

UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA

NAVY SEAL 1, et al.,)
)
) Plaintiffs,)
 v.)
) Case No. 8:21-cv-02429-SDM-TGW
 JOSEPH R. BIDEN, et al.,)
)
) Defendants.)
)

**DECLARATION OF ROBERT MALONE, MD, MS, IN SUPPORT OF PLAINTIFFS’
MOTION FOR A TEMPORARY RESTRAINING ORDER AND PRELIMINARY
INJUNCTION**

Dr. Robert Malone declares under penalty of perjury:

1. I am over the age of eighteen years, have personal knowledge and exposure to the matters set forth in this Declaration, and if called to testify to them, I would and could do so competently.

2. I am an original inventor of core mRNA and DNA vaccination technology; have been involved in developing, designing, and providing oversight of approximately forty phase 1 clinical trials and twenty phase 2 clinical trials, as well as five phase 3 clinical trials; have been involved in infectious disease pathogen advanced development oversight of HIV, Influenza, Plague, Anthrax, VEE/EEE/WEE, Tularemia, Tuberculosis, Ebola, Zika, Ricin toxin, and Engineered pathogens; and, since January 2020, have been leading a large team focused on clinical research design, drug development, computer modeling, and mechanisms of action of repurposed drugs for COVID-19 treatment.

3. I submit this declaration in support of Plaintiffs’ arguments that (a) the Pfizer-BioNTech COVID-19 Vaccine and COMIRNATY COVID-19 Vaccine are legally distinct; and (b) there are

no licensed SARS-CoV-2 vaccines currently available in the US. Rather, all currently available doses of SARS-CoV-2 vaccines are experimental medical products made available under the Emergency Use Statutes and Authorizations (EUA).

Education and Professional Experience

4. I graduated from the University of California, Davis with a Bachelor of Science degree in Biochemistry in 1984. I graduated from the University of California, San Diego with a Master's degree in Biology in 1989. I graduated from Northwestern University Medical School, Feinburg School of Medicine, in 1991.

5. I received one year of pathology residence training at University of California, Davis Sacramento Medical Center. I completed a Masters' Degree in Biology from University of California, San Diego in 1989 for work performed primarily at the Salk Institute in the Molecular Biology and Virology Laboratories and Laboratory of Dr. Inder Verma. This and subsequent work at the San Diego corporation "Vical" resulted in nine issued domestic US patents describing mRNA and DNA vaccine platform technology.

6. I completed a Giannini post-doctoral research fellowship at University of California, Davis Department of Pathology in 1992. I completed a Harvard Medical School Global Clinical Research Scholars fellowship in 2016. This fellowship included an emphasis on regulatory affairs, clinical development, bioethics, epidemiology and biostatistics.

7. I am currently licensed to practice medicine in the State of Maryland.

8. I have been extensively and repeatedly trained in clinical research bioethics over many years at a variety of institutions including intensive training by Dr. Adil Shamoo of the University of Maryland, Baltimore.

9. I served as Assistant and Associate Professor of Surgery and/or Pathology at University of California, Davis School of Medicine, University of Maryland School of Medicine, and the Uniformed University of the Health Sciences between 1992 and 2001. During this period, I was awarded numerous peer-reviewed and industrial grants and contracts relating to gene delivery technology, genetic vaccine development, the chemistry and formulation of gene delivery reagents such as those used for mRNA vaccines, mucosal genetic vaccine development and other related topics. This work resulted in numerous additional granted US Patents in these fields and the incorporation of biotechnology companies based on these discoveries including Inovio vaccines.

10. I served as Associate Director, Clinical Research at Dynport Vaccine Company LLC from 2002-2003, supporting the prime systems US DoD contract for all biodefense products under advanced development by the Department of Defense. I also served as Director, Business Development and Program Management for the Bill and Melinda Gates funded Aeras Global TB Vaccine Foundation from 2004-2005; Senior Medical Director, Summit Drug Development Services (a Regulatory Affairs and Clinical Research specialty contract research organization) from 2005-2006; Director, Clinical Development & Medical Affairs, Influenza for Solvay Pharmaceuticals (currently Abbvie) from 2006-2008; and Medical Director, Vaccines for the Beardsworth Consulting Group from 2010 – 2013.

11. I currently serve as CEO and Principal Consultant for RW Malone MD LLC, primarily supporting the US Department of Defense, Defense Threat Reduction Agency (via contracts held by Leidos and MIT-Lincoln Lab). I have been leading or serving as a principal consultant for teams developing both repurposed drugs or vaccines since January 4, 2020, resulting in multiple novel findings, published and pending manuscripts, three clinical trials involving repurposed drugs

(two in USA under DoD funding, one in India under funding from Reliance Healthcare) and one Phase 1 clinical trial for a novel SARS-CoV-2 vaccine.

12. I have a history of over a decade of service to the NIAID as either reviewer or study section chairperson for evaluating large contract bids for development of Biodefense and other Medical Countermeasures against emerging infectious diseases and biothreat agents.

13. I currently sit on the NIH/FNIH ACTIV COVID-19 Drug development panel.

14. I co-authored a book entitled “NOVEL CORONAVIRUS: A Practical Guide for Preparation and Protection (originally published Feb 2020).

15. I played a key role in the discovery and clinical development of the repurposed drugs Famotidine and Famotidine + Celecoxib as treatment for both outpatient and inpatient COVID-19 disease, and have academic publications relating to this work. This work has yielded FDA and Indian health authority approved INDs for clinically testing these agents in outpatient and inpatient randomized controlled trials.

