FEATURED ICONS

UPDATED RECOMMENDATION  NEW DATA  COMMUNICATION TIP  RESEARCH OPPORTUNITY

FEATURES

NEWS

• A window into the scope and impact of the COVID-19 pandemic in U.S. nursing homes will soon be available. De-identified clinical data on infectious diseases in long-term care facilities will be supplied by Real Time Medical Systems to the Institute for Health Metrics and Evaluation at the University of Washington. The data will come from weekly reports to the U.S. Centers for Disease Control and Prevention (CDC) as required recently by the U.S. Centers for Medicare and Medicaid Services.

• Community pharmacies are an important partner for addressing vaccination gaps. A study from Wisconsin shows community pharmacies administering 39% of zoster vaccine doses and 20% of influenza vaccine doses in that state (Vaccine. May 13, 2020. doi: 10.1016/j.vaccine.2020.04.043). Overall, 86% of pharmacies provide immunization services and 84% stock influenza vaccines, but only 21% stock human papillomavirus (HPV) vaccines. Addressing the obstacles limiting greater roles as immunizers, pharmacists “must engage in active communication with patients and be willing to collaborate with physicians,” the researchers concluded. Should a COVID-19 vaccine prove safe and effective in coming months, pharmacies will be an important element in vaccinating the U.S. population as quickly as possible.

• “A Map of Racial and Ethnic Disparities in Influenza Vaccine Uptake in the Medicare Fee-for-Service Program” was published in Advances in Therapy (2020;37(5):2224–2235). Looking at influenza vaccination among Medicare Fee-for-Service beneficiaries in 2015–16, the study showed that nonwhite beneficiaries, people dwelling in rural communities, and economically disadvantaged individuals are significantly less likely to receive influenza vaccine, especially newer, more effective formulations indicated for older adults.
RESOURCES

- Infectious disease expert Stanley Plotkin, MD, discusses development of COVID-19 vaccines in a recent episode of the Vax Talk podcast. Plotkin also has an informative set of YouTube videos on vaccines.

- COVID-19 is the topic of a 4-part bonus mini-season of the Pfizer podcast, The Antigen. The episodes look at past pandemics, outline potential coronavirus treatments in development, and look ahead to life after this crisis. The first episode of the bonus season features David Swerdlow, MD, who leads the Pfizer Medical Affairs team for COVID-19 and worked at the CDC during previous pandemics.

COVID-19: TESTING THE NEW VACCINE TECHNOLOGIES

With a pandemic virus circulating, the press is on to identify agents for treating COVID-19 and vaccines for preventing its spread. The speed at which the biopharma industry has responded has been historic, with several hundred potentially useful drugs, biologic agents, and vaccines already identified (Figure 1).

In addition to antiviral agents such as remdesivir, researchers are looking at monoclonal antibodies as promising agents to fill the treatment gap while vaccine development goes forward. Yet it is the safe and effective vaccine—or vaccines—that the world is counting on to eliminate the novel coronavirus 2019 as an existential threat to modern society.

CREATING “MULTIPLE SHOTS ON GOAL”

As medical researchers and biopharma companies began looking for a COVID-19 vaccine, their approaches were guided by past experiences with outbreaks of coronaviruses and the Ebola virus. Key lessons important in COVID-19 vaccine development are to develop vaccine materials that are ready for testing in phase 1 (human safety) trials, use proven technologies when possible, seek public and private funding sources, and if not a large manufacturing-ready company, bring on board partners capable of producing the hundreds of millions of doses needed quickly in this pandemic situation. During the 2.5 years of the Ebola virus outbreak in West Africa, several vaccines entered development. Two reached phase 3 (large human efficacy and safety) trials. One, a Merck vesicular stomatitis virus vaccine, was approved in the European Union in 2019 and is pending at the U.S. Food and Drug Administration (FDA). About 192,000 doses of this vaccine were administered during a 2019 Ebola outbreak in the Congo.

Of the COVID-19 investigational approaches shown in Figure 1, more than 100 are vaccine candidates. A few are repurposed products such as bacillus Calmette-Guerin (BCG) vaccine or products redirected from other target pathogens, but most are new candidates that rely on novel technologies such as mRNA, DNA, cellular, and protein vectors (Table 1).

Larger companies are testing multiple platforms that target different antigenic sites on the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) surface. This gives them not only “multiple shots on goal” in case one or more products perform better than others but also the opportunity to quickly respond if the virus mutates and becomes resistant to products that initially test well. Sanofi Pasteur, for example, is using a baculovirus recombinant vaccine platform to develop an adjuvanted COVID-19 spike protein. The company is also working with an mRNA platform to produce a second vaccine candidate that will rely on a second mechanism of action while adding manufacturing capacity.

