



COVID-19: Legal Considerations for Bringing a New Vaccine to Market

March 24, 2020

As the number of confirmed COVID-19 cases [increases at an accelerating rate](#), interest has grown in [developing a COVID-19 vaccine](#) as an avenue for addressing the pandemic. Media reports indicate that a number of [countries](#) and [companies](#) are working on developing a vaccine. The National Institute of Allergy and Infectious Diseases (NIAID) and the biotechnology company Moderna, Inc., recently initiated the [first clinical trials](#) of a potential vaccine in the United States at a hospital in Seattle. However, developing a new vaccine and obtaining approval to market it can take a long time. This Sidebar discusses the licensure (i.e., approval) process for vaccines under the Public Health Service Act (PHS Act) and the federal Food, Drug, and Cosmetic Act (FD&C Act), as well as potential legal avenues for expediting that process to bring a new vaccine to market sooner.

FDA Approval of New Vaccines

[Vaccines](#) are intended to prevent diseases and [generally work](#) by introducing pathogens to the human body (usually by injection) to trigger an immune response to the disease (i.e., producing antibodies to the pathogen). Vaccines are biological products [approved and regulated](#) by the U.S. Food and Drug Administration's (FDA's) Center for Biologics Evaluation and Research (CBER) under [Section 351](#) of the Public Health Service Act. A biologic such as a vaccine generally cannot be introduced into commerce unless FDA approves it. To be approved, FDA must determine that the vaccine is safe, potent, and pure based on data from laboratory studies and clinical trials. In general, this requirement means that the vaccine must achieve the desired effect (i.e., prevents the targeted disease or condition) and that the risk of adverse side effects is outweighed by the expected benefits.

Developing a new vaccine, or any other drug or biological product, begins in a laboratory. When a company (i.e., sponsor) is ready to test its new vaccine on humans in clinical trials, the sponsor submits an [investigational new drug application](#) (IND) to FDA. The IND contains information known about the vaccine so far and the sponsor's plan for the clinical studies, including the investigational plan and protocols for the studies. FDA uses the IND to [ensure](#) that clinical trials will protect the safety and rights of the participants and yield data with enough scientific integrity to evaluate the safety and effectiveness of the vaccine. The sponsor generally cannot begin clinical trials until FDA approves the IND.

Congressional Research Service

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LSB10427

If the clinical trials are successful, the sponsor may seek FDA approval to market its new vaccine. FDA approves new vaccines through biologics license applications (BLAs) reviewed by CBER. BLAs contain data from the laboratory and clinical studies and information about how and where the biologic will be manufactured. As [courts](#) have recognized, FDA exercises its scientific judgment when deciding whether to license vaccines based on such studies. Biologics that are approved through a BLA receive 12 years of regulatory exclusivity, during which time FDA cannot approve any biosimilars (i.e., abbreviated applications for the same biologic that depend on the clinical data in the BLA to demonstrate safety, potency, and purity). (These exclusivity rights and separate patent rights raise potential intellectual property questions that are discussed in more detail in this Sidebar.)

Options for Bringing a New Vaccine to Market Faster

The process of developing and testing a new vaccine to the point where it meets the safety, purity, and potency standard can be a [lengthy process](#). The FD&C Act provides several options that may allow a sponsor to bring a new vaccine to market faster. Generally, these options use one of two approaches. First, FDA can direct more of its resources to the product to accelerate the development and/or review processes (e.g., fast track product designation, breakthrough therapy designation, and priority review). Second, FDA can modify how it evaluates the risks and benefits of the vaccine before allowing its use, either by relying on different types of evidence (e.g., the accelerated approval process) or lowering the evidentiary standard in emergency situations (e.g., emergency use authorization). (For ease of reference, this section uses the general term “biologic” because vaccines are biological products, but the pathways discussed below are also available for traditional small molecule drugs.)

Shortening the Development and Review Processes

Several avenues are available for expediting the development and review processes for biologics used to treat or prevent serious or life-threatening conditions and diseases. In its [guidance](#), FDA generally considers a condition or disease *serious* if it substantially affects day-to-day functioning and is irreversible, persistent, or recurrent. A condition or disease may be found to be serious as a matter of clinical judgment based on its effect on survival, day-to-day functioning, or the likelihood that it will progress to a more serious condition if left untreated. As a matter of course, FDA considers any life-threatening condition or disease to be serious. The drug must also be intended to *treat* the serious condition or disease by having an effect on the disease itself or a serious aspect of the disease, such as a symptom or other manifestation. Among the examples FDA provides in its guidance is a product intended to *prevent* the serious condition. Given that COVID-19 is life-threatening, a vaccine intended to prevent COVID-19 seems likely to qualify as a drug used to treat or prevent a serious or life-threatening condition or disease—making it eligible for the following designations to accelerate the approval process.