16. I supported the Indian corporation Reliance in development of a second-generation SARS-CoV-2 vaccine that is now IND approved by the Indian health authority for initiation of clinical trials which are anticipated for Q4 2021.

17. I have previously served as an expert witness in cases relating to vaccine development, COVID-19, and related topics.

18. Together with Dr. Peter Navarro, I developed and published (lay press, Washington times) public policy recommendations involving targeting SARS-CoV-2 vaccine deployment to high risk groups (elderly, morbidly obese, immunodeficient and others), providing early COVID-19 treatment options (including antibody therapies), home diagnostic tests, and computational algorithms enabling individual assessment of COVID-19 risks.

19. Attached as **Exhibit A** is a true and correct copy of my curriculum vitae.

BioNTech’s COMIRNATY Vaccine is distinct from the Pfizer-BioNTech Vaccine

20. Defendants’ argument that the Pfizer-BioNTech vaccine is fully interchangeable with BioNTech’s COMIRNATY is incorrect. Even if the vaccines might be produced at the same facilities or with the “same formulation,” as defendants assert, does not mean they are fully interchangeable. The Pfizer-BioNTech vaccine is only authorized under the Emergency Use Authorization provision while the BioNTech vaccine received FDA approval. However, as will be addressed below, there is no FDA approved SARS-CoV-2 vaccine available. That is to say, the FDA approved BioNTech COMIRNATY vaccine is not available.

21. Although the FDA has stated that the two vaccines have the “same formulation . . . and can be used interchangeably to provide the vaccination series without presenting any safety or effectiveness concerns,” that does not mean they are the same vaccine. In fact, the FDA has explained that the two “products are legally distinct” but “with certain differences that do not impact safety or effectiveness.” *See* Letter United States Food and Drug Administration to Pfizer at 3, n. 10 (Sept. 22, 2021) (A true and correct copy of the letter is attached as **Exhibit B**); Letter United States Food and Drug Administration to Pfizer at 3, n. 11 (Oct. 20, 2021) (A true and correct copy of the letter is attached as **Exhibit C**); Letter United States Food and Drug Administration to Pfizer at 3 (A true and correct copy of the letter is attached as **Exhibit D**); CDC COVID-19 Vaccine Related Codes at 4 (A true and correct copy of the document is attached as **Exhibit E**).

22. The notion that the two legally distinct products are wholly interchangeable appears to be based on an incorrect understanding that a regulated product authorized for marketing by the FDA consists only of the active drug substance as delivered into a vial or other container in the case of

an injectable vaccine. However, the Pfizer-BioNTech vaccine and BioNTech COMIRNATY vaccine are legally distinct products, as described by the FDA documents available at <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine>. These vaccines and any other FDA regulated medicinal product consists of the entirety of the data supporting the safe and effective use of the product, as well as the quality systems, production methods and processes, laboratory assays (including in-process and release assays), materials, facilities & equipment, and packaging & labeling of the product. Packaging and labeling specifically includes a package insert summarizing the data supporting the intended safe and effective use, and also describing the risks associated with the medical product.

23. These packaging and labeling aspects for the Pfizer-BioNTech vaccine and BioNTech's COMIRNATY, which are intrinsic aspects of the regulated product, are explicitly not identical between these two legally distinct products. For example, BioNTech's COMIRNATY includes FDA approved labeling and a package insert designed to inform the recipient of the (incomplete, as recognized by the FDA) list of risks and benefits of the product, whereas the Pfizer-BioNTech vaccine does not. Therefore, the Pfizer-BioNTech vaccine and BioNTech's COMIRNATY are neither identical legally nor functionally.

24. There may be other differences between the Pfizer-BioNTech vaccine and BioNTech's COMIRNATY in the totality of the products in terms of quality systems, production methods and processes, laboratory assays (including in-process and release assays), materials, facilities & equipment. The provided FDA communication appears to assert that the materials used and final formulation is essentially identical, but potential differences in addition to the differences in packaging and labeling are not explicitly addressed.

25. On the basis of these facts and observations, it is my expert opinion that the Pfizer-BioNTech vaccine and BioNTech's COMIRNATY are not identical, and that the FDA has appropriately identified them as legally separate and distinct products. The assertions that the Pfizer-BioNTech vaccine and BioNTech's COMIRNATY are identical is not based in regulatory or legal fact.

BioNTech's COMIRNATY Vaccine is not available in the US

26. It is my expert opinion, based on the aforementioned FDA letters dated September 22, 2021 (Exhibit B at 6, n.12), October 20, 2021 (Exhibit C at 7, n. 13) , and October 29, 2021 (Exhibit D at 9, n. 17), as well as the September 13, 2021 National Institutes of Health news release (Exhibit F), and a CDC release of COVID-19 Vaccine Related Codes (Exhibit E), **that the FDA regulated product labeled COMIRNATY is the only FDA licensed SARS-CoV-2 vaccine** (A true and correct copy of the NIH press release is attached hereto as Exhibit F) **but it is not yet available for use in the U.S.** In the FDA letters dates September 22, 2021 and October 20, 2021 (both cited above), the FDA expressly states: "Although COMIRNATY (COVID-19 Vaccine, mRNA) is approved to prevent COVID-19 in individuals 16 years of age and older, **there is not sufficient approved vaccine available for distribution to this population in its entirety at the time of reissuance of this EUA.**" (emphasis added).

