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U.S. DISTRICT COURT
N.D. OF ALABAMA

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ALABAMA
SOUTHERN DIVISION

AMERICA'S FRONTLINE DOCTORS, *et al.*, Plaintiffs, v. UNITED STATES OF AMERICA, *et al.*, Defendants.	CIVIL ACTION NO. 2:21-CV-702-CLM

DECLARATION OF PETER MARKS, M.D., Ph.D.

I, Peter Marks, declare as follows:

1. I am the Director of the Center for Biologics Evaluation and Research ("CBER"), United States Food and Drug Administration ("FDA"), a position I have held since 2016. In this role, I direct the development and implementation of programs and policies for assuring the safety, purity, and potency of biological products, including vaccines, allergenic products, blood and blood products, and cellular, tissue, and gene therapies.

2. I joined FDA in 2012 as the Deputy Director for CBER, after practicing medicine, and working in industry and academia for several years. I received my graduate degree in cell and molecular biology and my medical degree at New York University, am board certified in internal medicine, hematology and medical oncology, and am a Fellow of the American College of Physicians.

3. In my capacity as Director of CBER, I am fully familiar with the instant matter and the facts stated herein. This declaration is based on my personal knowledge, my background, training, and experience and my review and consideration of information available to me in my official capacity, including information furnished by FDA personnel in the course of their official duties. My conclusions have been reached in accordance therewith.

4. Vaccines are biological products that are regulated under the Public Health Service Act ("PHSA"), 42 U.S.C. § 262(i)(1), as well as "drugs" subject to regulation under the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 321(g)(1)(B). Vaccines are approved for marketing through applications known as Biologics License Applications ("BLA"); a vaccine that is the subject of an approved BLA need not also obtain approval of a new drug application ("NDA") under 21 U.S.C. § 355. 42 U.S.C. § 262(a), (j).

5. Under the PHSA, FDA approves a BLA on the basis of a demonstration that: (1) the vaccine is "safe, pure, and potent"[1]; (2) the facility in which the vaccine is produced meets standards designed to assure that the vaccine continues to be safe, pure, and potent; and (3) the applicant consents to inspection of the manufacturing facility. 42 U.S.C. § 262(a)(2)(C). FDA may, but is not required to, consult with its standing advisory committee with scientific expertise in biological products, the Vaccines and Related Biological Products Advisory Committee, as part of the approval process. *See* 21 C.F.R. § 14.171(a). FDA has also issued several guidances and other public documents on the development of vaccines and other biologics. *See generally* Biologics License Applications (BLA)

[1] The standard for licensure of a biological product as potent under 42 U.S.C. § 262 has long been interpreted by FDA to include effectiveness. *See* 21 C.F.R. § 600.3(s); FDA Guidance, Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products at 4 (May 1998), available at https://www.fda.gov/media/71655/download.

Process, https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/biologics-license-applications-bla-process-cber; Guidance, Compliance & Regulatory Information (Biologics), https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics; Vaccine and Related Biological Product Guidances, https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/vaccine-and-related-biological-product-guidances; Vaccine Development 101, https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/vaccine-development-101.

6. On August 23, 2021, FDA approved a BLA for a COVID-19 vaccine known as Comirnaty, for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. *See* Comirnaty Approval Letter (August 23, 2021), attached as Exhibit 1. The Comirnaty BLA was approved based on six months of safety and efficacy data from two ongoing clinical trials as well as safety information from the millions of vaccine doses administered under the emergency use authorization ("EUA") for the Pfizer-BioNTech Covid-19 vaccine, as discussed below.

7. Comirnaty is an mRNA vaccine. It contains a piece of the SARS-CoV-2 virus's genetic material that instructs cells in the body to make the virus's distinctive "spike" protein. After a person is vaccinated, the body produces copies of the spike protein, which do not cause disease, and these copies trigger the immune system to learn to react defensively, producing an immune response against SARS-CoV-2. After delivering the instructions, the mRNA is rapidly broken down. It does not enter the nucleus of the cell and does not affect DNA.

