December 6, 2022

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Sent via email to: contact@interestofjustice.org

RE: Citizen Petition (Docket Number: FDA-2022-P-2411)

Dear Petitioner,

This letter responds to the citizen petition (the Petition) dated September 30, 2022 that you (Petitioner) submitted to the Food and Drug Administration (FDA, the Agency, we) requesting that FDA revoke the emergency use authorizations (EUAs) for certain COVID-19 vaccines.

This letter responds to the Petition in full. We have carefully reviewed the Petition and other information available to the Agency. Based on our review of these materials, and for the reasons described below, we conclude that the Petition does not contain facts demonstrating any reasonable grounds for the requested action. In accordance with Title 21 CFR (Code of Federal Regulations) 10.30(e)(3), and for the reasons stated below, FDA is denying the Petition.

Here is an outline of FDA's response:

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

I. BACKGROUND

There is currently a pandemic of respiratory disease, COVID-19, caused by a novel coronavirus, SARS-CoV-2. The COVID-19 pandemic presents an extraordinary challenge to global health. On January 31, 2020, the Department of Health and Human Services (HHS) issued a declaration of a public health emergency related to COVID-19.[1] On February 4, 2020, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the Secretary of HHS determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States (U.S.) citizens living abroad, and that involves the virus that causes COVID-19.[2] On the basis of such determination, on March 27, 2020, the Secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic ("COVID-19 EUA Declaration"),

[1] Secretary of HHS Alex M. Azar, Determination that a Public Health Emergency Exists (Originally issued on Jan. 31, 2020, and subsequently renewed), https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx.
[2] HHS, Determination of Public Health Emergency, 85 FR 7316, February 7, 2020, https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.

pursuant to section 564(b)(1) of the FD&C Act.[3] In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.[4]

Commercial vaccine manufacturers and other entities have developed and are developing COVID-19 vaccines, and clinical studies of these vaccines are underway and/or have been publicly reported. FDA has issued EUAs for vaccines to prevent COVID-19, including monovalent[5] vaccines sponsored by Pfizer Inc. (Pfizer)[6] and ModernaTX, Inc. (Moderna)[7] and bivalent[8] vaccines sponsored by Pfizer[9] and Moderna[10]. The EUAs have been amended since initial issuance.

On August 23, 2021, the Agency approved the Biologics License Application (BLA) for Comirnaty (COVID-19 Vaccine, mRNA), and the approval was granted to BioNTech Manufacturing GmbH.[11] Comirnaty is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older. On January 31, 2022, the Agency approved the BLA for Spikevax (COVID-19 Vaccine, mRNA), and the approval was granted to Moderna. Spikevax is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older.

II. VACCINES THAT ARE FDA-LICENSED OR RECEIVE AN EMERGENCY USE AUTHORIZATION MEET RELEVANT STATUTORY REQUIREMENTS

A. Investigational New Drugs

FDA's investigational new drug process applies to the development of new drugs and biological products, including vaccines.[12] Before a vaccine is licensed (approved) by FDA for use by the public, FDA requires that it undergo a rigorous and extensive development program to determine the vaccine's safety and effectiveness. This development program encompasses preclinical

[3] HHS, Emergency Use Authorization Declaration, 85 FR 18250, April 1, 2020, https://www.federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration.
[4] Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak, issued March 13, 2020, https://trumpwhitehouse.archives.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/.
[5] For the purposes of this letter, monovalent refers to any FDA authorized or approved COVID-19 vaccine that contains or encodes the spike protein of only the Original SARS-CoV-2.
[6] Hereinafter "Pfizer-BioNTech COVID-19 Vaccine".
[7] Hereinafter "Moderna COVID-19 Vaccine".
[8] For the purposes of this letter, unless otherwise specified, bivalent refers to any FDA authorized COVID-19 vaccine that encodes the spike protein of the Original SARS-CoV-2 and the Omicron BA.4/BA.5 SARS-CoV-2.
[9] Hereinafter "Pfizer-BioNTech COVID-19 Vaccine, Bivalent".
[10] Hereinafter "Moderna COVID-19 Vaccine, Bivalent".
[11] BioNTech Manufacturing GmbH is the biologics license holder for this vaccine, which is manufactured by Pfizer for BioNTech Manufacturing GmbH.
[12] See 21 CFR 312.2(a) (explaining that the regulations in 21 CFR Part 312 apply to clinical investigations of both drugs and biologics).

research (laboratory research, animal studies[13]) and clinical studies. At the preclinical stage, the sponsor focuses on collecting the data and information necessary to establish that the product will not expose humans to unreasonable risks when used in limited, early-stage clinical studies. Clinical studies, in humans, are conducted under well-defined conditions and with careful safety monitoring through all the phases of the investigational new drug process. FDA's regulations governing the conduct of clinical investigations are set out at 21 CFR Part 312.

Before conducting a clinical investigation in the U.S. in which a new drug or biological product is administered to humans, a sponsor must submit an investigational new drug application (IND) to FDA.[14] The IND describes the proposed clinical study in detail and, among other things, helps protect the safety and rights of human subjects.[15] In addition to other information, an IND must contain information on clinical protocols and clinical investigators.[16] Detailed protocols for proposed clinical studies permit FDA to assess whether the initial-phase trials will expose subjects to unnecessary risks. Information on the qualifications of clinical investigators (professionals, generally physicians, who oversee the administration of the investigational drug) permits FDA to assess whether they are qualified to fulfill their clinical trial duties. The IND includes commitments to obtain informed consent from the research subjects, to obtain review of the study by an institutional review board (IRB),[17] and to adhere to the IND regulations.

Once the IND is submitted, the sponsor must wait 30 calendar days before initiating any clinical trials, unless FDA informs the sponsor that the trial may begin earlier. During this time, FDA reviews the IND. FDA's primary objectives in reviewing an IND are, in all phases of the investigation, to assure the safety and rights of subjects, and, in Phase 2 and Phase 3, to help assure that the quality of the scientific evaluation of drugs is adequate to permit an evaluation of the drug's effectiveness and safety.[18]

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[13] We support the principles of the "3Rs," to reduce, refine, and replace animal use in testing when feasible. We encourage sponsors to consult with us if they wish to use a non-animal testing method they believe is suitable, adequate, validated, and feasible. We will consider if such an alternative method could be assessed for equivalency to an animal test method.

[14] See 21 CFR 312.20(a).

[15] For additional information regarding the IND review process and general responsibilities of sponsor-investigators related to clinical investigations see Investigational New Drug Applications Prepared and Submitted by Sponsor-Investigators; Draft Guidance for Industry, May 2015, https://www.fda.gov/media/92604/download. This draft guidance, when finalized, will represent the current thinking of the Agency on this topic.

[16] See, e.g., 21 CFR 312.23(a)(6).

[17] The IRB is a panel of scientists and non-scientists in hospitals and research institutions that oversees clinical research. IRBs approve clinical study protocols, which describe the type of people who may participate in the clinical study; the schedule of tests and procedures; the medications and dosages to be studied; the length of the study; the study's objectives; and other details. IRBs make sure that the study is acceptable, that participants have given consent and are fully informed of the risks, and that researchers take appropriate steps to protect patients from harm. See The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective web page, last updated November 2017, https://www.fda.gov/drugs/drug-information-consumers/fdas-drug-review-process-ensuring-drugs-are-safe-and-effective.

[18] 21 CFR 312.22(a).

FDA's regulations provide that, once an IND is in effect, the sponsor may conduct a clinical investigation of the product, with the investigation generally being divided into three phases. With respect to vaccines, the initial human studies, referred to as Phase 1 studies, are generally safety and immunogenicity studies performed in a small number of closely monitored subjects. Phase 2 studies may include up to several hundred individuals and are designed to provide information regarding the incidence of common short-term side effects such as redness and swelling at the injection site or fever and to further describe the immune response to the investigational vaccine. If an investigational new vaccine progresses past Phase 1 and Phase 2 studies, it may progress to Phase 3 studies. For Phase 3 studies, the sample size is often determined by the number of subjects required to establish the effectiveness of the new vaccine, which may be in the thousands or tens of thousands of subjects. Phase 3 studies provide the critical documentation of effectiveness and important additional safety data required for licensing.