27. As stated in the CDC COVID-19 Vaccine Related Codes document (Exhibit E), **"COMINARTY products are not orderable at this time. NDCs are listed per FDA Structured Product Label (SPL) document for the BLA licensed product. These codes are not included in CDC Vaccine Code Set files at this time. Pfizer has provided the following statement regarding the COMINARTY branded NDCs and labels:** 'Pfizer received FDA BLA license on 8/23/2021 for its COVID-19 vaccine for use in individuals 16 and older (COMIRNATY). At that

time, the FDA published a BLA package insert that included the approved new COVID-19 vaccine tradename COMIRNATY and listed 2 new NDCs (0069-1000-03, 0069-1000-02) and images of labels with the new tradename. **At present, Pfizer does not plan to produce any product with these new NDCs and labels over the next few months while EUA authorized product is still available and being made available for U.S. distribution. As such, the CDC, AMA, and drug compendia may not publish these new codes until Pfizer has determined when the product will be produced with the BLA labels.**” (Exhibit E) (first bolding in original, second bolding emphasis added).

28. On September 13, 2021, the NIH published the identical Pfizer statement: **“At present, Pfizer does not plan to produce any product with these new NDCs and labels over the next few months while EUA authorized product is still available and being made available for U.S. distribution. As such, the CDC, AMA, and drug compendia may not publish these new codes until Pfizer has determined when the product will be produced with the BLA labels.”** (Exhibit F) (emphasis added).

29. Based on all information available to me, it is my expert opinion that **none** of the SARS-CoV-2 vaccines currently available in the U.S. are FDA approved and licensed for use. All doses currently available (Pfizer-BioNTech, Moderna, and Johnson & Johnson) are experimental medical products made available as such by the FDA and the Department of Health and Human Services under the Emergency Use Statutes and Authorizations (EUA). Under the EUA, and the FDA Fact Sheets for Pfizer-BioNTech, Moderna, and Johnson & Johnson, individuals have the “option to accept or refuse” the products.

VERIFICATION

I, Robert Malone, MD, MS, am over the age of eighteen years and a Declarant in this action. The statements and allegations that pertain to me or which I make in this DECLARATION are true and correct, and based upon my personal knowledge (unless otherwise indicated). If called upon to testify to their truthfulness, I would and could do so competently. I declare under penalty of perjury, under the laws of the United States, that the foregoing statements are true and correct to the best of my knowledge.

Dated: November 9, 2021

A handwritten signature in black ink, appearing to read "R. Malone", is written above a horizontal line.

Robert Malone, MD, MS

Robert W. Malone, MD, MS

Robert W. Malone, MD, MS
Madison, VA 22727
rwmalonemd@gmail.com
(434) 979-0090

EXHIBIT A

PROFESSIONAL EXPERIENCE

The original inventor of mRNA and DNA vaccination technologies (1989); including in-vitro and in-vivo RNA transfection. Dr. Malone is a specialist in clinical research, medical affairs, regulatory affairs, project management, proposal management (large grants and contracts), vaccines and biodefense. This includes writing, developing, reviewing and managing vaccine, bio-threat and biologics clinical trials and clinical development strategies. He has been involved in developing, designing, and providing oversight of approximately forty phase 1 clinical trials and twenty phase 2 clinical trials, as well as five phase 3 clinical trials. He has served as medical director/medical monitor on both phase 1, phase 2 and phase 3 clinical trials, including those run at a well-known vaccine-focused Clinical Contract Research Organizations. He has served as principal investigator on some of these. Examples of his infectious disease pathogen advanced (clinical phase) development oversight experience include HIV, Influenza (seasonal and pandemic), Plague, Anthrax, VEE/EEE/WEE, Tularemia, Tuberculosis, Ebola, Zika, Ricin toxin, Botulinum toxin, and Engineered pathogens. In many cases, this experience has included vaccine product development, manufacturing, regulatory compliance, and testing (manufacturing release and clinical) aspects. In most cases, his oversight responsibilities have included clinical trial design, regulatory and ethical compliance, and laboratory assay strategy, design, testing and performance.

Dr. Malone has a history of assembling and managing expert teams that focus on solving complicated biodefense challenges to meet US Government requirements. He was instrumental in enabling the PHAC/rVSV ZEBOV (“Merck Ebola”) vaccine to move forward quickly towards BLA and (now recently granted) licensure. Dr. Malone got the project on track in support of DoD/DTRA and NewLink Genetics, recruited organizations to team with USAMRIID/WRAIR to develop the immunoassays, put WHO and Norwegian government philanthropic leadership in touch with Pentagon leadership to expedite the initial WRAIR clinical and ring vaccination trials, recruited a management team, recruited Merck vaccines to purchase the product candidate from NewLink, helped write and edit the clinical trials developed by the World Health Organization and lead the development of the BARDA and DTRA contracts - yielding over 200M\$ in resources. Dr. Malone’s early involvement in this project allowed for the Merck vaccine to be developed very rapidly.

