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August 6, 2020

The Honorable Alex M. Azar II
Secretary of Health and Human Services
Office of the Secretary
U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Stephen M. Hahn, M.D.
Commissioner
Food and Drug Administration
U.S. Department of Health and Human Services
9000 Rockville Pike
Bethesda, Maryland 20892

Peter Marks, M.D., Ph.D.
Director
Center for Biologics Evaluation and Research
Food and Drug Administration
U.S. Department of Health and Human Services
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Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
U.S. Department of Health and Human Services
5601 Fishers Lane
Bethesda, MD 20892

Dear Secretary Azar, Commissioner Hahn, Dr. Marks, and Dr. Fauci:

Public Citizen, a consumer advocacy organization with more than 500,000 members and supporters nationwide, is writing to strongly urge you to promptly end the current dangerous consideration being given to issuing Emergency Use Authorizations (EUAs) for vaccines to prevent coronavirus disease 2019 (COVID-19).

COVID-19 vaccines should be marketed and distributed in the U.S. only after all the essential clinical trials routinely needed to establish safety and efficacy have been completed, the data from those trials has been submitted to and analyzed by the Food and Drug Administration (FDA) and presented at public meetings of the advisory committees that normally review vaccine products, and the agency has approved Biologics License Applications (BLAs) for the vaccines. If the FDA were to issue an EUA and thus allow premature widespread use of COVID-19 vaccines, a significant number of people inevitably would choose not to be vaccinated under such uncertain circumstances, which would significantly impair the country's response to the ongoing public health crisis caused by the coronavirus pandemic.

Below we elaborate on the following serious concerns regarding the potential use of EUAs for COVID-19 vaccines:

- Current EUA use consideration by the FDA

- Dangers of the FDA's June 2020 guidance on the development and licensure of COVID-19 vaccines, which inappropriately facilitates EUA use for such vaccines
- No evidence that the FDA has ever issued an EUA for any vaccine for a pandemic/epidemic-causing infectious agent
- A previously published national opinion survey poll on widespread negative attitudes toward vaccination if the use of the then-experimental H1N1 swine flu vaccine was to have been authorized under an EUA rather than under an approved BLA (an EUA was wisely not issued).

FDA consideration of EUAs

Last week, Dr. Peter Marks, Director of the FDA's Center for Biologics Evaluation and Research — which approves vaccines — and FDA Commissioner Steven Hahn each spoke about COVID-19 vaccine development progress and made references to the possibility of issuing EUAs for these products.

Dr. Marks on July 29 told an online Disease Control and Prevention Summit that the FDA could issue an EUA for a COVID-19 vaccine in a matter of weeks once the vaccine meets efficacy requirements.[1]

In a livestream interview with *Journal of the American Medical Association* Editor Dr. Howard Bauchner on July 30, Dr. Hahn indicated that there was a possibility that his agency would use the EUA pathway for a COVID-19 vaccine if the risks of the vaccine were much lower than the risks of not having the vaccine and were outweighed by the potential benefit of having the vaccine. Dr. Hahn repeatedly stressed that the FDA would resist pressure for a quicker vaccine approval and that it was the science and the data that would determine the FDA's decision about any vaccine.[2]

The FDA's guidance on the development and licensure of COVID-19 vaccines

Dr. Marks and Commissioner Hahn were both referring to the FDA's *Guidance for Industry: Development and Licensure of Vaccines to Prevent COVID-19*, which was published on June 30. Statements in the guidance that address the use of EUAs for COVID-19 vaccines include the following:

> An Emergency Use Authorization (EUA) may be issued only after several statutory requirements are met (section 564 of the FD&C Act (21 U.S.C. 360bbb2))… Among

[1] CNN. FDA could issue Covid-19 vaccine emergency authorization weeks after evidence it works safely. July 30, 2020. https://www.cnn.com/world/live-news/coronavirus-pandemic-07-29-20-intl/h_07b1b159cdd369bf5a42d5a754136acd. Accessed August 5, 2020.

[2] YouTube. COVID-19 and the FDA, with FDA Commissioner Stephan Hahn, MD. July 30, 2020. https://www.youtube.com/watch?v=UdmaU2-C_wE&feature=youtu.be. Accessed August 5, 2020. See discussion at 32 to 33.5 minutes.

> these requirements is a determination by FDA that the known and potential benefits of a product, when used to diagnose, prevent, or treat serious or life-threatening diseases, outweigh the known and potential risks of the product.
>
> Issuance of an EUA…may be appropriate for a COVID-19 vaccine provided the standard for issuing an EUA is met. Issuance of an EUA for a COVID-19 vaccine prior to the completion of large randomized clinical efficacy trials could reduce the ability to demonstrate effectiveness of the investigational vaccine in a clinical disease endpoint efficacy trial to support licensure, and such clinical disease endpoint efficacy trials may be needed to investigate the potential for vaccine-associated [enhanced respiratory disease]. Thus, for a vaccine for which there is adequate manufacturing information, issuance of an EUA may be appropriate once studies have demonstrated the safety and effectiveness of the vaccine but before the manufacturer has submitted and/or FDA has completed its formal review of the biologics license application.[3]

In other words, under this guidance, the FDA could issue an EUA for a COVID-19 vaccine based on a safety and efficacy data set that contains less data than would later be available when a BLA for the vaccine is submitted to the agency for approval. The issuance of the EUA would be followed later by a formal BLA submission to the FDA and the FDA's normal review. Thus, the evaluation of whether the known and potential benefits of a COVID-19 vaccine outweigh the known and potential risks under the EUA process will by its very nature be based on more limited data and a less complete and robust FDA review than would occur under the full, better-informed BLA review and approval process.