Additionally, FDA regulations require that an IRB must review clinical investigations involving children as subjects covered by 21 CFR part 50, subpart D and only approve those clinical investigations involving children as subjects that satisfy the criteria in 21 CFR part 50, subpart D, Additional Safeguards for Children in Clinical Investigations. As explained in the preamble to the final rule, "[t]hese safeguards are intended to ensure that the rights and welfare of children who participate in clinical investigations are adequately protected."[19]

At any stage of development, if data raise significant concerns about either safety or effectiveness, FDA may request additional information or studies; FDA may also halt ongoing clinical studies. The FD&C Act provides a specific mechanism, called a "clinical hold," for prohibiting sponsors of clinical investigations from conducting the investigation (section 505(i)(3) of the FD&C Act; 21 U.S.C. § 355(i)(3)), and FDA's IND regulations in 21 CFR 312.42 identify the circumstances that may justify a clinical hold. Generally, a clinical hold is an order issued by FDA to the sponsor of an IND to delay a proposed clinical investigation or to suspend an ongoing investigation.[20]

B. Licensed Vaccines Are Safe, Pure, and Potent

FDA has a stringent regulatory process for licensing vaccines.[21, 22] The Public Health Service Act (PHS Act) authorizes FDA to license biological products, including vaccines, if they have been demonstrated to be "safe, pure, and potent."[23] Prior to approval by FDA, vaccines are extensively tested in non-clinical studies and in humans. FDA's regulations describe some of the

[19] Additional Safeguards for Children in Clinical Investigations of Food and Drug Administration-Regulated Products, 78 FR 12937 at 12938, February 26, 2013, https://www.federalregister.gov/documents/2013/02/26/2013-04387/additional-safeguards-for-children-in-clinical-investigations-of-food-and-drug.
[20] 21 CFR 312.42(a).
[21] CDC, Ensuring the Safety of Vaccines in the United States, February 2013, https://www.cdc.gov/vaccines/hcp/patient-ed/conversations/downloads/vacsafe-ensuring-bw-office.pdf.
[22] Vaccine Safety Questions and Answers, last updated March 2018, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/vaccine-safety-questions-and-answers.
[23] Section 351(a)(2)(C)(i)(I) of the PHS Act.

extensive data and information that each sponsor of a BLA for a vaccine must submit to FDA in order to demonstrate the product's safety, purity, and potency before FDA will consider licensing the vaccine. FDA requires that the sponsor's application include, among other things, data derived from nonclinical and clinical studies showing the product's safety, purity, and potency; a full description of manufacturing methods for the product; data establishing the product's stability through the dating period; and representative sample(s) of the product and summaries of results of tests performed on the lot(s) represented by the sample.[24]

As is evident from the language of the PHS Act and FDA's regulations, the licensure process for a vaccine requires the sponsor to establish, through carefully controlled laboratory and clinical studies, as well as through other data, that the product is safe and effective for its proposed uses. FDA's multidisciplinary review teams then rigorously evaluate the sponsor's laboratory and clinical data, as well as other information, to help assess whether the safety, purity, and potency of a vaccine have been demonstrated.[25] Only when FDA's standards are met is a vaccine licensed.

FDA regulations explicitly state that "[a]pproval of a biologics license application or issuance of a biologics license shall constitute a determination that the establishment(s) and the product meet applicable requirements to ensure the continued safety, purity, and potency of such products."[26] Therefore, the manufacturers of vaccines that have been licensed in the U.S. have necessarily demonstrated the safety, purity, and potency of the vaccines within the meaning of the applicable statutory and regulatory provisions before the vaccines were licensed and allowed to be marketed.

C. An Emergency Use Authorization for a COVID-19 Preventative Vaccine Is Issued Only If the Relevant Statutory Standards Are Met

Congress established the EUA pathway to ensure that, during public health emergencies, potentially lifesaving medical products could be made available before being approved. The EUA process allows the Secretary of HHS, in appropriate circumstances, to declare that EUAs are justified for products to respond to certain types of threats. When such a declaration is made, FDA may issue an EUA, which is different from the regulatory process for vaccine licensure.

Section 564 of the FD&C Act authorizes FDA to, under certain circumstances, issue an EUA to allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by chemical, biological, radiological, or nuclear (CBRN) threat agents when there are no adequate, approved, and available alternatives.

On February 4, 2020, pursuant to section 564(b)(1)(C) of the FD&C Act, the Secretary of HHS 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 the

[24] 21 CFR 601.2(a).
[25] FDA, Vaccines, last updated August 2022, https://www.fda.gov/vaccines-blood-biologics/vaccines.
[26] 21 CFR 601.2(d).

virus that causes COVID-19.[27] On the basis of such determination, on March 27, 2020, the Secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to section 564(b)(1) of the FD&C Act.[28]

Based on this declaration and determination, under section 564(c) of the FD&C Act, FDA may issue an EUA during the COVID-19 pandemic after FDA concludes that the following statutory requirements are met:

- The agent referred to in the COVID-19 EUA Declaration by the Secretary (SARS-CoV-2) can cause a serious or life-threatening disease or condition.

- Based on the totality of scientific evidence available, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing such serious or life-threatening disease or condition that can be caused by SARS-CoV-2.

- The known and potential benefits of the product, when used to diagnose, prevent, or treat the identified serious or life-threatening disease or condition, outweigh the known and potential risks of the product.

- There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the disease or condition.

Although EUAs are governed under a different statutory framework than BLAs, FDA has made clear that issuance of an EUA for a COVID-19 vaccine would require that the vaccine demonstrated clear and compelling safety and efficacy in a large, well-designed Phase 3 clinical trial. In the guidance document Emergency Use Authorization for Vaccines to Prevent COVID-19 (EUA Vaccine Guidance), FDA has provided recommendations that describe key information that would support issuance of an EUA for a vaccine to prevent COVID-19.[29] In the EUA Vaccine Guidance, FDA explained that, in the case of such investigational vaccines, any assessment regarding an EUA will be made on a case-by-case basis considering the target population, the characteristics of the product, the preclinical and human clinical study data on the product, and the totality of the available scientific evidence relevant to the product.[30] FDA has also stated, in this guidance, that for a COVID-19 vaccine for which there is adequate manufacturing information to ensure its quality and consistency, issuance of an EUA would require a determination by FDA that the vaccine's benefits outweigh its risks based on data from at least one well-designed Phase 3 clinical trial that demonstrates the vaccine's safety and efficacy in a clear and compelling manner.[31]

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[27] HHS, Determination of Public Health Emergency, 85 FR 7316, February 7, 2020, https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.
[28] COVID-19 EUA Declaration.
[29] Emergency Use Authorization for Vaccines to Prevent COVID-19; Guidance for Industry, March 2022, (EUA Vaccine Guidance), https://www.fda.gov/media/142749/download.
[30] *Id.* at 4.
[31] *Id.*

A Phase 3 trial of a vaccine is generally a clinical trial in which a large number of people are assigned to receive the investigational vaccine or a control. In general, in Phase 3 trials that are designed to show whether a vaccine is effective, neither people receiving the vaccine nor those assessing the outcome know who received the vaccine or the comparator.

In a Phase 3 study of a COVID-19 vaccine, the efficacy of the investigational vaccine to prevent disease will be assessed by comparing the number of cases of disease in each study group. For Phase 3 placebo- controlled efficacy trials, FDA has recommended to manufacturers in guidance that the vaccine should be at least 50% more effective than the comparator, and that the outcome be reliable enough so that it is not likely to have happened by chance.[32] During the entire study, subjects will be monitored for safety events. If the evidence from the clinical trial meets the pre-specified criteria for success for efficacy and the safety profile is acceptable, the results from the trial can potentially be submitted to FDA in support of an EUA request.

During the current public health emergency, manufacturers may, with the requisite data and taking into consideration input from FDA, choose to submit a request for an EUA. It is FDA's expectation that, following submission of an EUA request and issuance of an EUA, a sponsor would continue to evaluate the vaccine and would also work towards submission of a BLA as soon as possible.[33]

D. FDA Periodically Reviews Authorizations and May Revise or Revoke an Emergency Use Authorization if the Issuance Criteria Are No Longer Met

An EUA will remain in effect until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products is terminated under section 564(b)(2) of the FD&C Act or the EUA is revoked under section 564(g) of the FD&C Act. Section 564(g) provides that "[t]he Secretary shall periodically review the circumstances and the appropriateness of an authorization" under section 564. In addition, section 564(g)(2) states the Secretary "may revise or revoke an authorization" if:

- the circumstances described under [section 564(b)(1) of the FD&C Act] no longer exist;
- the criteria under [section 564(c) of the FD&C Act] for issuance of such authorization are no longer met; or
- other circumstances make such revision or revocation appropriate to protect the public health or safety.