Currently, Dr. Malone is leading a large team since January 10, 2020, focused on clinical research design, drug development, computer modeling and mechanisms of action of repurposed drugs for COVID-19 treatment. This work has included multiple manuscripts summarizing most recent findings relating to famotidine and overall insights into the mechanism of COVID-19 disease, and others focused on celecoxib and famotidine are being reviewed for publication. He has developed and wrote the initial clinical trial design: A Single Center, Randomized, Double Blinded Controlled Crossover Observational Outpatient Trial of the Safety and Efficacy of Oral Famotidine for the Treatment of COVID-19 in Non-Hospitalized Symptomatic Adults. Another project he has been involved with is a DTRA/DOMANE-funded development and performance of a virtual outpatient clinical trial designed to test new monitoring and data capture technology while using COVID19 as a live-fire example. He has helped open two IND for famotidine and celecoxib use for treatment and prevention of COVID19 disease including an associated

drug master file, and has enabled teaming/pharmaceutical supply arrangements with two major pharmaceutical firms.

Dr. Malone is an internationally recognized scientist and is the original inventor of mRNA Vaccination, DNA Vaccination, and multiple non-viral DNA and RNA/mRNA delivery technologies. Dr. Malone holds numerous fundamental domestic and foreign patents in the fields of gene delivery, delivery formulations, and vaccines: including DNA and RNA/mRNA vaccines. His expertise includes virology, immunology, molecular biology, pathology and pharmacology.

Scientifically trained at UC Davis, UC San Diego, and at the Salk Institute Molecular Biology and Virology laboratories, Dr. Malone received his medical training at Northwestern University (MD) and Harvard University (Clinical Research Post Graduate Fellowship) medical schools, and in Pathology at UC Davis.

He has extensive research and development experience (bench to bedside) in the areas of pre-clinical discovery research, clinical trials, vaccines, gene therapy, bio-defense, repurposing drugs for infectious diseases, high throughput screening and immunology. He has over twenty years of management and leadership experience in academia, pharmaceutical and biotechnology industries, as well as in governmental and non-governmental organizations. He often serves as study section chairperson for NIAID contract study sections relating to biodefense medical product development. He is currently a topic editor for the journal *Frontiers in Pharmacology*, in the area of “Treating COVID-19 With Currently Available Drugs.”

Dr. Malone has approximately 100 peer-reviewed publications and published abstracts and has about 12,000 citations of his peer reviewed publications and patents, as verified by Google Scholar. His google scholar ranking is “outstanding” for impact factors. He has been an invited speaker at over 50 conferences, has chaired numerous conferences and he has sat on or served as chairperson on numerous NIAID and DoD study sections.

SUMMARY OF ACCOMPLISHMENTS / SKILLS

- Inventor of mRNA and DNA vaccination.
- Inventor of lipid mediated and naked mRNA delivery (transfection).
- Inventor of in-vivo electroporation (particularly for skin delivery).
- A senior executive and scientist with a highly successful track record of leading bench and discovery research through FDA Phase I, II, and III clinical trials, protocol development and submission, and related regulatory submissions including pIND and IND.
- Significant expertise in drug development and delivery.
- Specialist in Medical Affairs.
- Special in Regulatory Affairs.
- Domestically trained, Maryland Licensed Physician/Scientist.
- Experienced capturing and managing large federal contracts (including BARDA) with over 9 billion in ID/IQ awards and almost a billion USD in government contracts won and/or managed in the last decade.
- Expertise in pathology, infectious disease, pandemic clinical trials, influenza, regulatory affairs, project management, biodefense, HIV and Ebola. A verified list of capture is available upon request.
- Significant expertise with federal contracting, grants, international NGO health related research and development coupled with professional relationships at CDC, DoD, HHS (BARDA, CDC, FDA and NIAID).
- Prior and current service on many federal study sections and oversight boards involving infectious disease, vaccine, and biodefense.
- Experienced and formally trained as a Business Development Professional, project manager, capture/proposal manager, color team reviewer and editor for projects valued from 10M\$ up to 1B\$ US, with experience managing processes and teams in a wide variety of non-profit and for-profit corporate cultures including both matrix and traditional environments.
- Highly skilled in fostering a culture of innovative problem solving within project teams.
- DoD Secret Clearance authorized.
- Expert witness experience, with extensive training from some of the top attorneys/law firms in the USA.
- Rated outstanding for impact factors, by Google scholar.
- Graduated from the Harvard Medical School Global Clinical Scholars Research Training Program with distinction, a year-long program focused on international clinical research. This program combines on-site (London & Boston) as well as distance learning, with an average of 15h per week lecture and practicum exercises.

RW Malone MD, LLC***CEO and Principal Consultant:*** 2001-Present

Dr. Malone has been involved in developing, designing, and providing oversight of approximately forty phase-1 clinical trials and twenty phase-2 clinical trials, as well as five phase 3 clinical trials. He has served as medical director/medical monitor on approximately forty phase-1 clinical trials, and on twenty phase-2 clinical trials, including those run at vaccine-focused Clinical Research Organizations. He has served as principal investigator on some of these. Providing business development, proposal management, clinical trials development, expert witness, regulatory and medical affairs support for pharmaceutical, vaccines-related and biologics companies as well as related regulatory submissions including pIND and IND.