<table>
<thead>
<tr>
<th>Vaccines/Candidates</th>
<th>Sponsors/Partners [Funding]</th>
<th>Vaccine Type</th>
<th>Phase of Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG Vaccine</td>
<td>Merck, Pasteur Institute, and others PreP Biopharm</td>
<td>Cell</td>
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<tr>
<td>Ad5-nCoV</td>
<td>CanSino Biologics, Beijing Institute of Biotechnology</td>
<td>RNA</td>
<td>2</td>
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<tr>
<td>Vaccine (Inactivated)</td>
<td>Sinopharm, Wuhan Institute of Virology</td>
<td>Protein</td>
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<tr>
<td>LV-SMENP-DC Vaccine</td>
<td>Shenzhen Genoimmune Medical Institute</td>
<td>Virus</td>
<td>1/2</td>
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<td>Bria-1MT</td>
<td>BriaCell Therapeutics Corp.</td>
<td>Cell</td>
<td>1/2</td>
</tr>
<tr>
<td>BNT162 mRNA vaccine</td>
<td>BioNTech AG, Pfizer</td>
<td>RNA</td>
<td>1/2</td>
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<td>RITI Vaccine</td>
<td>ArchiVet Farma S.L.</td>
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<td>Pathogen-specific aAPC Vaccine</td>
<td>Shenzhen Genoimmune Medical Institute</td>
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<tr>
<td>mRNA-1273</td>
<td>Moderna, NIH, [CSPI], Lonza (manufacturing)</td>
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<tr>
<td>INO-4800 DNA Vaccine</td>
<td>Inovio, Beijing Advaccine Biotechnology Co.</td>
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<td>ChAdOx1 nCoV-19</td>
<td>University of Oxford, ChAdOx1 consortium, [Horizon 2020], AstraZeneca</td>
<td>Recombinant virus</td>
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<tr>
<td>bacTIRI-Spike</td>
<td>Symvivo Corp.</td>
<td>Cell</td>
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**TABLE 1. Most Advanced COVID-19 Vaccine Candidates**

COMPRESSED R&D TIMELINES

The most optimistic but realistic scenario for the pandemic in the United States goes something like this: COVID-19 infections drop to a low level over the summer of 2020 and are just beginning to rise when results of a phase 2/3 vaccine trial lead to an emergency use authorization during the winter months. Production has been ramped up so that hundreds of millions of doses are available quickly, people line up to receive the vaccine, and COVID-19 is a thing of the past.

If a COVID-19 vaccine can be developed that rapidly, it would not just be historic. In fact, if a vaccine were ready for market in about a decade, that would be fast by vaccine standards. As listed in the current edition of Plotkin’s Vaccines (Table 4.3), development timelines for vaccines have been 25–30 years for varicella and FluMist, 14–16 years for HPV and rotavirus, and 10–12 years for pediatric combination vaccines. The vaccines developed most quickly, mumps and Ebola vaccines, required 4 years to reach the market. That’s years, not the months people are talking about for COVID-19 vaccine.

This severely compressed timeline depends first on finding a vaccine that works and passes initial safety screens, something that has yet to happen for pathogens such as human immunodeficiency virus. Initial signs for COVID-19 are positive though. Moderna announced SARS-CoV-2 antibody levels in 8 normal volunteers who received the mRNA-based vaccine in a phase 1 trial. The University of Oxford’s adenovirus-based product was safe in phase 1 trials, and because the platform was validated previously by the British regulatory authority, the COVID-19 vaccine was able to begin moving directly into larger clinical trials.

PLANNING FOR APPROVAL, PRODUCTION

Everything from masks and swabs to medications and ventilators has been in short supply during the COVID-19 pandemic. Should one or more vaccines prove safe and effective, the competition for the products could eclipse anything seen thus far. In fact, the competition has already begun among countries as to where vaccine products should be initially distributed. Supplies for vaccine production and administration (e.g., glass vials, syringes, alcohol swabs) will also be in high demand.

This illustrates the importance for larger biopharma companies to ramp up production capabilities now and to work with regulatory authorities regarding what will be required in interim analyses of pivotal trials of safety and efficacy. One unknowable variable—the status of the COVID-19 pandemic at the time results become available—will affect the willingness of FDA and other regulatory authorities to allow emergency use. Furthermore, the companies need to know whether phase 2 proof-of-concept studies will suffice and what types of robust animal viral challenge data could be useful.

Companies are also beginning to look at other important considerations. Will vaccines require refrigeration (as opposed to freezing)? Will multidose vials be produced for maximizing supply with the fewest number of vials? Or will the single-dose vials and syringes more commonly found in the United States be produced? Producing a vaccine product is complicated, and the process can be undermined by one weak link in the supply chain.
The final piece in a COVID-19 vaccine protecting the world from this novel coronavirus is for people to get vaccinated if and when the opportunity comes. However, just as some nonvaccinating individuals have personal and religious opposition to vaccines and others are vaccine hesitant, some people in the population will refuse the COVID-19 product. That group is likely to be small, but it will get media attention. Additionally, the negative reaction of some people to state and local physical distancing orders has steeled their opposition to public health mandates, including vaccines.

To ensure an adequate vaccination rate to achieve herd immunity—estimated to be 55% to 82% for COVID-19—authors of a recent op-ed article in JAMA suggested these approaches:

- As soon as a COVID-19 vaccine is shown to be safe and effective, it should be delivered and distributed equitably to those at highest risk for complications and disease transmission.
- Before the vaccine is available, an educational program should be designed to address obstacles to vaccine acceptance and launched using linguistically and culturally competent messages.
- This robust educational campaign should include traditional and social media and focus in particular on social influencers and sources of misinformation.
- Vaccine advocates, including frontline health care workers, should be trained to provide strong recommendations for COVID-19 vaccination. Messaging should include their personal experiences with COVID-19 and the vaccine when relevant.

**SOURCES AND RESOURCES**