[32] Development and Licensure of Vaccines to Prevent COVID-19; Guidance for Industry, June 2020, (Vaccine Development and Licensure Guidance), https://www.fda.gov/media/139638/download.
[33] *Id.*

Consistent with these provisions and section 564(g)(1) of the FD&C Act, FDA periodically reviews the circumstances and appropriateness of an EUA and revises or revokes an EUA if the criteria in section 564(g)(2) are met and if certain circumstances exist.[34]

III. DISCUSSION

On August 31, 2022, FDA authorized the Moderna COVID-19 Vaccine, Bivalent for use as a single booster dose in individuals 18 years of age and older and also authorized the Pfizer-BioNTech COVID-19 Vaccine, Bivalent for use as a single booster dose in individuals 12 years of age and older. The "Action Requested" section of the Petition refers to these August 31, 2022 authorizations, stating, "[o]n August 31, 2022, the FDA amended [EUAs] of the Moderna COVID-19 Vaccine and the Pfizer-BioNTech COVID-19 Vaccine to authorize bivalent formulations of the vaccines . . . ."[35] Petitioner then states, "[t]his petition DEMANDS that you revoke this authorization, or at minimum, IMMEDIATELY suspend it . . . ."[36]

We interpret this as a request for FDA to revoke[37] the EUA for the Moderna COVID-19 Vaccine, Bivalent and the EUA for the Pfizer-BioNTech COVID-19 Vaccine, Bivalent. We note that on October 12, 2022, FDA amended the EUAs for the Moderna COVID-19 Vaccine, Bivalent and the Pfizer-BioNTech COVID-19 Vaccine, Bivalent to authorize their use as a single booster dose in younger age groups (see additional discussion in section III.A.i of this letter). Although the Petition was submitted prior to October 12, 2022 and does not reference FDA's authorization of the Moderna COVID-19 Vaccine, Bivalent and the Pfizer-BioNTech COVID-19 Vaccine, Bivalent in these younger age groups, this response explains that the Petition provides no basis for FDA to revoke the EUA for the Moderna COVID-19 Vaccine, Bivalent or the EUA for the Pfizer-BioNTech COVID-19 Vaccine, Bivalent in any age group.

Although the "Action Requested" section of the Petition focuses on FDA's authorization of bivalent mRNA COVID-19 vaccines (i.e., the Moderna COVID-19 Vaccine, Bivalent and the Pfizer-BioNTech COVID-19 Vaccine, Bivalent), we note that certain language in other sections of the Petition refers more broadly to mRNA COVID-19 vaccines. For example, the Petition states, "[t]his is a Citizens Petition to revoke . . . all other authorization for mRNA Gene Therapies misbranded as vaccines" and "[w]e invoke the right to demand the EUA for all mRNA products revoked today . . . ."[38] To the extent the Petition can be interpreted as requesting that FDA revoke the EUAs for other authorized mRNA COVID-19 vaccines, this response explains that the Petition provides no basis for such an action.

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[34] Emergency Use Authorization of Medical Products and Related Authorities; Guidance for Industry and Other Stakeholders, January 2017, (EUA Guidance), at 29, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities.

[35] Petition at 2.

[36] *Id.* at 3.

[37] In responding to the request in the Petition that FDA "revoke this authorization, or at a minimum, IMMEDIATELY suspend it," this letter uses the terminology used in section 564 of the FD&C Act, which describes circumstances under which FDA may revise or revoke an EUA. See Petition at 3 and section 564(g)(2) of the FD&C Act. Because the Petition does not request a revision to the EUAs, this letter focuses on the grounds for revocation.

[38] Petition at 1 and 9.

A. Petitioner's Request that FDA Revoke Authorizations for the Moderna and Pfizer-BioNTech Bivalent COVID-19 Vaccines

As explained above, we interpret the Petition as requesting that FDA revoke the EUA for the Moderna COVID-19 Vaccine, Bivalent and the EUA for the Pfizer-BioNTech COVID-19 Vaccine, Bivalent. Below we address this request and the information submitted by Petitioner in support of this requested action.

i. EUAs for the Pfizer-BioNTech and Moderna COVID-19 Vaccines

a. EUA for the Pfizer-BioNTech COVID-19 Vaccine

On December 11, 2020, FDA issued an EUA for emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 in individuals 16 years of age and older. The EUA was subsequently amended.[39] Currently, the Pfizer-BioNTech COVID-19 Vaccine[40] is authorized for emergency use as a:

- Two-dose primary series for individuals 5 years of age and older,
- Third primary series dose for individuals 5 years of age and older who have been determined to have certain kinds of immunocompromise,
- Three-dose primary series for individuals 6 months through 4 years of age.

On August 31, 2022, the EUA was amended to authorize the Pfizer-BioNTech COVID-19 Vaccine, Bivalent as a single booster dose for the prevention of COVID-19 in individuals 12 years of age and older. On October 12, 2022, the EUA was amended to authorize the Pfizer-BioNTech COVID-19 Vaccine, Bivalent as a single booster dose for the prevention of COVID-19 in individuals 5 through 11 years of age. Currently, the Pfizer-BioNTech COVID-19 Vaccine, Bivalent is authorized for emergency use in individuals 5 years of age and older as a single booster dose administered at least 2 months after either:

- completion of primary vaccination with any FDA authorized or approved monovalent COVID-19 vaccine, or
- receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine.

The Agency issued the EUA after a thorough evaluation of scientific data regarding the safety, effectiveness, and manufacturing information and after reaching a determination that the vaccine

[39] For a description of all revisions to the EUA, see Pfizer-BioNTech COVID-19 Vaccine Letter of Authorization, October 12, 2022. This Letter of Authorization is posted on www.fda.gov.

[40] Comirnaty is the proprietary name for the product licensed under the BLA. The Pfizer-BioNTech COVID-19 Vaccine has been available since December 11, 2020, pursuant to EUA. The two approved formulations of Comirnaty are the same formulations, respectively, as the two FDA-authorized monovalent formulations of Pfizer-BioNTech COVID-19 Vaccine for individuals ≥12 years, and vials of the BLA-compliant vaccine may bear the name "Pfizer-BioNTech COVID-19 Vaccine." Because of these features, and because Comirnaty is commonly referred to as the "Pfizer vaccine" or the "Pfizer-BioNTech COVID-19 Vaccine," certain references in this section to "Pfizer-BioNTech COVID-19 Vaccine" may also be applicable to uses of Comirnaty that are authorized under EUA.

meets the statutory requirements under section 564 of the FD&C Act. This letter incorporates by reference the EUA Review Memoranda,[41] which discuss this determination, and the data upon which it was based, in detail.[42]

b. EUA for the Moderna COVID-19 Vaccine

On December 18, 2020, FDA issued an EUA for emergency use of the Moderna COVID-19 Vaccine for the prevention of COVID-19 for individuals 18 years of age and older. The EUA was subsequently amended.[43] Currently, the Moderna COVID-19 Vaccine[44] is authorized for emergency use as a:

- Two-dose primary series for individuals 6 months of age and older,
- Third primary series dose for individuals 6 months of age and older who have been determined to have certain kinds of immunocompromise.

On August 31, 2022, the EUA was amended to authorize the Moderna COVID-19 Vaccine, Bivalent as a single booster dose for the prevention of COVID-19 in individuals 18 years of age and older. On October 12, 2022, the EUA was amended to authorize the Moderna COVID-19 Vaccine, Bivalent as a single booster dose for the prevention of COVID-19 in individuals 6 through 17 years of age. Currently, the Moderna COVID-19 Vaccine, Bivalent is authorized for emergency use in individuals 6 years of age and older as a single booster dose administered at least 2 months after either:

- a completion of primary vaccination with any FDA authorized or approved monovalent COVID-19 vaccine, or
- receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine.

The Agency issued the EUA after a thorough evaluation of scientific data regarding the safety, effectiveness, and manufacturing information and after reaching a determination that the vaccine

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[41] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memoranda and Addenda to Decision Memoranda, dated December 11, 2020; May 10, 2021; August 12, 2021; September 22, 2021; October 20, 2021; October 29, 2021; November 18, 2021; November 19, 2021; December 8, 2021; December 30, 2021; January 6, 2022; March 28, 2022; May 17, 2022; June 16, 2022; August 31, 2022; October 11, 2022 (referred to collectively in this response as "FDA's Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memoranda and Addenda"), available at https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine.

[42] This letter incorporates by reference FDA's Summary Basis for Regulatory Action (SBRA) for Comirnaty, available at https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine#comirnaty.

[43] For a description of all revisions to the EUA, see Moderna COVID-19 Vaccine Letter of Authorization, October 12, 2022. This Letter of Authorization is posted on www.fda.gov.

[44] Spikevax is the proprietary name for the product licensed under the BLA. The Moderna COVID-19 Vaccine has been available since December 18, 2020, pursuant to EUA. The approved formulation of Spikevax and the FDA-authorized Moderna COVID-19 Vaccine for providing the primary series in individuals ≥12 years are the same formulation. Because of these features, and because Spikevax may be commonly referred to as the "Moderna vaccine" or the "Moderna COVID-19 Vaccine," certain references in this section to "the Moderna COVID-19 Vaccine" may also be applicable to uses of Spikevax that are authorized under EUA.

meets the statutory requirements under section 564 of the FD&C Act. This letter incorporates by reference the EUA Review Memoranda, which discuss this determination,[45] and the data upon which it was based, in detail.[46]

ii. The Standard for Revocation of EUAs Is Not Met

Section 564(g)(2) of the FD&C Act provides the standard for revocation of an EUA. Under this statutory authority, FDA may revise or revoke an EUA if:

> (A) the circumstances described under [section 564(b)(1) of the FD&C Act] no longer exist;
> (B) the criteria under [section 564(c) of the FD&C Act] for issuance of such authorization are no longer met; or
> (C) other circumstances make such revision or revocation appropriate to protect the public health or safety.

