

## Reassuring the Public and Clinical Community About the Scientific Review and Approval of a COVID-19 Vaccine

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**Public perception** of the review of medications and vaccines for coronavirus disease 2019 (COVID-19) has become enmeshed in politics. The pressure on the US Food and Drug Administration (FDA) and Commissioner Stephen Hahn, MD,



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to approve the broad use of a COVID-19 vaccine in the coming months will be immense.

However, a lack of clarity about the agency's approach—coupled with a stream of announcements from various federal agencies and pharmaceutical companies—has led to confusion and concern. Greater clarity and transparency about the review process as well as the full engagement of the relevant federal advisory committees can inspire understanding and trust.

A flurry of recent statements has captured headlines. Commissioner Hahn indicated that the FDA is willing to use an Emergency Use Authorization (EUA) for vaccines before phase 3 trials are complete.<sup>1</sup> An EUA provides a rapid approach to facilitate availability and use of biologics, drugs, vaccines, devices, and diagnostic tests (referred to as “medical countermeasures”) during a public health emergency.<sup>2</sup> Some medical experts have suggested that this approach is inappropriate. On August 27, 2020, the US Centers for Disease Control and Prevention (CDC) instructed states to begin to prepare for distribution of a vaccine in the coming months.<sup>3</sup> On September 3, the chief executive officer (CEO) of Pfizer announced that the company will have sufficient data to know if its vaccine is effective by the end of October and will consider filing for EUA.<sup>4,5</sup> But on September 4, the White House chief advisor for the coronavirus vaccine development program, Operation Warp Speed, announced that it was “extremely unlikely but not impossible” that a vaccine could be available by the end of October.<sup>6</sup>

On September 8 the CEOs of 9 pharmaceutical companies released a joint pledge that they are committed to “developing and testing potential vaccines for COVID-19 in accordance with high ethical standards and sound scientific principles.”<sup>7</sup> The pledge indicates that they would “only submit for approval or emergency use authorization after demonstrating safety and efficacy through a Phase 3 clinical study that is designed and conducted to meet requirements of expert regulatory authorities such as FDA.” The statement does not include any commitment or suggestion that the data underpinning their application be shared with any other group.<sup>8</sup> These announcements have left some clinicians, public health officials, and members of the public bewildered about what is actually happening and concerned that vaccines will be made available before safety and effectiveness are fully established.

The goal of making available a safe and effective COVID-19 vaccine is widely seen as critical for ending the pandemic, and Operation Warp Speed has accelerated the development, testing, and eventual distribution of such a vaccine. However, recent polls of adults suggest that as few as 50% of US adults are committed to receiving a COVID-19 vaccine,<sup>9</sup> and misinformation and conspiracy theories about a vaccine abound. Prematurely approving a vaccine could undermine COVID-19 vaccination efforts and erode confidence in vaccines more generally.

The path forward starts with support, not mistrust, of the career FDA scientists and officials with the expertise to determine whether emerging vaccine candidates are ready for use in specific populations. The director of the FDA center responsible for vaccine review, Peter Marks, MD, told the *Washington Post* that the COVID-19 vaccine will only be authorized or licensed when it meets the existing guidelines for safety and efficacy.<sup>10</sup> This statement of agency policy is reassuring. Rather than prejudging any decision, and consistent with the scientific method, FDA staff should have the ability to evaluate the data from phase 3 trials and make the case for whether those trials establish safety and effectiveness. The staff scientists should then be able to recommend either an EUA or full licensure to provide access to a safe and effective vaccine as quickly as possible. If the recommendation is for an EUA, the staff scientists should explain why this path was taken and how this would not mean compromising on the answers to critical questions.

Beyond internal deliberations within the FDA, a thorough and transparent review process of data supporting vaccine approval is essential to building public confidence in a COVID-19 vaccine.

Important safeguards should be established to reassure the clinical community and the public about any vaccine approval. The FDA should explain the role of the data and safety monitoring boards (DSMBs) for the vaccine trials, the first “independent” group that reviews the data, and any correspondence between the DSMB and the project investigators should be shared with the public. Two additional groups have an important consultant responsibility to the government and the public: the FDA Vaccines and Related Biological Products Advisory Committee<sup>11,12</sup> and the Advisory Committee on Immunization Practices (ACIP).<sup>13</sup> These advisory groups are composed of medical, scientific, health policy, and public health experts who review data and develop recommendations for the use of vaccines.

The FDA should share all allowable and available data about a vaccine candidate with the FDA vaccine advisory committee

and ACIP prior to making any decision about an EUA or approval. Typically, the FDA's vaccine committee makes recommendations prior to agency action, and ACIP soon afterward. In this challenging situation, the FDA should seek the input of both committees prior to making a decision. An FDA decision consistent with the advice of these independent experts will then reassure the public. However, if the FDA goes in a different direction, the agency will need to explain the reasons well to avoid confusion and vaccine hesitancy. If either panel is excluded from reviewing data, the FDA may struggle to convince the public and clinical community about the strength of the evidence, and vaccine uptake may be adversely affected.

Some have expressed concern that political appointees in the executive branch may insist on an EUA for a vaccine over the recommendation of FDA career scientists. Such interference would both present a direct risk to the US public and cause incalculable damage to public trust in the federal government's ability to make critical scientific decisions. The FDA should be clear at the time of the announcement of an EUA or approval of a vaccine if such an EUA or approval had been man-

dated by members of the executive branch against the advice of the agency scientists. In such a scenario, Congress should take action to protect the public.

A more nuanced issue is the potential effect of an EUA or approval on ongoing research. The agency should work with the National Institutes of Health (NIH) to develop a joint approach to support ongoing vaccine trials, including further research on the vaccines in question. It would be unfortunate for the FDA and NIH to present conflicting views of a vaccine, as happened with convalescent plasma for treatment of severe COVID-19.

This is a time of great societal upheaval, and the response to the pandemic has required difficult decisions. An effective COVID-19 vaccine, if widely available and with substantial uptake, will allow society over time to return to some semblance of normalcy. The FDA remains the agency to answer the core question of when vaccines are safe and effective for the US population. It also remains essential for the FDA to be fully informed by independent scientific experts, to promote trust and confidence on the path to ending the pandemic.

#### ARTICLE INFORMATION

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