Projects include:

- Working with Reliance Life Sciences (India) to develop RelCovax™, a second-generation multivalent SARS-CoV-2 vaccine candidate designed to meet global vaccination demands. 2020-present.
Led a large team since January 10, 2020, focused on drug development, computer modeling and mechanisms of action for COVID-19 and is now preparing a manuscript summarizing most recent findings relating to famotidine and overall insights into the mechanism of COVID-19 disease.
- Accelerated COVID-19 Therapeutic Interventions and Vaccines: ACTIV Therapeutics Clinical Working Group, NIH. Invited Participant. June, 2020-present.
- Clinical trials protocol development: Developed and wrote initial clinical trial design: A Single Center, Randomized, Double Blinded Controlled Crossover Observational Outpatient Trial of the Safety and Efficacy of Oral Famotidine for the Treatment of COVID-19 in Non-Hospitalized Symptomatic Adults.
- Proposed is a DOMANE/WRAIR joint development and performance of outpatient clinical trial designed to test new monitoring and data capture technology while using COVID19 as a live-fire example.
- Opening IND for famotidine use for treatment and prevention of COVID19 disease with associated drug master file.
- Principal Regulatory Consultant, Clinical Network Services (CNS)/Novotech, 2018-2019. Regulatory, clinical and business development support.
- Served as an expert witness with specialized training, 2017 - present.
- Ebola vaccine project for NewLink/Bioprotection Systems (rVSVdG ZEBOV Ebola vaccine project), resulting in well over 100M USD non-dilutive capital to NL/BPS. This also included working with the World Health Organization as well as initial set up of the licensing deal to Merck Vaccines of the Ebola vaccine.
- Served as Medical Director, Beardsworth, half time position on retainer, 2010 – 2013.
- Service on federal biotechnology/vaccines proposal study sections (multiple).
- Served as Editor-In-Chief of Journal of Immune Based Therapies and Vaccines 2007-2012
- Service on Safety Monitoring Committee, Phase 1 safety/immunogenicity of novel Influenza vaccine
- Consulting support for multiple vaccine-focused clinical sites in US and Latin America.
- Served as Medical Director, Vaccines with Accelovance, Inc. (2008 – 2009).
- Served as medical monitor for multiple seasonal and pandemic (H1N1) studies.

Robert W. Malone, MD, MS

- Review and edit clinical protocols.
- Examples of multi-year contract clients include Accelovance, Alchem Laboratories, Avancer, Beardsworth, Chesapeake Perl, Corium, DOAR, ITS, ITT-Exelis, EpiVax, Jean Brown Research, Opgen, Quest Diagnostics (Focus), PaxVax, SAI, Soligenix, TASC, Univ of MA.
- Commercial intelligence work for two of the largest pharmaceutical companies in the world (sub-contractor).
- Partnering with Galloway and Associates (Darrell Galloway) 2012-2014.
- Acting as *Managing Director, Clinical Development and Government Affairs* for the Avancer Group. April 2012 – 2016.
- Proposal development (patch-based vaccine delivery, Tularemia vaccine, CDC contract for clinical trials site development, international government and NGO contract and grant solicitations) – Aeras Global TB Vaccine Foundation 2003-2005.
- Proposal development (plague vaccine- HHS), Technical diligence – VaxGen Corporation.
- Consulting services for EpiVax, 2005-2018 (member, Scientific Advisory Board), 2020.
- Consulting services for Aldevron, LLC. 2001-2005 (operating as Gene Delivery Alliance).
- Business and proposal development in the areas of Bioinformatics and Life Sciences (including telemedicine) and research at the University of Bern, Switzerland.
- Consulting services for Molecular Histology, Inc. with the title of Medical Director.
- Collaboration with Inovio, including incorporation of company in the USA.
- Consulting services for MSD, Inc. for business/ technology development planning.

Alchem Laboratories
Chief Medical Officer

This position was as a consultant, but then full time FTE. Consulting for Alchem and/or its CEO: 2012 – 2019. CMO 11/2019 to 4/2020.

- Led a high through-put screening and research team for drug development 2019-2020.
- Dr. Malone began modeling and focusing on the Plpro (papain-like protease) and Mpro (main protease) of then novel coronavirus (now SARS-CoV-2) using computational tools including Modeller to generate homology-modeled crystal structures for the SARS-CoV-2 Plpro and Mpro. Which generated a candidate list for COVID-19, which was reduced to a few candidates, based on binding sites, safety, licensure, efficacy, bioavailability of drug candidates.
- Lead the discovery and development of famotidine for the Treatment of COVID-19.
- Technical Lead/writer for funded full proposal under BAA-18-100-SOL-00003 Amendment 15 entitled: “A Multi-site, Randomized, Double-Blind, Multi-Arm Historical Control, Comparative Trial of the Safety and Efficacy of Hydroxychloroquine, and the Combination of Hydroxychloroquine and Famotidine for the Treatment of COVID-19 in Hospitalized Adults.”
- Developed and wrote initial clinical trial design for a comparative trial of the safety and efficacy of hydroxychloroquine, and the combination of hydroxychloroquine and famotidine for the treatment of COVID-19 in hospitalized adults.

Robert W. Malone, MD, MS

Atheric Pharmaceutical, LLC

CEO, and Co-founder.

Feb 2016-Dec 2017. Atheric™ Pharmaceutical LLC was a biopharmaceutical company focused on the rapid development and commercialization of re-purposed drugs to prevent and treat Zika and other Flavivirus disease. Optimization of high through-put screening techniques for anti-viral drug development.