At the outset, we note that Congress has provided FDA with discretion under section 564 of the FD&C Act and nothing in the statute *requires* FDA to *revoke* existing EUAs in any circumstance. Rather, section 564(g)(2) of the FD&C Act says that, in certain circumstances, FDA "*may* revise or revoke" an EUA.[47] The verb "may" is ordinarily permissive, particularly when the statute elsewhere uses the term "shall" to confer a mandatory duty.[48] Further underscoring FDA's discretion, the EUA statute explicitly provides that all decisions regarding EUAs are "committed to agency discretion."[49]

A permissive reading of "may" also accords with the statutory purpose of giving FDA flexibility to "permit rapid distribution of promising new drugs and antidotes in the most urgent

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[45] FDA, Moderna COVID-19 Vaccine EUA Decision Memoranda and Addenda to Decision Memoranda, dated December 18, 2020; August 12, 2021; October 20, 2021; November 18, 2021; November 19, 2021; December 30, 2021; January 6, 2022; March 28, 2022; June 16, 2022; August 31, 2022; September 20, 2022; September 26, 2022; September 28, 2022; October 6, 2022; October 11, 2022; October 14, 2022; October 20, 2022; October 28, 2022; November 4, 2022; November 19, 2022; November 28, 2022 (referred to collectively in this response as "FDA's Moderna COVID-19 Vaccine EUA Decision Memoranda and Addenda"), available at https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/spikevax-and-moderna-covid-19-vaccine.

[46] This letter incorporates by reference FDA's Summary Basis for Regulatory Action (SBRA) for Spikevax, available at https://www.fda.gov/vaccines-blood-biologics/spikevax.

[47] Section 564(g)(2) of the FD&C Act (emphasis added).

[48] See *Old Line Life Ins. Co. of Am. v. Garcia*, 411 F.3d 605, 614-615 (6th Cir. 2005); *Goodman v. City Prods. Corp, Ben Franklin Div.*, 425 F.2d 702, 703 (6th Cir. 1970); *Anderson v. Yungkau*, 329 U.S. 482, 485 (1947) ("[W]hen the same Rule uses both 'may' and 'shall,' the normal inference is that each is used in its usual sense—the one act being permissive, the other mandatory."); see also A. Scalia & B.A. Garner, *Reading Law: The Interpretation of Legal Texts* 112 (2012) ("The traditional, commonly repeated rule is that *shall* is mandatory and *may* is permissive. . ."). There is nothing to indicate that section 564(g)(2) of the FD&C Act departs from this ordinary meaning of "may."

[49] See section 564(i) of the FD&C Act. *See also Association of American Physicians & Surgeons v. FDA*, 2020 WL 5745974, at *3 (6th Cir. Sept. 24, 2020) (citing to section 564(i) of the FD&C Act for the proposition that "emergency-use authorizations are exempt from review under the [Administrative Procedure Act].").

circumstances,"[50] because it allows the Agency to permit continued distribution of EUA products and thereby removes the need for manufacturers to limit supply or delay seeking approval to exhaust supplies of authorized product.

FDA's EUA Guidance notes that once an EUA is issued for a product, in general, that EUA will remain in effect for the duration of the EUA declaration under which it was issued, "unless the EUA is revoked because the criteria for issuance . . . are no longer met or revocation is appropriate to protect public health or safety (section 564(f),(g) [of the FD&C Act])."[51] Thus, in this section, we assess whether any of the statutory conditions under which FDA may revoke an EUA are met, namely: (1) whether the circumstances described under section 564(b)(1) of the FD&C Act no longer exist, (2) whether the criteria for their issuance under section 564(c) of the FD&C Act are no longer met, and (3) whether other circumstances make a revision or revocation appropriate to protect the public health or safety.

a. Circumstances Described under Section 564(b)(1) of the FD&C Act Continue to Exist

Section 564(b)(1) of the FD&C Act describes the circumstances under which the HHS Secretary may declare that circumstances exist justifying the issuance of EUAs. As explained above, on February 4, 2020, pursuant to section 564(b)(1)(C) of the FD&C Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of HHS 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 the virus that causes COVID-19.[52] On the basis of such determination, on March 27, 2020, the Secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to section 564(b)(1) of the FD&C Act (21 U.S.C. § 360bbb-3(b)(1)).[53]

Based on this declaration and determination, under section 564(c) of the FD&C Act (21 U.S.C. § 360bbb-3(c)), FDA may issue an EUA during the COVID-19 pandemic after FDA concludes that the statutory requirements provided in section 564(c) are met. Section 564(b)(2) sets forth the statutory standard for termination of an EUA declaration. An EUA declaration remains in place until the earlier of: (1) a determination by the HHS Secretary that the circumstances that precipitated the declaration have ceased (after consultation as appropriate with the Secretary of Defense) or (2) a change in the approval status of the product such that the authorized use(s) of the product are no longer unapproved.

The Petition does not demonstrate, nor does the Petition assert any claim(s), that the circumstances described under section 564(b)(1) no longer exist. The Petition therefore has not shown that there are grounds for revoking the EUA for the Moderna COVID-19 Vaccine,

[50] See 2004 U.S.C.C.A.N. S17, S18 (Statement of President Bush Upon Signing P.L. 108-276, PROJECT BIOSHIELD ACT OF 2004).
[51] EUA Guidance at 28.
[52] HHS, Determination of Public Health Emergency, 85 FR 7316, February 7, 2020, https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.
[53] COVID-19 EUA Declaration.

Bivalent, or for revoking the EUA for the Pfizer-BioNTech COVID-19 Vaccine, Bivalent, on the basis of section 564(g)(2)(A) (i.e., on the basis that the circumstances described under section 564(b)(1) no longer exist).

b. The Criteria for the Issuance of the EUA Continue to Be Met

Section 564(g)(2)(B) of the FD&C Act provides that FDA may revise or revoke an authorization if the criteria for issuance of the authorization under section 564(c) of the FD&C Act are no longer met. This section describes why the Petition has not demonstrated that the criteria under section 564(c) of the FD&C Act are no longer met with respect to the Moderna COVID-19 Vaccine, Bivalent or the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and why, therefore, FDA is not revoking the EUAs for the Pfizer-BioNTech COVID-19 Vaccine, Bivalent or the Moderna COVID-19 Vaccine, Bivalent under the authority in section 564(g)(2)(B) of the FD&C Act.

1. Serious or Life-Threatening Disease or Condition

As explained above in section II.C of this letter, section 564(c)(1) of the FD&C Act requires that, for an EUA to be issued for a medical product, the "agent[s] referred to in [the HHS Secretary's EUA declaration] can cause a serious or life-threatening disease or condition." FDA has concluded that SARS-CoV-2, which is the subject of the EUA declaration, meets this standard.

The SARS-CoV-2 pandemic continues to present an extraordinary challenge to global health and, as of November 15, 2022, has caused more than 635 million cases of COVID-19 and claimed the lives of more than 6.61 million people worldwide.[54] In the United States, as of November 15, 2022, more than 97 million cases and over 1 million deaths have been reported to the Centers for Disease Control and Prevention (CDC).[55] On January 31, 2020, the Secretary of HHS declared a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS, and the U.S. President declared a national emergency in response to COVID-19 on March 13, 2020. Additional background information on the SARS-CoV-2 virus and COVID-19 pandemic may be found in FDA's EUA decision memoranda.[56]

As explained above, FDA has concluded that SARS-CoV-2 can cause a serious or life-threatening disease or condition. Petitioner has not provided any data, and FDA is not aware of any data, that change the conclusion that SARS-CoV-2 can cause a serious or life-threatening disease or condition. The Petition thus fails to establish that the criterion under section 564(c)(1) is no longer met for the Pfizer-BioNTech COVID-19 Vaccine, Bivalent or for the Moderna COVID-19 Vaccine, Bivalent.

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[54] Johns Hopkins University School of Medicine, Coronavirus Resource Center, https://coronavirus.jhu.edu/map.html (accessed November 15, 2022).
[55] CDC, COVID Data Tracker, https://covid.cdc.gov/covid-data-tracker/#datatracker-home (accessed November 15, 2022).
[56] See FDA's Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memoranda and Addenda and FDA's Moderna COVID-19 Vaccine EUA Decision Memoranda and Addenda.