Fast Track Product Designation

[Section 506](#) of the FD&C Act allows FDA to designate certain biologics as fast track products, which receive FDA assistance in expediting development and review. A biologic may be designated as a [fast track product](#) if FDA determines that the biologic will treat or prevent a serious or life-threatening disease or condition and fill an unmet medical need. An unmet medical need exists when available therapies do not adequately address treating or diagnosing a condition or disease. FDA recognizes in its [guidance](#) that an unmet medical need necessarily exists if there is no available therapy. Sponsors may provide FDA with nonclinical or clinical data to demonstrate that the drug has the potential to fill that unmet medical need. Given that there are no approved vaccines for COVID-19, any vaccine that showed potential to prevent COVID-19 in laboratory or clinical trials would seem likely to qualify for fast track designation.

At its discretion, the biologic's sponsor requests fast track designation for its product. It may request fast track designation when it submits an IND or any time thereafter. FDA has 60 days to determine if the biologic qualifies for the designation. Once FDA designates a biologic as a fast track product, FDA must facilitate its development and expedite review of the biologic. In [practice](#), this process generally means that the biologic's sponsor has greater access to FDA through written and in-person communications during the development and testing process to improve efficiency and ensure that appropriate data are collected. FDA may also review the BLA for a fast track product on a rolling basis as sections are complete (rather than waiting for a completed application) if initial clinical testing shows the biologic may be effective.

Breakthrough Therapy Designation

[Section 506](#) of the FD&C Act also allows FDA to designate certain biologics as breakthrough therapies, which similarly heightens FDA involvement in the development and review process. Breakthrough therapy designation is based on preliminary clinical evidence showing the biologic may be a substantial improvement over available therapies for one or more clinically significant endpoints. [Endpoints](#) measure the outcome of a clinical trial. Under [FDA guidance](#), a clinically significant endpoint generally measures an effect on irreversible morbidity or mortality or on symptoms representing serious consequences of the disease or condition. Unlike fast track product designation, which can be based on laboratory data, breakthrough therapy designation requires evidence from clinical trials. FDA exercises its judgment in determining whether the data show a [substantial improvement](#) over existing therapies, taking into consideration both the magnitude of the biologic's effects on the endpoint and the importance of the effect measured by that endpoint to treating the disease or condition. When there are no existing therapies, such as with a COVID-19 vaccine, FDA compares the biologic to a placebo or well-documented historical control. A COVID-19 vaccine may be eligible for breakthrough therapy designation if the sponsor can demonstrate potential effectiveness in early clinical trials.

At its discretion, the sponsor requests breakthrough therapy designation and may do so with submission of an IND or at any time thereafter. FDA must determine whether the biologic qualifies as a breakthrough therapy within 60 days of receipt. As with fast track product designation, the FD&C Act directs FDA to expedite the development and review of applications for breakthrough therapies. Per [FDA guidance](#), expedited development and review of breakthrough therapies entails (1) intensive assistance from FDA on efficient development and clinical trial design; (2) organizational commitment from FDA, including senior management and experienced staff; (3) rolling review of the BLA; and (4) other actions to expedite review, such as priority review discussed below. Extensive FDA assistance during the development process and the involvement of senior managers distinguishes breakthrough therapy designation from fast track product designation.

Accelerated Approval

[Section 506](#) of the FD&C Act also allows FDA to approve certain biologics based on surrogate or intermediate endpoints, referred to as [accelerated approval](#). In general, sponsors select endpoints that directly measure the clinical outcome (i.e., the benefits expected from the biologic), such as whether the patient feels better or lives longer. Surrogate and intermediate endpoints do not measure the clinical benefit directly but instead measure an effect that is expected to predict a clinical benefit. For example, a drug to treat strokes would have an intended clinical outcome of reducing the incidence or severity of strokes. But rather than measuring the incidence of strokes directly, an investigator might measure the drug's effect on blood pressure as a surrogate endpoint due to the strong correlation between strokes and blood pressure.

To qualify for accelerated approval, (1) the biologic must treat a serious or life-threatening condition or disease and (2) FDA must determine that the biologic has an effect on a surrogate or intermediate

endpoint that is reasonably likely to predict a clinical benefit. When deciding whether to approve a biologic on this basis, FDA must consider how severe, rare, or prevalent the condition is and the availability of alternative treatments. A vaccine for COVID-19 could qualify for accelerated approval if investigators identified a surrogate or intermediate endpoint that could reasonably predict the vaccine would be effective against the virus.

Priority Review

Once a BLA is submitted, FDA can designate the BLA for standard review or [priority review](#). FDA aims to act on priority review applications within 6 months, compared to 10 months or more for standard review applications. FDA makes this determination for every application, though a sponsor can expressly request priority review. FDA may designate a BLA for priority review if it represents a “significant improvement” over existing treatments in terms of safety or effectiveness in treating, diagnosing, or preventing the disease or condition. In the absence of any approved vaccine for COVID-19, FDA would likely designate for priority review any BLA for such a vaccine.