No evidence that the FDA has ever issued an EUA for any vaccine for a pandemic/epidemic-causing infectious agent

Not surprisingly, given that vaccines for common infections are used by hundreds of millions of people, we found no evidence in online FDA records of the agency issuing an EUA for any vaccine for preventing or mitigating an epidemic or pandemic. A search of the FDA's databases showed that no currently active EUAs[4] or previously granted EUAs that are no longer in effect[5] authorized use of such a vaccine. There have been multiple EUAs granted for other FDA-regulated products, including protective equipment, diagnostic tests, and treatments for viral diseases such as influenza and COVID-19, but the agency appears to date to have drawn the line against issuing EUAs for vaccines, with one exception: At the request of the Department of

[3] Food and Drug Administration. Development and licensure of vaccines to prevent COVID-19; guidance for industry. June 2020. https://www.fda.gov/media/139638/download. Accessed August 5, 2020.
[4] Food and Drug Administration. Emergency Use Authorization. https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization. Accessed August 5, 2020.
[5] Food and Drug Administration. Emergency Use Authorization--archived information. https://wayback.archive-it.org/7993/20180424110451/https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm264224.htm. Accessed August 5, 2020.

Defense, the FDA issued an EUA for an anthrax vaccine because of the purported threat of biological warfare involving anthrax, a circumstance that is irrelevant to a COVID-19 vaccine.[6]

These observations provide a strong signal that the FDA has long recognized the importance of allowing the marketing of a vaccine for a common infectious disease only after clinical trials necessary for BLA approval have been completed and thoroughly evaluated by FDA staff and the appropriate advisory committees.

Prior public opinion poll showing widespread negative attitudes toward use of a vaccine made available under an EUA

In 2009, in the midst of the H1N1 swine flu pandemic, a study was published with the results of a national opinion survey of 1,543 representative U.S. adults designed to measure respondents' willingness to accept a new, unapproved vaccine.[7] When asked, if they had to make a decision now, would they be willing to take "a new but not yet approved vaccine for swine flu," 63.5% indicated they would not take it, 27.8% were undecided, and only 8.7% were willing to take the vaccine. Overall, 48.8% said they would be very or extremely worried if they "were offered a flu vaccine that was recently developed and not yet approved by the U.S. Food and Drug Administration," and an additional 28.4% said they were moderately worried.

Another telling finding was that a significantly larger proportion of those who would refuse the vaccine (65.4%) were confident about their decision than were those who would accept (45.8%) or were unsure about accepting (25.9%) the vaccine ($p<0.001$).

The survey study authors also discussed improvements in communication with potential vaccine recipients that could provide more information about the process wherein an EUA for a vaccine is granted. Despite the usefulness of some of these suggestions, the striking difference between the significantly smaller amount of efficacy and safety data required for issuing an EUA than for FDA approval of a BLA is inescapable.

Unfortunately, present vaccine hesitation based, for example, on concern about vaccines causing autism — despite the clear evidence discounting such a link — will surely grow if the FDA allows an EUA for a COVID-19 vaccine. Already, the agency's decisions to issue EUAs for chloroquine and hydroxychloroquine for treatment of COVID-19 and for several poorly performing COVID-19 diagnostic tests have heightened public distrust about the agency's decision-making process and whether it is compromising its scientific standards.

If COVID-19 vaccines were to be made available under the EUA pathway, there clearly would be less efficacy and safety data and less thorough FDA evaluation than if BLA approval were

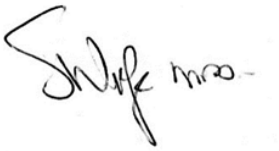
[6] Food and Drug Administration. Notice: Authorization of emergency use of anthrax vaccine adsorbed for prevention of inhalation anthrax by individuals at heightened risk of exposure due to attack with anthrax; availability. *Federal Register*. February 2, 2005. https://www.federalregister.gov/documents/2005/02/02/05-2028/authorization-of-emergency-use-of-anthrax-vaccine-adsorbed-for-prevention-of-inhalation-anthrax-by. Accessed August 5, 2020.

[7] Quinn SC, Kumar S, Freimuth VS, et al. Public willingness to take a vaccine or drug under Emergency Use Authorization during the 2009 H1N1 Pandemic. *Biosecur Bioterror*. 2009;7(3):275-290.

required. The "logic" of saving several months by a faster but riskier EUA pathway will surely be outweighed by the loss in public confidence in the vaccine, accompanied by decreased willingness to be vaccinated.

We therefore strongly urge you to promptly end any further consideration of issuing EUAs for COVID-19 vaccines. Thank you for your attention to this urgent public health matter.

Sincerely,



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