8. Prior to approval, beginning in December 2020, the same formulation of the vaccine as that approved on August 23, known as Pfizer-BioNTech Covid-19 vaccine, was available under an EUA. FDA has discretion to issue an EUA for

an FDA-regulated product if: (1) the Secretary of the Department of Health and Human Services has declared a public health emergency involving a biological or other agent that can cause a serious or life-threatening disease or condition; (2) it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing that disease or condition, and the known and potential benefits of the product outweigh the known and potential risks of the product; and (3) there is no "adequate, approved, and available" alternative to the product. 21 U.S.C. § 360bbb-3(c).[2]

9. Even after FDA approved Comirnaty, FDA authorized continued use of the Pfizer-BioNTech Covid-19 vaccine under an EUA for indications that included the approved use. FDA determined that there is not sufficient approved vaccine available for distribution to the 16 years and older population in its entirety at the time of FDA's reissuance of the EUA. *See* Letter to Pfizer, Inc. reissuing EUA authorization for Covid-19 vaccine, p. 9, n.18 (December 16, 2021), attached as Exhibit 2. FDA also determined that there are no products that are approved to prevent COVID-19 in additional populations covered by the EUA, as the vaccine remains available under the EUA for uses that have not been approved, specifically for individuals ages 5 through 15 years old; for a third dose in certain populations; and for a "booster" dose in certain circumstances.

10. On October 29, 2021, FDA authorized a new formulation of the Pfizer-BioNTech vaccine for use in children 5 to 11 years of age when diluted to a lower strength. *Id.* at 3 n.12. FDA also authorized the new formulation, without dilution, for individuals 12 years of age and older. *Id.* The new formulation

[2] Distribution of a product pursuant to an EUA is not a "clinical trial" subject to the requirements for clinical trials conducted under an investigational new drug ("IND") application. 21 U.S.C. §§ 360bbb-3(k); 355(i). Clinical trials must be conducted in accordance with an approved IND and involve only enrolled study participants. Only clinical trial participants enrolled in a clinical study conducted according to an approved IND receive the study drug.

contains the same mRNA and lipids, and the same quantity of these ingredients, per 0.3 mL dose, as the original formulation. *Id.* at 11. The two formulations differ only with respect to certain inactive ingredients and have been shown to be analytically comparable. *Id.* Specifically, the original formulation uses "phosphate buffered saline" as a buffer and is thus called the PBS formulation. The new formulation uses tromethamine ("Tris") buffer and is thus called the Tris formulation.

11. On December 16, 2021, FDA approved a supplemental BLA for Comirnaty to include the use of the Tris formulation in individuals 16 years of age and older. *See* Comirnaty Supplement Approval Letter (December 16, 2021), attached as Exhibit 3. Both the original (PBS) formulation and the new (Tris) formulation are now approved for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. *See* Comirnaty Prescribing Information, purple cap (December 16, 2021), attached as Exhibit 4; Comirnaty Prescribing Information, gray cap (December 16, 2021), attached as Exhibit 5.

12. FDA determined that "for individuals 12 years of age and older, the two formulations of COMIRNATY (COVID-19 Vaccine, mRNA) and the two formulations of the Pfizer-BioNTech COVID-19 Vaccine, when prepared according to their respective instructions for use, can be used interchangeably without presenting any safety or effectiveness concerns." *See* EUA Letter of Authorization, Exhibit 2, p. 12. FDA provided this information in the Letter of Authorization to make clear that pharmacies and other healthcare practitioners could provide the vaccination series to recipients using Pfizer-BioNTech, Comirnaty, or both (*e.g.*, first dose of Pfizer-BioNTech followed by

second dose of Comirnaty, or vice versa), regardless of formulation,[3] because the products are medically interchangeable and are made by the same manufacturer under current good manufacturing practice requirements. FDA included this clarification in the authorization letter to avoid the unnecessary operational complications that may have resulted if pharmacies or other healthcare practitioners had believed that the authorization did not include use in individuals who had received Pfizer-BioNTech for the first dose and Comirnaty for the second dose, or vice versa. Either formulation of either Comirnaty or the Pfizer-BioNTech vaccine is also authorized to provide a booster dose. *Id.*

13. While FDA determined Comirnaty and Pfizer-BioNTech Covid-19 vaccine are medically interchangeable, there are legal distinctions between BLA-approved and EUA-authorized products. For example, products approved under BLAs are required to have the labeling that was approved as part of the BLA, whereas products authorized under the EUA would have the EUA labeling, and there may also be differences in manufacturing sites for the BLA and EUA vaccine. Both the EUA and BLA processes have required the sponsor to identify specific facilities that will manufacture the vaccine. *See* Summary Basis for Regulatory Action – Comirnaty ("SBRA"), p. 11-13 (Aug. 23, 2021), attached as Exhibit 6.