2. Evidence of Effectiveness

Section 564(c)(2)(A) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude based on the totality of scientific evidence available[57] to the Secretary, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition that can be caused by SARS-CoV-2.

FDA has determined that based on the totality of scientific evidence available, it is reasonable to believe that the Pfizer-BioNTech COVID-19 Vaccine, Bivalent may be effective to prevent COVID-19 in individuals 5 years of age and older when administered as a booster dose at least 2 months after completion of primary vaccination or receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine. Likewise, FDA has also determined that based on the totality of scientific evidence available, it is reasonable to believe that the Moderna COVID-19 Vaccine, Bivalent may be effective to prevent COVID-19 in individuals 6 years of age and older when administered as a booster dose at least 2 months after completion of primary vaccination or receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine. The basis for the determination for authorization for both of these vaccines is explained in detail in FDA's decision memoranda regarding the Pfizer-BioNTech COVID-19 Vaccine, Bivalent[58] and the Moderna COVID-19 Vaccine, Bivalent[59] EUAs.

Petitioner presents no new data regarding the effectiveness of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent or the Moderna COVID-19 Vaccine, Bivalent that is of the scientific rigor that FDA would rely on for our scientific and regulatory decisions. However, Petitioner makes

[57] Petitioner makes multiple statements asserting that FDA did not consider the totality of the scientific evidence available. For example, Petitioner states, "**FDA'S AUTHORIZATION BASED ON 'A TOTALITY OF EVIDENCE' IS A FRAUD. OUR EVIDENCE WAS NOT CONSIDERED.**" Petition at 12. We disagree with these assertions and note that Petitioner does not identify any specific data or information that FDA failed to consider. As such, these assertions are not further discussed in this response.

[58] See FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) in Individuals 12 Years of Age and Older (Aug. 31, 2022), https://www.fda.gov/media/161595/download.; FDA Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) in Individuals 5 through 11 Years of Age (Oct. 11, 2022), https://www.fda.gov/media/162410/download.

[59] See FDA, Moderna COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) in Individuals 18 Years of Age and Older (Aug. 31, 2022), https://www.fda.gov/media/161554/download.; FDA, Moderna COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) in Individuals 6 Through 17 Years of Age (Oct. 11, 2022), https://www.fda.gov/media/162515/download.

several unsupported assertions relating to the effectiveness of the vaccines.[60] For example, Petitioner asserts that "[w]e have learned a fatal flaw about the Pfizer and Moderna COVID vaccines: they do not prevent people from becoming infected with, or transmitting COVID-19."[61] Additionally, Petitioner asserts that "[t]he EUA was issued to prevent COVID, it's a fraud of law to continue under that prong of the EUA law, which of course makes the approval VOID ab inito because it was always known by FDA that it couldn't work as a preventative or to confer immunity."[62] Petitioner further states that "[a]t this time no mRNA product has ever been found to be effective for the prevention or prophylactics of infectious diseases."[63] Petitioner also asserts that the authorization "erroneously ties immune response to 'protection' which is irrational and unscientific."[64]

It is important to note that the Pfizer-BioNTech COVID-19 Vaccine, Bivalent, and the Moderna COVID-19 Vaccine, Bivalent are authorized to prevent COVID-19, not to prevent SARS-CoV-2 infection or transmission. Additionally, a vaccine does not need to be 100% effective in preventing the target disease to meet the licensure or EUA standard. It is expected that some vaccinated individuals will contract the target disease despite having been vaccinated against it.

No FDA licensed or authorized vaccine is 100% effective, but scientific data have nevertheless demonstrated that vaccinations have been a very effective approach to protecting the public's health in the United States.[65] Similarly, a COVID-19 vaccine need not be 100% effective in preventing COVID-19, or even close to 100% effective in doing so, in order to have a significant effect in altering the course of the COVID-19 pandemic and for the known and potential benefits to outweigh the known and potential risks.

Authorization of both the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent were based, in part, on immunogenicity data accrued with bivalent vaccines encoding the spike protein of the Original SARS-CoV-2 and the spike protein of an Omicron strain (B.A.1). With regard to Petitioner's assertion that linking immune response to protection is "irrational and unscientific," Petitioner presents no new data that is of the scientific rigor that FDA would rely on for our scientific and regulatory decisions that would undermine FDA's approach. FDA notes that consideration of immunogenicity data is consistent with FDA guidance for industry.[66] As explained by FDA in the EUA Vaccine Guidance, "the effectiveness

[60] Some of these assertions are premised on the Petitioner's characterization of the vaccines as "investigational." For example, Petitioner states, "[i]t is not yet proven safe, effective because it is investigational." Petition at 3. To clarify, the clinical use of a product within the scope of an EUA is not a clinical investigation. Section 564(k) of the FD&C Act specifies that the use of a product within the scope of an EUA "shall not be considered to constitute a clinical investigation" for purposes of the statutes governing such investigations.
[61] Petition at 6.
[62] *Id.*
[63] *Id.* at 7.
[64] *Id.* at 12.
[65] FDA, Vaccine Safety Questions and Answers, last updated March 2018, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/vaccine-safety-questions-and-answers.
[66] EUA Vaccine Guidance, https://www.fda.gov/media/142749/download.

of a modified COVID-19 vaccine against a particular SARS-CoV-2 variant of concern (VOC) can be evaluated based on:

- The efficacy of primary vaccination with the manufacturer's authorized or approved prototype COVID-19 vaccine made by the same process and for which a clinical disease endpoint efficacy study has been conducted that met FDA pre-specified success criteria, AND
- Comparison of immune responses (assessed by neutralizing antibody) induced by the modified vaccine and the prototype vaccine."[67]

The Petition provides no information, nor is FDA aware of any information, that would undermine FDA's determinations that the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent may be effective to prevent COVID-19 when administered as a single booster dose at least 2 months after completion of primary vaccination or receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine. Therefore, the criterion under section 564(c)(2)(A) of the FD&C Act continues to be met.

3. Benefit-Risk Analysis

Section 564(c)(2)(B) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude that "the known and potential benefits of the product, when used to diagnose, prevent, or treat [the identified serious or life-threatening disease or condition], outweigh the known and potential risks of the product." FDA authorized the Pfizer-BioNTech COVID-19 Vaccine, Bivalent for emergency use in individuals 5 years of age older, and the Moderna COVID-19 Vaccine, Bivalent for emergency use in individuals 6 years of age and older, after reaching a determination that, among other things, the known and potential benefits of these vaccines, when used as a single booster dose to prevent COVID-19 in these populations, outweigh their known and potential risks.[68]

In this section, we address Petitioner's arguments relevant to the risks and benefits of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent and explain why they do not alter the Agency's determination that the criterion in section 564(c)(2)(B) is satisfied. For the reasons discussed in this section, the criterion under section 564(c)(2)(B) of the FD&C Act continues to be met.

[67] *Id.* at 20.

[68] For an extensive discussion of FDA's analysis of the data regarding the risks and benefits of these vaccines, see FDA's Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memoranda and Addenda and FDA's Moderna COVID-19 Vaccine EUA Decision Memoranda and Addenda.

Petitioner's Assertions Regarding Potential Risks Associated with Human Gene Therapy Products

Throughout the Petition, Petitioner refers to statements regarding potential risks of adverse events following exposure to human gene therapy products in FDA's January 2020 guidance document, "Long Term Follow-Up After Administration of Human Gene Therapy Products" (the "January 2020 Guidance").[69] For example, Petitioner states, "FDA January 2020 guidance . . . states the use of these experimental products affects DNA with an unreasonable risk to use in more than a few people at a time."[70] To clarify, the preceding statement does not appear in the January 2020 Guidance.

Moreover, the January 2020 Guidance specifies that it does not apply to vaccines for infectious disease indications.[71] Thus, the January 2020 Guidance does not apply to the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent. The January 2020 Guidance applies to all gene therapy clinical studies and to licensed gene therapy products for which long term follow-up observations are warranted based on analyses of available preclinical and clinical safety data for the product that raises concerns for delayed adverse events.[72]

FDA finds no basis in Petitioner's statements regarding potential risks with gene therapy products to change its conclusion that the known and potential benefits of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent outweigh the known and potential risks.