Kennesaw State University

Adjunct Associate Professor 2009-2013

Beardsworth Consulting Group, Inc

Medical Director, Vaccines (RW Malone MD, LLC under contract to Beardsworth)

2010-2013

Dr. Malone functioned as the in-house medical vaccine expert for medical monitoring and Scientific Liaison

- Medical liaison to investigator sites including oversight of clinical monitoring
- Provided medical monitoring input including CRF review, 24x7 accessibility to site personnel, assess enrollment waiver requests, SAE review, etc.
- Safety Officer and Medical Representative on project teams
- Medical consultant to clients
- Business development/proposal writing/government contracting

Solvay Pharmaceuticals, Inc (currently Abbvie)

Director, Clinical Development & Medical Affairs, Influenza 2006-2008

Led an extended clinical team (both internal and CRO components), providing project and clinical trials management oversight, serving as primary author on clinical protocols, strategic documents including clinical development plans, DSMB/SMC charters, and all clinical documents required to support IND filing. Support and review of outcomes including safety data assessment

Generated and managed cost projections and budgetary oversight, providing strategic management and serving as a communication hub for clinical aspects of a \$300 million USD federal contract to develop and license a cell-based influenza vaccine

Solvay's US Government contract for cell-based influenza vaccine was terminated around the end of 2007. At which point the cell-based influenza vaccine project was dissolved.

Summit Drug Development Services

Senior Medical Director 2005-2006

Directed due diligence assessments and strategic drug development planning and prepared regulatory submissions and implemented, monitored, and analyzed clinical trials for clients (oncology, vaccines, biologicals, cell/stem cell therapies). Primary author of three pIND, two IND, an Appendix M submission. Served as proposal manager and primary author for a 129M USD federal contract submission focused on pandemic influenza.

AERAS Global TB Vaccine Foundation

Director, Business Development and Program Management 2004-2005

Initially serving as consultant, provided leadership primarily focused on tuberculosis vaccine development and proposal development to NGO (B&M Gates), USG (CDC, NIH, DoD).

Dynport Vaccine Company, LLC

Associate Director, Clinical Research 2002-2003

- Served as liaison between product development teams and clinical research support groups.
- Prepared planning documents and product development plans.
- Participated in and supported safety review and assessment of smallpox vaccine product.
- Identified new technologies relevant to product development teams, facilitating integration of same in product development plans.
- Created documents for clinical trials including investigator brochures. Prepared proposal solicitations, technical review of subcontractor proposals. Performed technical review of potential subcontractors, new technologies.
- Assisted business development group in strategic evaluation and planning concerning new business opportunities and managed in-house Publication.

Intradigm, Corp

Co-Founder (one of three co-founders), CSO, Board of Director Member 2000-2001

Intradigm was a biotechnology company that develops gene therapeutic technology based on RNA interference. Intradigm merged with Silence Technologies in 2009 and the merged company is now publicly traded. Silence Technologies is involved in developmental research of targeted RNAi therapeutics for the treatment of serious diseases.

Dr. Malone co-founded and helped to secure \$2.3 million in V.C. funding, including monies from the Novartis Venture Fund, ETP Venture Capital Fund and the State of Maryland. Performed facilities set-up, infrastructure set-up and Intellectual Property Development. Business and technology development planning, including in-depth business and scientific plan.

Uniformed Services University of the Health Sciences

Dept of Surgery, Clinical Breast Care Program (CBCP) through the Henry M. Jackson Foundation
Adjunct Associate Professor

Chief of Laboratory Science and Director of Tissue Banking 2000-2001

- Worked closely with architect firm to design space, set-up laboratory facilities for the Clinical Breast Care Project, including new facilities design (tissue banking facilities, laboratory, animal rooms, animal surgical suite, office suites) at USUHS and Windber Medical Center, PA
- Hired faculty, technicians, staff for CBCP at both sites, including writing and initiating job descriptions, job interviews, hiring decisions, set-up for re-locations
- Laboratory Supervisor: Tissue banking immunology, cell culture, gene transfer, genetic vaccination research, animal research.

University of Maryland, Baltimore School of Medicine, Dept. of Pathology

Assistant Professor 1997-2000

Set-up and ran successful research laboratory in immunology (genetic vaccination) and gene transfer.

University of California, Davis Department of Medical Pathology

1991-1997

Assistant Professor 1993-1997

Director and Founder, Gene Therapy Program (pulmonary, dermal, heart, liver, mucosal and parenteral vaccines).

Research Fellow, Pathology Resident 1991-1993

Vical, Inc

***Research Scientist* 1989**

- Set up Vical's molecular biology laboratory.
- Initiated and carried out research in non-viral gene therapy and DNA vaccination.
- Inventor of "naked DNA" gene therapy. (see issued patents for details).
- Inventor of DNA vaccination (see issued patents for details).
- Inventor of "mRNA" gene therapy. Salk institute.
- Inventor of mRNA vaccination. Salk institute.
- Inventor of "mRNA as a drug" or "transient gene therapy", terms both coined by Dr. Malone. Salk Institute.

LICENSURE / CERTIFICATIONS

Physician and Surgeon, State of Maryland License 1997-present. #DOO55466

BOARD OF DIRECTOR POSITIONS:

Discovery Cure, Inc. Founding Board of Director. 2018-2020

Epivax, Scientific Advisory Board, 2012-2019.