14. Vaccine manufactured at sites listed in the BLA also undergoes lot release, which is designed to ensure conformity with standards applicable to the product. 21 C.F.R. § 610.1; *see also* https://www.fda.gov/vaccines-blood-

[3] The Pfizer-BioNTech COVID-19 Vaccine that uses PBS buffer and COMIRNATY (COVID-19 Vaccine, mRNA) that uses PBS buffer have the same formulation. Additionally, the Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer and COMIRNATY (COVID-19 Vaccine, mRNA) that uses Tris buffer have the same formulation. EUA Letter of Authorization, Exhibit 2, at 11. FDA has determined that the two-dose vaccination series can be administered using the approved or authorized versions of the PBS or Tris formulations, in any combination. *Id.* at 11-12.

biologics/biologics-post-market-activities/lot-release#lotrelease. Vaccine manufactured at sites that are not listed in the BLA is not subject to the lot release requirement.[4] Manufacturing of the BLA and EUA vaccine must adhere to FDA's current good manufacturing practice regulations, which are designed to ensure that the products meet specified standards of safety, purity, and potency. *See* 21 C.F.R. Part 211 (CGMP regulations for drugs), § 211.1(b) (applicability of CGMP regulations to drugs that are also biological products); Exhibit 2 at 16.

15. In conjunction with the August 23 approval of Comirnaty, FDA asked the applicant to identify available lots of vaccine that were manufactured at facilities listed in the BLA that had undergone lot release. For these lots and other lots produced at facilities listed in the BLA, at this time, FDA is exercising its enforcement discretion with respect to certain labeling requirements, in that FDA is not taking enforcement with respect to vials that bear the EUA label.[5] FDA considers these lots to be manufactured in compliance with the BLA and they are not subject to the EUA requirements when used for the approved indication. Thus, the conditions in the Letter of Authorization for the EUA—including the condition requiring vaccination providers to provide recipients with the Fact Sheet for Recipients, which advises recipients that "under the EUA, it is your choice to receive or not receive the vaccine"—do not apply when these lots or other BLA-

[4] Although not subject to lot release, as a condition of the EUA, Pfizer-BioNTech submits to the EUA file Certificates of Analysis for each drug product lot at least 48 hours prior to vaccine distribution; these Certificates include the established specifications and specific results for each quality control test performed on the final drug product lot. Additionally, also as a condition of the EUA, Pfizer-BioNTech submits quarterly manufacturing reports to the EUA file that include specified information about each lot of vaccine manufactured. *See* Exhibit 2 at 16.

[5] Each vial contains six doses of vaccine and a dose is withdrawn from the vial immediately before injection into a recipient, who would not ordinarily be handling the vial or viewing its label. Fact Sheet for Healthcare Providers Administering Vaccine (purple cap, pp. 7-11 (Dec. 16, 2021), available at https://www.fda.gov/media/153713/download; Fact Sheet for Healthcare Providers Administering Vaccine (gray cap, pp. 6-10 (Dec. 16, 2021), available at https://www.fda.gov/media/153715/download.

compliant lots are used for the approved indication. FDA worked with the applicant to develop a Dear Health Care Provider letter and website to identify those lots. Summary Basis for Regulatory Action – Comirnaty ("SBRA"), Exhibit 6. Also because, after licensure of Comirnaty, recipients may receive either the BLA or EUA vaccine, the vaccine has been distributed with unified Fact Sheets—with separate versions for providers and recipients—that provide information about the EUA and BLA products. *See* Fact Sheet for Recipients and Caregivers 12 Years of Age and Older (Dec. 16, 2021), available at https://www.fda.gov/media/153716/download.