Petitioner's Claims Concerning Immune Responses and Antibody Dependent Enhancement

Petitioner makes various assertions relating to risks associated with immune responses and antibody dependent enhancement. For example, Petitioner states "Moderna says the bivalent vaccines create even more antibodies than the monovalent" and asserts that the immune response "to self antigens from gene therapy may introduce the risk for autoimmune like reactions…the

[69] Petitioner also refers in some places to what Petitioner characterizes as a "2018 gene therapy guidance." For example, Petitioner asserts that "FDA published serious risks and concerns about these same types of gene therapy products in 2018, but to approve these products today, the same FDA is now ignoring risks and FDA guidance recommendations they published just 4 years ago." Petition at 4. Petitioner further asserts that "FDA's 2018 gene therapy guidance recommendations (which FDA says is their 'current thinking on the matter') says 'there is an unreasonable risk' in widespread use of this gene therapy which they say can affect DNA and cause cancers, auto immune like disorders and long term adverse effects." Petition at 3. We note that the January 2020 Guidance finalized the draft guidance of the same title dated July 2018 (the "July 2018 Draft Guidance"). FDA interprets Petitioner's references to a 2018 gene therapy guidance as references to the July 2018 Draft Guidance. The July 2018 Draft Guidance noted that it was "for comment purposes only" and that it would reflect FDA's current thinking "when finalized."

[70] Petition at 1.

[71] Long Term Follow-Up After Administration of Human Gene Therapy Products; Guidance for Industry, January 2020, (January 2020 Guidance), at 2, https://www.fda.gov/media/113768/download.

[72] *Id*.

bivalents double the risk."[73] Petitioner claims that "UK Government data and all kinds of data that has been censored by the FDA and their cohorts within the CDC and WHO absolutely show that these bivalent and gene therapy products . . . are destroying people['s] immune system[s] causing antibody dependent enhancement."[74] Petitioner further states, "it's dangerous and recklessly endangering life by giving people Antibody Dependent Enhancement like AIDS."[75] Petitioner asserts that "FDA breached duty when they authorized these products with the facts sheet omitting a warning of the risk of autoimmune like reactions . . . ."[76]

Petitioner provides no evidence to support these assertions that is of the scientific quality FDA would consider in making scientific and regulatory decisions.[77] Therefore, Petitioner's assertions regarding immune response and antibody dependent enhancement do not alter FDA's determination that the known and potential benefits of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent outweigh the known and potential risks.

Petitioner's Statements Regarding Adverse Events

Petitioner asserts that the "EUA should be revoked and no composition changes allowed due to large numbers of credible reports of adverse events (number or severity) linked to, or suspected of being caused by, the EUA product."[78] Petitioner provides no references to support this claim, and Petitioner does not cite to any specific statistics regarding adverse events.

Additionally, Petitioner makes several other assertions regarding deaths that Petitioner argues are related to COVID-19 mRNA vaccines. For example, Petitioner asserts "[i]t violates much more than Federal law that the FDA is failing to inform the public about the risk of death…[f]or FDA to know a % of people will die yet continue to give the mRNA and gene products to people outside clinical trials without informing people death is listed as common in 1.1% of users is a

[73] Petition at 7.
[74] *Id.* at 8.
[75] *Id.* at 7.
[76] *Id.* at 8.
[77] In some instances, Petitioner attempts to support these assertions by pointing to statements regarding gene therapy products in the January 2020 Guidance; however, as previously explained, the January 2020 Guidance does not apply to vaccines for infectious disease indications.
[78] Petition at 8.

violation of Nuremberg Code Article 1 and Siracusa Principles 69(b)."[79, 80] Referring to slides that Petitioner presented during the public comment session of the June 28, 2022 meeting of FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC), Petitioner further refers to "the phase 4 data in our slides showing death is common and illegally omitted in the fact sheets."[81] The Petition provides no reference or citation to support the claim that death is "common in 1.1% of users."[82]

FDA is monitoring the safety of authorized and approved COVID-19 vaccines through both passive and active safety surveillance systems. FDA is doing so in collaboration with the Centers for Disease Control and Prevention (CDC), the Centers for Medicare and Medicaid Services (CMS), the Department of Veterans Affairs (VA), and other academic and large non-government healthcare data systems.

There are extensive vaccine safety surveillance efforts in place, including the Vaccine Adverse Event Reporting System (VAERS) for COVID-19 vaccines. VAERS is a national passive surveillance vaccine safety database that receives unconfirmed reports of possible adverse events following the use of a vaccine licensed or authorized in the United States. Passive surveillance is defined as unsolicited reports of adverse events that are sent to a central database or health authority. In the United States, these are received and entered into VAERS, which is co-managed by FDA and CDC. In the current pandemic, these reports are being used to monitor the occurrence of both known and unknown adverse events, as vaccination providers of COVID-19 vaccines are required to report serious adverse events to VAERS.

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[79] *Id.* at 5.

[80] Throughout the Petition, Petitioner alleges violations of international laws and norms, referring specifically to the Nuremberg Code, Siracusa Principles 69(b), and "the treaty on protecting the rights of children." Petition at 11. These assertions appear to be premised on Petitioner's contention that that use of authorized vaccines within the scope of their EUAs is investigational. For example, Petitioner states, "You CANNOT skip trials and be in compliance with international laws regarding investigational medicines, no matter what errors FDA believes." Petition at 9. Petitioner further asserts that "when FDA violates the international norms it affects other countries that rely on FDA. For instance, Costa Rica is the first country in the world to mandate the bivalent vaccine 3 doses for 6 months to 5 years, and is using FDA's authorization to do so in an expedited decree, even though the emergency was dropped." Petition at 5. To be clear, FDA complies with applicable legal requirements, including international legal obligations. And as explained earlier in this response (see footnote 60), the clinical use of a product within the scope of an EUA is not a clinical investigation. Additionally, FDA does not mandate use of vaccines and does not make recommendations about whether other entities should mandate vaccines. Concerns about vaccination requirements are better addressed to any government or private entity that may issue requirements related to vaccination.

[81] Petition at 9.

[82] We note that the VRBPAC slides Petitioner references cite to the following website in support of a similar assertion regarding a 1.1% rate of deaths: https://www.ehealthme.com/vs/pfizer-biontech-covid-vaccine/death/. See recording of the June 28, 2022 VRBPAC meeting at 5:07:00, https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-june-28-2022-meeting-announcement. Notably, the referenced website purports to show the percentage of people who died out of the total number of people who reported side effects after receiving the Pfizer-BioNTech COVID-19 Vaccine. It does not purport to show the percentage of people who died after receiving the Pfizer-BioNTech COVID-19 Vaccine (or any other vaccine). We further note that although the website claims to reference CDC and FDA data, it is not clear from where the data on the website originated.

As part of FDA and CDC's multi-system approach to post-licensure and post-authorization vaccine safety monitoring, VAERS is designed to rapidly detect unusual or unexpected patterns of adverse events, also known as "safety signals." VAERS reports generally cannot be used to determine if a vaccine caused or contributed to an adverse event or illness. If the VAERS data suggest a possible link between an adverse event and vaccination, the relationship may be further studied in a controlled fashion.[83]

We note that a large number of COVID-19 vaccine doses have been administered in the United States and that certain adverse event reporting by vaccination providers is required for all currently authorized COVID-19 vaccines. As of November 9, 2022, over 646,000,000 doses of authorized COVID-19 vaccines have been administered in the United States.[84] N We note that the crude number of VAERS reports of death is extremely small compared to the large number of people who have been vaccinated. The VAERS reporting rate for deaths (which is the number of VAERS death reports received out of the number of individuals vaccinated) for the authorized COVID-19 vaccines is actually very low (17,392 out of 646 million doses or 0.0027% as of November 9, 2022).[85] Furthermore, although VAERS reports provide a very important tool in monitoring vaccine safety, these reports alone cannot be used to determine if a vaccine caused or contributed to an adverse event or illness.[86] For example, under the EUAs for the authorized COVID-19 vaccines, unlike for previously approved vaccines, vaccination providers are required to report to VAERS serious adverse events following vaccination with the COVID-19 vaccines "irrespective of attribution to vaccination."[87]

For the reasons discussed above, Petitioner's assertions regarding adverse events do not change FDA's conclusion that the known and potential benefits of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent, outweigh their known and potential risks.

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[83] FDA, VAERS Overview, https://www.fda.gov/vaccines-blood-biologics/vaccine-adverse-events/vaers-overview.
[84] CDC, COVID Data Tracker, COVID-19 Vaccinations in the United States, https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-total-admin-rate-total (accessed November 15, 2022).
[85] CDC, Selected Adverse Events Reported after COVID-19 Vaccination, https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html (accessed November 15, 2022).
[86] VAERS Data Disclaimer, https://vaers.hhs.gov/data.html
[87] See, e.g., Pfizer-BioNTech COVID-19 Fact Sheets for Healthcare Providers Administering Vaccine (Vaccination Providers), Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors, https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccines#additional; Moderna COVID-19 Fact Sheets for Healthcare Providers Administering Vaccine (Vaccination Providers), Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors, https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccines#additional; Janssen COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors, https://www.fda.gov/media/146304/download; Novavax COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors, https://www.fda.gov/media/159897/download.

