Address Manufacturing Challenges

Why GAO Did This Study

As of February 5, 2021, the U.S. had over 26 million cumulative reported cases of COVID-19 and about 449,020 reported deaths, according to the Centers for Disease Control and Prevention. The country also continues to experience serious economic repercussions, with the unemployment rate and number of unemployed in January 2021 at nearly twice their pre-pandemic levels in February 2020. In May 2020, OWS was launched and included a goal of producing 300 million doses of safe and effective COVID-19 vaccines with initial doses available by January 2021. Although FDA has authorized two vaccines for emergency use, OWS has not yet met its production goal. Such vaccines are crucial to mitigate the public health and economic impacts of the pandemic.

GAO was asked to review OWS vaccine development efforts. This report examines: (1) the characteristics and status of the OWS vaccines, (2) how developmental processes have been adapted to meet OWS timelines, and (3) the challenges that companies have faced with scaling up manufacturing and the steps they are taking to address those challenges.

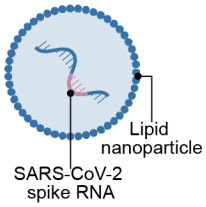
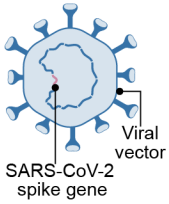
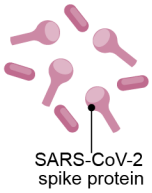
GAO administered a questionnaire based on HHS's medical countermeasures TRL criteria to the six OWS vaccine companies to evaluate the COVID-19 vaccine development processes. GAO also collected and reviewed supporting documentation on vaccine development and conducted interviews with representatives from each of the companies on vaccine development and manufacturing.

View GAO-21-319. For more information, contact Karen L. Howard and Candice N. Wright at (202) 512-6888 or howardk@gao.gov or wrightc@gao.gov.

What GAO Found

Operation Warp Speed (OWS)—a partnership between the Departments of Health and Human Services (HHS) and Defense (DOD)—aimed to help accelerate the development of a COVID-19 vaccine. GAO found that OWS and vaccine companies adopted several strategies to accelerate vaccine development and mitigate risk. For example, OWS selected vaccine candidates that use different mechanisms to stimulate an immune response (i.e., platform technologies; see figure). Vaccine companies also took steps, such as starting large-scale manufacturing during clinical trials and combining clinical trial phases or running them concurrently. Clinical trials gather data on safety and efficacy, with more participants in each successive phase (e.g., phase 3 has more participants than phase 2).

Vaccine Platform Technologies Supported by Operation Warp Speed, as of January 2021

	mRNA platform	Replication-defective live-vector platform	Recombinant-subunit-adjuvanted protein platform
			
Description	Encapsulated genetic instructions that allow vaccinated individuals to produce the spike protein of SARS-CoV-2 to stimulate immune system but cannot cause COVID-19.	Non-replicating virus that delivers genetic instructions to allow vaccinated individuals to produce the spike protein of SARS-CoV-2 to stimulate immune system but cannot cause COVID-19.	Fully-formed spike protein of SARS-CoV-2 delivered with adjuvant, which helps to stimulate immune system of vaccinated individuals but cannot cause COVID-19.
Operation Warp Speed candidates (most advanced clinical trial phase)	**Moderna** (phase 3) **Pfizer/BioNTech** (phase 3)	**Janssen** (phase 3) **AstraZeneca** (phase 3)	**Sanofi/GSK** (phase 2) **Novavax** (phase 3)

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-21-319

As of January 30, 2021, five of the six OWS vaccine candidates have entered phase 3 clinical trials, two of which—Moderna's and Pfizer/BioNTech's vaccines—have received an emergency use authorization (EUA) from the Food and Drug Administration (FDA). For vaccines that received EUA, additional data on vaccine effectiveness will be generated from further follow-up of participants in clinical trials already underway before the EUA was issued.

Technology readiness. GAO's analysis of the OWS vaccine candidates' technology readiness levels (TRL)—an indicator of technology maturity—showed that COVID-19 vaccine development under OWS generally followed traditional practices, with some adaptations. FDA issued specific guidance that identified ways that vaccine development may be accelerated during the pandemic. Vaccine companies told GAO that the primary difference from a non-pandemic environment was the compressed timelines. To meet OWS timelines,

some vaccine companies relied on data from other vaccines using the same platforms, where available, or conducted certain animal studies at the same time as clinical trials. However, as is done in a non-pandemic environment, all vaccine companies gathered initial safety and antibody response data with a small number of participants before proceeding into large-scale human studies (e.g., phase 3 clinical trials). The two EUAs issued in December 2020 were based on analyses of clinical trial participants and showed about 95 percent efficacy for each vaccine. These analyses included assessments of efficacy after individuals were given two doses of vaccine and after they were monitored for about 2 months for adverse events.

Manufacturing. As of January 2021, five of the six OWS vaccine companies had started commercial scale manufacturing. OWS officials reported that as of January 31, 2021, companies had released 63.7 million doses—about 32 percent of the 200 million doses that, according to OWS, companies with EUAs have been contracted to provide by March 31, 2021. Vaccine companies face a number of challenges in scaling up manufacturing to produce hundreds of millions of doses under OWS's accelerated timelines. DOD and HHS are working with vaccine companies to help mitigate manufacturing challenges, including:

- Limited manufacturing capacity: A shortage of facilities with capacity to handle the vaccine manufacturing needs can lead to production bottlenecks. Vaccine companies are working in partnership with OWS to expand production capacity. For example, one vaccine company told GAO that HHS's Biomedical Advanced Research and Development Authority helped them identify an additional manufacturing partner to increase production. Additionally, the U.S. Army Corps of Engineers is overseeing construction projects to expand capacity at vaccine manufacturing facilities.
- Disruptions to manufacturing supply chains: Vaccine manufacturing supply chains have been strained by the global demand for certain goods and workforce disruptions caused by the global pandemic. For example, representatives from one facility manufacturing COVID-19 vaccines stated that they experienced challenges obtaining materials, including reagents and certain chemicals. They also said that due to global demand, they waited 4 to 12 weeks for items that before the pandemic were typically available for shipment within one week. Vaccine companies and DOD and HHS officials told GAO they have undertaken several efforts to address possible manufacturing disruptions and mitigate supply chain challenges. These efforts include federal assistance to (1) expedite procurement and delivery of critical manufacturing equipment, (2) develop a list of critical supplies that are common across the six OWS vaccine candidates, and (3) expedite the delivery of necessary equipment and goods coming into the United States. Additionally, DOD and HHS officials said that as of December 2020 they had placed prioritized ratings on 18 supply contracts for vaccine companies under the Defense Production Act, which allows federal agencies with delegated authority to require contractors to prioritize those contracts for supplies needed for vaccine production.
- Gaps in the available workforce: Hiring and training personnel with the specialized skills needed to run vaccine manufacturing processes can be challenging. OWS officials stated that they have worked with the Department of State to expedite visa approval for key technical personnel, including technicians and engineers to assist with installing, testing, and certifying critical equipment manufactured overseas. OWS officials also stated that they requested that 16 DOD personnel be detailed to serve as quality control staff at two vaccine manufacturing sites until the organizations can hire the required personnel.