EDUCATION

- **HARVARD MEDICAL SCHOOL** *Global Clinical Scholars Research Training Program (fellowship)*
A year-long comprehensive program that combines on-site (London, Boston) and distance learning, with an average of 15h per week lecture and practicum exercises. 2015-2016. Graduation with distinction (top 5% of graduating class).
- **UNIVERSITY OF CALIFORNIA, DAVIS: RESEARCH FELLOWSHIP, 1992 – 1993**
Postgraduate Fellowship Award
- **UNIVERSITY OF CALIFORNIA, DAVIS MEDICAL CENTER: 1992**
Clinical Pathology Internship
- **NORTHWESTERN UNIVERSITY MEDICAL SCHOOL: 1991**
Doctor of Medicine
- **UNIVERSITY OF CALIFORNIA, SAN DIEGO: 1988**
Master of Science, Biology
- **UNIVERSITY OF CALIFORNIA, DAVIS: 1984**
Bachelor of Science, Biochemistry

TEACHING EXPERIENCE

Kennesaw State University

Associate Professor:

BTEC 4490 Experimental Design and Analysis (2009): Survey course focused on advanced product development and regulatory aspects of biotechnology and vaccines products.

University of Maryland, Medical School

Assistant Professor:

Fundamentals of Molecular Biology (Graduate Course, Winter 2000)

Host defenses and Infectious Diseases, small group instructor Year 2 Medical School core curriculum. 1998, 1999

University of California, Davis

Assistant Professor:

MD 410A/410B. General Systemic Pathology (1992, 1993, 1994, 1995, 1996)

PTX 202. Principles of Pharmacology and Toxicology-Lecturer (1995, 1996)

BCM 214-414. Molecular Medicine-Lecturer (1995, 1996)

IM 295 Cytokines-Lecturer (1996), IDI 280. Molecular Basis of Disease-Lecturer (1996)

University of California, San Diego

Biology 111. Cell Biology (Fall 1988). Teaching Assistant under Dr. M. Montal

Biology 123. Embryology laboratory (Spring 1988). Teaching Assistant under Dr. C.Holt

Santa Barbara City College

Computer Laboratory (Spring 1981) Teaching Assistant

PROFESSIONAL OFFICES AND MEMBERSHIPS

- Royal Society of Medicine, Fellow 2021-Present.
- Harvard Medical School Alumni, 2016- present.
- American Society of Tropical Medicine and Hygiene Member (ASTMH): 2016-2018.
- Virginia Bio: 2016-2018
- IEEE Genomics and Bioinformatics Working Group Member: 2002
- Northern Virginia Technology Council BioMedTech Committee: Co-chair: 2002 – 2003
- Intradigm, Corp. – a new start-up from Novartis, Inc.: Scientific Advisory Board: 2000 – 2001
- Novartis, Inc. (GTI/Systemix & Pharmacokinetics): Scientific Advisory Board and External Portfolio Reviewer: 1999 – 2001
- University of Maryland, Medical School: Pathology Education Policy Committee: 1999 – 2000
- UC Davis:
 - Education Policy Committee Graduate Group in Comparative Pathology: 1996 – 1/1997
 - Member, Biochemistry and Molecular Biology Graduate Group: 1993 – 1/1997
 - Member, Comparative Pathology Graduate Group: 1995 – 1/1997
- Boehringer Mannheim: Scientific Advisory Board: 1992 – 1993

EDITORIAL BOARDS

- Topic Editor, *Frontiers in Pharmacology (Respiratory Pharmacology)*: “Treating COVID-19 with Currently Available Drugs,” 2020-2021.
- Editor-In-Chief, *Journal of Immune Based Therapies and Vaccines*. 2009 – 2012, Editor: 2012.
- Gene Therapy/Molecular Biology International Society. 1997 – 2014.
- Reviewer for: Numerous peer-reviewed journals on infectious disease, public health 2016 to present.
- *Nucleic Acids Research*: 2001 – 2002.
- *Molecular Therapy*: 1999 – 2001.

ACADEMIC HONORS

- Harvard Medical School, Global Clinical Scholar Post Graduate: graduation with distinction (top 5% of graduating class).
- “DNA Vaccine” Recognizes Robert W. Malone, MD, MS, 2013.
- Trainee Investigator Award, American Federation for Clinical Research: 1993.
- Bank of America – Giannini Foundation Medical Research Fellow: 1992 – 1993.
- Henry Christian Award for Excellence in Research, American Federation for Clinical Research: 1992.
- UCDCM Medical Scholars Grant: 1992 – 1993.
- DNA and RNA Transfection and Vaccination (Abstract). First Place, Northwestern AOA Research Symposium Competition for Medical Students: 1989.
- USPHS Pre-Doctoral Fellowship: 1986 – 1988.
- San Diego Supercomputer Grant for RNA Structure Modeling: 1988.
- Northwestern University MD/ PhD Scholarship: 1984 – 1986.
- Dean's List, UC Davis: 1982 – 1984.
- President's Undergraduate Fellowship Grant for Investigation of Oncogene Expression in Breast Tumor Tissue: 1983 – 1984.
- Edmonson Summer Fellowship, Department of Pathology, UC Davis Medical School: 1984.