Petitioner's Claims Regarding Other Risks

Petitioner asserts that "new facts came out since the FDA authorized these products which shows a 44% increased risk of transmission, auto immune like reaction and that there is 92% more risk than benefit."[88] Petitioner provides no citation or further information regarding these statistics referenced, nor does Petitioner provide any new data or information that would change FDA's evaluation of the benefit-risk profile of authorized COVID-19 vaccines.

Petitioner's above-referenced claims regarding "new facts" and these vaccines having "more risk than benefit" do not alter FDA's determination that the known and potential benefits of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent outweigh their known and potential risks.

Petitioner's Claims Regarding FDA's Assessment of Benefits and Risks

Petitioner asserts that the authorization "is supported by flawed facts" and that "[i]t cites, for the proposition that the product is safe and effective, only a single observational study of 8 mice, which was unsuccessful, which could lead to an overestimation of the benefit of the experiments and an underestimation of the potential and known harms."[89]

Petitioner provides no data to support the assertion that FDA overestimated benefits or underestimated risks when authorizing the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent. Additionally, Petitioner incorrectly characterizes the safety and effectiveness data evaluated by FDA to support authorization of these vaccines.

For each of the bivalent COVID-19 vaccines currently authorized by FDA, the Agency evaluated immunogenicity and safety data from a clinical study of a booster dose of a bivalent COVID-19 vaccine that contained an mRNA component corresponding to the Original strain of SARS-CoV-2 and an mRNA component of Omicron variant BA.1 lineage. The FDA considers such data as relevant and supportive of vaccines containing a component of the Omicron variant BA.4 and BA.5 lineages. Furthermore, data pertaining to the safety and effectiveness of the monovalent

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[88] Petition at 2.

[89] *Id.* at 12. FDA interprets Petitioner's reference to "a single observational study of 8 mice" as referring to nonclinical data discussed by Pfizer during the June 28, 2022 Vaccines and Related Biological Products Advisory Committee Meeting (Vaccines and Related Biological Products Advisory Committee June 28, 2022 Meeting Presentation- Pfizer/BioNTech COVID-19 Omicron-Modified Vaccine Options, https://www.fda.gov/media/159496/download). For a complete discussion of the data evaluated by FDA to support the emergency use authorization of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent, see FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) in Individuals 12 Years of Age and Older (Aug. 31, 2022), https://www.fda.gov/media/161595/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) in Individuals 5 through 11 Years of Age (Oct. 11, 2022), https://www.fda.gov/media/162410/download.

mRNA COVID-19 vaccines, which have been administered to millions of people, including during the Omicron waves of COVID-19, contributed to the agency's evaluation.

The totality of data evaluated by FDA to support authorization of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent included:

- clinical safety and immunogenicity data in individuals greater than 55 years of age from a study in which participants received a second booster dose of either the monovalent Pfizer-BioNTech COVID-19 Vaccine or Pfizer-BioNTech's investigational bivalent COVID-19 vaccine (Original and Omicron BA.1), which is manufactured by the same process as the monovalent Pfizer-BioNTech COVID-19 Vaccine and the Pfizer-BioNTech COVID-19 Vaccine, Bivalent;
- safety and effectiveness data from clinical trials and observational studies which evaluated primary and booster (homologous and heterologous) vaccination with the monovalent Pfizer-BioNTech COVID-19 Vaccine;
- post-marketing safety surveillance data with primary series and booster doses of the monovalent Pfizer-BioNTech COVID-19 Vaccine; and
- supportive non-clinical immunogenicity data from a study with the Pfizer-BioNTech COVID19 Vaccine, Bivalent.[90]

The totality of data evaluated by FDA to support authorization of the Moderna COVID-19 Vaccine, Bivalent included:

- clinical safety and immunogenicity data in individuals 18 years of age and older from a study in which participants received a second booster dose of either the monovalent Moderna COVID-19 Vaccine or Moderna's investigational bivalent COVID-19 vaccine (Original and Omicron BA.1), which is manufactured by the same process as the monovalent Moderna COVID-19 Vaccine and the Moderna COVID-19 Vaccine, Bivalent;
- safety and effectiveness data from clinical trials and observational studies which evaluated primary and booster (homologous and heterologous) vaccination with the monovalent Moderna COVID-19 Vaccine;
- post-marketing safety surveillance data with primary series and booster doses of the monovalent Moderna COVID-19 Vaccine; and

[90] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) in Individuals 12 Years of Age and Older (Aug. 31, 2022), at 4-5, https://www.fda.gov/media/161595/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) in Individuals 5 through 11 Years of Age, (Oct. 11, 2022), at 3-4, https://www.fda.gov/media/162410/download.

- supportive non-clinical immunogenicity data from a study with the Moderna COVID-19 Vaccine, Bivalent.[91]

Petitioner's assertions regarding FDA's assessment of benefits and risks do not alter FDA's determination that the known and potential benefits of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent outweigh their known and potential risks.

4. No Alternatives

For a product to be granted an EUA, section 564(c)(3) of the FD&C Act requires that "there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating [the serious or life-threatening disease or condition]." The Petition does not argue for revocation of the EUAs for the Pfizer-BioNTech Vaccine, Bivalent and Moderna COVID-19 Vaccine, Bivalent on the grounds that there is an adequate, approved, and available alternative to prevent COVID-19, nor does it provide persuasive information to support that such an alternative exists.

Currently, the only FDA-approved drugs or biological products indicated to prevent COVID-19 in any population are Comirnaty and Spikevax. Comirnaty is approved for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older. Spikevax is approved for the prevention of COVID-19 in individuals 18 years of age or older. The approved COVID-19 vaccines are monovalent vaccines, meaning that they contain or encode the spike protein of only the Original SARS-CoV-2. There are no approved COVID-19 vaccines that are based on currently circulating variants of concern, and there are no COVID-19 vaccines approved for use as a booster dose. Therefore, for the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent, there are no adequate, approved and available alternatives, and the criterion under section 564(c)(3) of the FD&C Act is met.

c. No Other Circumstances Make a Revision or Revocation Appropriate to Protect the Public Health or Safety

As noted above, section 564(g)(2) of the FD&C Act provides that FDA may revise or revoke an EUA if circumstances justifying its issuance (under section 564(b)(1)) no longer exist, the criteria for its issuance are no longer met, or other circumstances make a revision or revocation appropriate to protect the public health or safety. The EUA guidance explains that such other circumstances may include:

[91] FDA, Moderna COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) in Individuals 18 Years of Age and Older (Aug. 31, 2022), at 5-6, https://www.fda.gov/media/161554/download; FDA, Moderna COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) in Individuals 6 Through 17 Years of Age (Oct. 11, 2022), at 5-7, https://www.fda.gov/media/162515/download.

> significant adverse inspectional findings (e.g., when an inspection of the manufacturing site and processes has raised significant questions regarding the purity, potency, or safety of the EUA product that materially affect the risk/benefit assessment upon which the EUA was based); reports of adverse events (number or severity) linked to, or suspected of being caused by, the EUA product; product failure; product ineffectiveness (such as newly emerging data that may contribute to revision of the FDA's initial conclusion that the product "may be effective" against a particular CBRN agent); a request from the sponsor to revoke the EUA; a material change in the risk/benefit assessment based on evolving understanding of the disease or condition and/or availability of authorized MCMs; or as provided in section 564(b)(2), a change in the approval status of the product may make an EUA unnecessary.[92]

Petitioner asserts that "[a]nother possible option for consideration…is to review the phase 4 data and review the circumstances and appropriateness of an EUA, including circumstances that might warrant revocation of the EUA."[93] Petitioner further asserts that "FDA has a duty to determine that it is appropriate to protect the public health or safety to revoke all failing mRNA products."[94]

FDA determined the EUA standard is met for both the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent because data submitted by the sponsors demonstrated in a clear and compelling manner that the known and potential benefits of these vaccines, when used to prevent COVID-19, outweigh the known and potential risks, and that there is no adequate, approved, and available alternative for diagnosing, preventing, or treating COVID-19.

FDA finds no basis in the information submitted in the Petition to support a revocation of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent EUA or the Moderna COVID-19 Vaccine, Bivalent EUA. As described above, the Petition has not provided information demonstrating that that the known and potential benefits of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent or the Moderna COVID-19 Vaccine, Bivalent are outweighed by the known and potential risks of these products. Furthermore, Petitioner has not demonstrated that other circumstances make a revision or revocation of the EUA for the Pfizer-BioNTech COVID-19 Vaccine, Bivalent or the EUA for the Moderna COVID-19 Vaccine, Bivalent appropriate to protect the public health or safety. FDA therefore sees no justifiable basis upon which to take any action based on Petitioner's request regarding the Pfizer-BioNTech COVID-19 Vaccine, Bivalent EUA and the Moderna COVID-19 Vaccine, Bivalent EUA. Accordingly, as noted above, we deny Petitioner's request.