Emergency Use Authorizations Before Approval

In certain emergency situations, [Section 564](#) of the FD&C Act allows FDA to authorize the use of a drug or biologic (e.g., a vaccine) before it is approved (i.e., an [Emergency Use Authorization](#) or EUA). FDA may issue an EUA only if the Secretary of Health and Human Services has declared that circumstances exist justifying emergency authorized use of the medical product. Of relevance to the COVID-19 pandemic, on [February 4, 2020](#), the Secretary determined that there is a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad, and that involves a biological, chemical, radiological, or nuclear agent (BCRN agent)—namely, the virus that causes COVID-19. Based on this determination, the Secretary has authorized the emergency use of several [diagnostic tests](#). On [March 2, 2020](#), the Secretary determined that circumstances exist to allow for the emergency use of certain respirators not approved by the agency, and FDA [issued an EUA](#) allowing for the emergency use of such respirators.

After the Secretary determines a public health emergency exists (one of four bases for declaring an emergency or threat), FDA may issue an EUA for a specific product if the Secretary concludes that:

- the BCRN agent can cause a serious or life-threatening disease or condition;
- it is reasonable to believe, based on the totality of the scientific evidence available, that:
 - The product may be effective in diagnosing, treating, or preventing the disease or condition caused by the BCRN agent; and
 - The known and potential benefits of the product outweigh the known and potential risks; and
- there is no adequate, approved, and available alternative to the product.

In evaluating a product for an EUA, FDA uses a [lower evidentiary standard](#), determining whether the product “may be effective” in diagnosing, treating, or preventing a disease rather than evaluating its “effectiveness” in doing so. As discussed above, COVID-19 is a serious or life-threatening disease, confirmed by the fact that FDA has [already issued](#) EUAs in connection with COVID-19 for diagnostic tests and certain personal protective equipment. There is also [no alternative](#) to a COVID-19 vaccine at this time. Any decision by FDA to issue an EUA for a COVID-19 vaccine would accordingly depend on whether the totality of the evidence available to FDA shows that it is reasonable to believe (1) the vaccine may be effective in preventing COVID-19 and (2) that those benefits outweigh any known or potential risks from the vaccine. FDA would have to conduct this evaluation for each vaccine that is developed and submitted for an EUA.

The [FD&C Act](#) requires FDA to impose certain conditions on EUAs as necessary and appropriate to protect the public health. The conditions vary depending on whether the product is unapproved or approved but for a different use. In general, the conditions provide for monitoring, reporting, and recordkeeping as well as ensuring that the health care professionals administering the product and the individuals being treated with the product are informed about the benefits and risks of using the product. FDA may also waive good manufacturing practices (GMP) and certain prescription requirements when issuing an EUA and may impose conditions related to advertising the product.

Considerations for Congress

The current legal regime for approving new pharmaceutical products such as vaccines generally aims to strike a balance between bringing products to market sooner and ensuring that products on the market are safe and effective. For serious or life-threatening diseases and conditions or in emergency situations, the law gives FDA a certain amount of discretion to shift that balance. FDA generally expedites the process one of two ways: shifting its resources or shifting its standard in evaluating the risks and benefits.

In considering avenues to facilitate the development of a COVID-19 vaccine, Congress has similar options. Congress could consider providing additional resources to FDA to exercise its existing authorities. Congress is already employing this approach: The [Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020](#), enacted on March 6, appropriated \$61 million to FDA “to prevent, prepare for, and respond to coronavirus, domestically or internationally, *including the development of necessary medical countermeasures and vaccines*, advanced manufacturing for medical products, the monitoring of medical product supply chains, and related administrative activities.” Alternatively, Congress could direct FDA to strike a different balance when evaluating the risks versus the benefits specifically in the context of potential COVID-19 vaccines. In assessing that balance, Congress and FDA would face weighing the benefits from disseminating a vaccine to the public sooner (e.g., limiting the spread of the virus or reducing the economic consequences) against the risk that the vaccine may have been authorized prematurely and prove ineffective or unsafe, potentially leading to worse public health outcomes. Any alteration to this balance that requires FDA to exceed or contradict its existing authority would require an act of Congress to amend the agency’s statutory authority.

Should FDA authorize or approve a COVID-19 vaccine, other considerations may come to bear. For example, registered manufacturers may not be able to produce an adequate supply of the vaccine. FDA is currently addressing [hand sanitizer](#) shortages by exercising its enforcement discretion with respect to production by [over-the-counter drug manufacturers](#) and [compounders](#). Congress may consider other avenues for increasing supply of the vaccine. In addition, existence of a vaccine would raise questions of mandatory vaccination to address the public health crisis, which is addressed in a separate Sidebar.

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