16. As discussed above, FDA approved Comirnaty based on data from two clinical studies. These clinical studies demonstrated that the overall efficacy rate in the 16 and older subject population was 91.1% for the prevention of COVID-19 infection and between 95% and 100% for the avoidance of severe infection. Comirnaty Prescribing Information (August 23, 2021), attached as Exhibit 7. FDA also considered the safety data from the two clinical studies, in addition to safety information from EUA use. *Id.* at 6-13. In summary, based on its review of the clinical, pre-clinical, and product-related data submitted in the Comirnaty BLA, FDA determined that the product had a favorable benefit/risk balance, and was safe, pure, and potent. The agency approved the license for Comirnaty on August 23, 2021. Exhibit 1, FDA Approval Letter (Aug. 23, 2021).

17. FDA collects adverse event reports from the general population receiving the vaccine via the Vaccine Adverse Event Reporting System (VAERS). 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. VAERS reports provide a very important tool in monitoring vaccine safety, but these reports alone cannot be used to determine if a vaccine caused or contributed to an adverse event or illness. *See*

VAERS Data Disclaimer, https://vaers.hhs.gov/data.html. There are particular scientific limitations in comparing VAERS reports for COVID-19 vaccines with reports for previously approved vaccines for other conditions. 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" and regardless of how long after vaccination the adverse event occurs. In addition, CDC deployed the smartphone-based active-surveillance "v-safe" system only for the COVID-19 vaccines. V-safe has solicited adverse event reports directly from those who have received the vaccine, which are then included in VAERS, but this system has only been deployed for COVID-19 vaccines and not for other vaccines. Finally, another potential factor that limits comparisons between VAERS reports for COVID-19 vaccines and reports for other vaccines is the concept of "stimulated reporting." Because of extensive media coverage and awareness of the public health emergency – and of the authorized COVID-19 vaccines and their reported side effects – vaccine recipients, health care providers, and others are more likely to report adverse events for these vaccines than for other vaccines that have been widely available for longer periods of time. Although VAERS is not designed to assess causality, FDA and CDC actively monitor VAERS reports and engage in additional studies or investigations if VAERS monitoring suggests that a vaccine might be causing a health problem.

18. In approving the BLA for Comirnaty, FDA applied its scientific expertise to evaluate the data contained in the application and determined that Comirnaty's benefits outweigh its risks and that it is safe, pure, potent, and effective for its proposed use. In response to the urgent public health emergency presented by COVID-19, FDA worked expeditiously to provide guidance to entities seeking to develop vaccines for this disease, and to review the BLA for

Comirnaty once it was submitted to the agency to ensure it fully met the statutory standards for approval, to further the objective of protecting the public health.

19. An injunction affecting the Pfizer-BioNTech vaccine EUA would greatly harm the public, particularly at a time during the spread of the Omicron variant of SARS-CoV-2, when public health agencies are evaluating concerns that other medical countermeasures for COVID-19 treatment may become ineffective. Safe and effective vaccines are currently the most powerful tool we have against the pandemic and have been estimated to have already saved hundreds of thousands of lives. *See* Eric C. Schneider *et al.*, *The U.S. COVID-19 Vaccination Program at One Year: How Many Deaths and Hospitalizations Were Averted?* The Commonwealth Fund, Dec. 14, 2021, https://www.commonwealthfund.org/publications/issue-briefs/2021/dec/us-covid-19-vaccination-program-one-year-how-many-deaths-and. An injunction based on the Court's evaluation of the Pfizer-BioNTech EUA vaccine would call into question the data supporting FDA's determination that the Pfizer-BioNTech EUA vaccine and Comirnaty, which are medically interchangeable, are safe and effective. The consequence could be to undermine the vaccine development process, if vaccine developers see that courts are willing to disregard FDA's rigorous review process and remove products from the market on the basis of mere allegations. In addition, another serious consequence could be to undermine the government's efforts to encourage vaccination in all eligible populations by exacerbating vaccine hesitancy. One of the most significant barriers to widespread vaccination is vaccine hesitancy and vaccine misinformation. There would also likely be considerable public and administrative confusion as to the effect of the injunction because the Pfizer-BioNTech EUA vaccine and Comirnaty are medically interchangeable. Even a more limited injunction, somehow limited to these plaintiffs, would generate extraordinary doubt and confusion.

I declare under penalty of perjury that the foregoing is true and correct to the best of my information, knowledge, and belief.

Dated: December 17, 2021

Peter Marks, M.D., Ph.D.
Director, Center for Biologics Evaluation
and Research
United States Food and Drug Administration