[92] EUA Guidance at 29.
[93] Petition at 9.
[94] *Id*.

B. Petitioner's Discussion Regarding Revocation of EUAs for Other mRNA COVID-19 Vaccines

As explained, although the "Actions Requested" section of the Petition focuses on revocation of the EUAs for the bivalent mRNA COVID-19 Vaccines, other sections of the Petition reference revocation more broadly (e.g., Petitioner refers to revocation of authorization for "all mRNA products"[95]). To the extent the Petition can be interpreted as requesting that FDA revoke the EUAs for the monovalent Pfizer-BioNTech COVID-19 Vaccine and Moderna COVID-19 Vaccine ("the Authorized Monovalent mRNA COVID-19 Vaccines"), which are the only other mRNA vaccines available under EUA besides the bivalent vaccines discussed in section III.A, this section explains that Petitioner has provided no basis for such action.

i. The Standard for Revocation of EUAs Is Not Met

The Agency issued the EUAs for Authorized Monovalent mRNA COVID-19 Vaccines after a thorough evaluation of scientific data regarding the safety, effectiveness, and manufacturing information (which helps ensure product quality and consistency) and after determining that the vaccines meet the statutory requirements under section 564 of the FD&C Act. FDA's Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memoranda and Addenda, and FDA's Moderna COVID-19 Vaccine EUA Decision Memoranda and Addenda, discuss these determinations and the data upon which they were based, in detail.

In the following sections we address whether the Petition demonstrates that any of the statutory conditions under which FDA may revoke an EUA are met with respect to the Authorized Monovalent mRNA COVID-19 Vaccines, namely: (1) whether the circumstances described under section 564(b)(1) of the FD&C Act no longer exist, (2) whether the criteria under section 564(c) of the FD&C Act are no longer met, and (3) whether other circumstances make a revision or revocation appropriate to protect the public health or safety.

a. Circumstances Described under Section 564(b)(1) of the FD&C Act Continue to Exist

For the reasons described in section III.A.ii.a of this response, the Petition does not demonstrate that the circumstances described under section 564(b)(1) no longer exist.

b. The Criteria for the Issuance of the EUA Continue to Be Met

This section describes why the Petition has not demonstrated that the criteria under section 564(c) of the FD&C Act are no longer met with respect to the Authorized Monovalent mRNA COVID-19 Vaccines. Below we briefly address each criterion.

[95] *Id.*

1. Serious or Life-Threatening Disease or Condition

As explained above in section II.C of this letter, section 564(c)(1) of the FD&C Act requires that, for an EUA to be issued for a medical product, the "agent[s] referred to in [the HHS Secretary's EUA declaration] can cause a serious or life-threatening disease or condition." FDA has concluded that SARS-CoV-2 can cause a serious or life-threatening disease or condition. Petitioner has not demonstrated that the criterion under section 564(c)(1) is no longer met for the reasons described in section III.A.ii.b.1 of this letter.

2. Evidence of Effectiveness

Section 564(c)(2)(A) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition that can be caused by SARS-CoV-2.

FDA has determined that based on the totality of scientific evidence available, it is reasonable to believe that the Authorized Monovalent mRNA COVID-19 Vaccines may be effective to prevent COVID-19. The basis for this determination is explained in detail in FDA's decision memoranda regarding the Pfizer-BioNTech COVID-19 Vaccine EUA and the Moderna COVID-19 Vaccine EUA.[96] FDA is not aware of any data that change this conclusion, nor has Petitioner provided any such data in the Petition. Petitioner presents no new data regarding the effectiveness of the Authorized Monovalent mRNA COVID-19 Vaccines that is of the scientific rigor that FDA would rely on for our scientific and regulatory decisions. To the extent Petitioner's arguments relating to effectiveness are applicable to the Authorized Monovalent mRNA COVID-19 Vaccines, those arguments are addressed in section III.A.ii.b.2 of this letter.[97] The criterion under section 564(c)(2)(A) of the FD&C Act continues to be met with respect to the Authorized Monovalent mRNA COVID-19 Vaccines.

3. Benefit-Risk Analysis

Section 564(c)(2)(B) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude that "the known and potential benefits of the product, when used to diagnose, prevent, or treat [the identified serious or life-threatening disease or condition], outweigh the known and potential risks of the product . . . ."

FDA authorized for emergency use the Authorized Monovalent mRNA COVID-19 Vaccines after reaching determination that, among other things, the known and potential benefits of these

[96] See FDA's Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memoranda and Addenda and FDA's Moderna COVID-19 Vaccine EUA Decision Memoranda and Addenda.

[97] Additionally, we note that—like the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the Moderna COVID-19 Vaccine, Bivalent—the Authorized Monovalent mRNA COVID-19 Vaccines are authorized to prevent COVID-19, not to prevent SARS-CoV-2 infection or transmission.

vaccines, when used to prevent COVID-19, outweigh their known and potential risks. These determinations are explained in detail in FDA's Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memoranda and Addenda and FDA's Moderna COVID-19 Vaccine EUA Decision Memoranda and Addenda.

Petitioner presents no information that alters FDA's assessment of the known and potential benefits of the Authorized Monovalent mRNA COVID-19 Vaccines, or whether such known and potential benefits outweigh the known and potential risks. To the extent Petitioner's arguments relating to benefit-risk analysis are applicable to the Authorized Monovalent mRNA COVID-19 Vaccines, those arguments are addressed in section III.A.ii.b.3 of this letter.

Petitioner has not provided any data, nor is FDA aware of any data, that changes FDA's conclusion that the known and potential benefits of the Authorized Monovalent mRNA COVID-19 Vaccines, when used to prevent COVID-19, outweigh their known and potential risks. The criterion under section 564(c)(2)(B) of the FD&C Act continues to be met with respect to the Authorized Monovalent mRNA COVID-19 Vaccines.

4. No Alternatives

For a product to be granted an EUA, section 564(c)(3) of the FD&C Act requires that "there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating [the serious or life-threatening disease or condition]." The Petition does not argue that FDA should revoke authorization of Authorized Monovalent mRNA COVID-19 Vaccines on the grounds that there is an adequate, approved, and available alternative for preventing COVID-19, nor does it provide persuasive information to support that such an alternative exists. As discussed above, the only FDA-approved drugs or biological products currently indicated to prevent COVID-19 in any population, are Comirnaty and Spikevax. Comirnaty is approved for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older. Spikevax is approved for the prevention of COVID-19 in individuals 18 years of age or older.

Although there are two approved COVID-19 vaccines, that does not mean that there is now an "adequate, approved, and available" alternative such that continuation of the EUAs for the Authorized Monovalent mRNA COVID-19 Vaccines is no longer justified. Although the two approved vaccines are approved to prevent COVID-19 in certain individuals who fall within the scope of the authorizations for the Authorized Monovalent mRNA COVID-19 Vaccines, there is not sufficient approved vaccine available for distribution to this population in its entirety. Additionally, there are no COVID-19 vaccines that are approved to provide COVID-19 vaccination in individuals younger than 12 years of age or a third primary series dose to certain immunocompromised populations.

Therefore, there is no adequate, approved, and available alternative to the Authorized Monovalent mRNA COVID-19 Vaccines for preventing COVID-19. The criterion under section 564(c)(3) of the FD&C Act continues to be met.

c. No Other Circumstances Make a Revision or Revocation Appropriate to Protect the Public Health or Safety

FDA determined the EUA standard is met for the Authorized Monovalent mRNA COVID-19 Vaccines because data submitted by the sponsors demonstrated in a clear and compelling manner that the known and potential benefits of these vaccines, when used to prevent COVID-19, outweigh the known and potential risks, and that there is no adequate, approved, and available alternative for diagnosing, preventing, or treating COVID-19.

FDA finds no basis in the information submitted in the Petition to support a revocation of the EUAs for the Authorized Monovalent mRNA COVID-19 Vaccines. The Petition has not provided information demonstrating that that the known and potential benefits of the Authorized Monovalent mRNA COVID-19 Vaccines are outweighed by the known and potential risks of these products. Furthermore, Petitioner has not demonstrated that other circumstances make a revision or revocation of the EUAs for the Authorized Monovalent mRNA COVID-19 Vaccines appropriate to protect the public health or safety. FDA therefore sees no justifiable basis upon which to revoke the EUAs. Accordingly, to the extent the Petition can be interpreted as requesting that FDA revoke the EUAs for the Authorized Monovalent mRNA COVID-19 Vaccines, we deny such request.

IV. CONCLUSION

FDA has considered Petitioner's request for FDA to revoke the EUAs for certain COVID-19 vaccines. For the reasons given above, FDA denies the Petition in its entirety.

Sincerely yours,

Peter Marks, MD, PhD
Director
Center for Biologics Evaluation and Research

cc: Dockets Management Staff