PATENTS ISSUED:

1. Lipid-mediated polynucleotide administration to deliver a biologically active peptide and to induce a cellular immune response. Assigned to Vical, Inc and licensed to Merck. No. 7,250,404, date of issue: 7/31/07. Priority date 3/21/1989. **Citations: 105 articles.**
2. Lipid-mediated polynucleotide administration to reduce likelihood of subject's becoming infected. Assigned to Vical, Inc and licensed to Merck. US Pat. Ser. No. 6,867,195 B1, date of issue: 3/15/05. Priority date 3/21/1989.
3. Generation of an immune response to a pathogen. Assigned to Vical, Inc and licensed to Merck. US Pat. Ser. No. 6,710,035, date of issue: 3/23/04. Priority date 3/21/1989. **Citations: 37 articles.**

4. Expression of exogenous polynucleotide sequences in a vertebrate, mammal, fish, bird or human Assigned to Vical, Inc, licensed to Merck. US Pat. Ser. No. 6,673,776, date of issue: 1/6/04. Priority date 3/21/1989.
5. Methods of delivering a physiologically active polypeptide to a mammal. Assigned to Vical, Inc, licensed to Merck. US Pat. Ser. No. 6.413.942, date of issue: 7/2/02. Priority date 3/21/1989.
Citations: 150 articles.
6. Induction of a protective immune response in a mammal by injecting a DNA sequence (includes mRNA). Assigned to Vical, Inc, licensed to Merck. US Pat. Ser. No. 6,214,804, date of issue: 4/10/01. Priority date 3/21/1989. **Citations: 359 articles.**
7. DNA vaccines for eliciting a mucosal immune response (includes mRNA). US Pat. Ser. No. 6,110,898, date of issue: 8/29/00. Priority date 1996. **Citations: 40 articles.**
8. Formulations and methods for generating active cytofectin: polynucleotide transfection complexes. US Pat. Ser. No. 5,925,623 7/20/99.
9. Cationic Transport Reagents. US Pat. Ser. No. 5,892,071 issued 4/06/99.
10. Polyfunctional cationic cytofectins, formulations and methods for generating active cytofectin: polynucleotide transfection complexes. US Pat. Ser. No. 5,824,812 issued 10/20/98.
11. Cationic Transport Reagents. US Pat. Ser. No. 5,744,625 issued 4/28/98.
12. Generation of antibodies through lipid mediated DNA delivery. Assigned to Vical, Inc, licensed to Merck. US Pat. Ser. No. 5,703,055, date of issue: 12/30/97. Priority date 3/21/1989. **Citations: 463 articles.**
13. Induction of a protective immune response in a mammal by injecting a DNA sequence (includes mRNA). Assigned to Vical, Inc, licensed to Merck. US Pat. Ser. No. 5,589,466, date of issue: 12/31/96. Priority date 3/21/1989. **Citations: 889 articles.**
14. Delivery of exogenous DNA sequences in a mammal (includes mRNA). Assigned to Vical, Inc, licensed to Merck. US Pat. Ser. No. 5,580,859, date of issue: 12/3/96. Priority date 3/21/1989. **Citations: 1234 articles.**
15. Cationic Transport Reagents. US Pat. Ser. No. 5,527,928, date of issue: 6/18/96.

Of note: Cationic Lipid-Mediated RNA and DNA Transfection (“RNA as a Drug”). 1988 patent application, Salk institute assignee, patent abandoned without inventor permission or knowledge. Inventor: Robert Malone. Available upon request.

PUBLICATIONS (selected)

COVID-19 Disease, Women’s Predominant Non-Heparin Vaccine-Induced Thrombotic Thrombocytopenia and Kounis Syndrome: A Passepartout Cytokine Storm Interplay. Kounis, N.G.; Koniari, I.; ... Malone, R.W. *Biomedicines* 2021, 9, 959. <https://doi.org/10.3390/biomedicines9080959>

Famotidine and Celecoxib COVID-19 Treatment Without and With Dexamethasone; Retrospective Comparison of Sequential Continuous Cohorts, Submitted to Nature, Scientific Reports, May 2021. Robert W Malone, Kevin M Tomera, Leo Egbujiobi, Joseph K Kittah
Preprint at Research Square <https://www.researchsquare.com/article/rs-526394/v1>

More Than Just Heartburn: Does Famotidine Effectively Treat Patients with COVID-19? Malone RW. *Dig Dis Sci.* 2021 Feb 24:1–2. doi: 10.1007/s10620-021-06875-w. PMID: 33625612; PMCID: PMC7903029.

COVID-19: Famotidine, Histamine, Mast Cells, and Mechanisms. Malone RW, et. al. *Frontiers in Pharmacology*, 23 March 2021. <https://doi.org/10.3389/fphar.2021.633680> Cited in 46 articles.

COVID-19: Famotidine, Histamine, Mast Cells, and Mechanisms. Malone RW, et al *DO.Res Sq.* 2020 Jun 22:rs.3.rs-30934. doi: 10.21203/rs.3.rs-30934/v2. Preprint.PMID: 32702719 <https://www.researchsquare.com/article/rs-30934/v2> Cited in 26 articles.

Hospitalized COVID-19 Patients Treated With Celecoxib and High Dose Famotidine Adjuvant Therapy Show Significant Clinical Responses (July 8, 2020). Tomera, K, Malone, R and Kittah, J. Available at SSRN: <https://ssrn.com/abstract=3646583> or <http://dx.doi.org/10.2139/ssrn.3646583> Cited in 10 articles.

Medical Countermeasures Analysis of 2019-nCoV and Vaccine Risks for Antibody-Dependent Enhancement (ADE). Ricke, D.O.; Malone, R.W. Preprints 2020, 2020030138 (doi: 10.20944/preprints202003.0138.v1). May, 2020 https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3646583 Cited in 32 articles.

Molecular evolution of Zika virus as it crossed the Pacific to the Americas. Schneider AB, Malone RW, et al. *Cladistics*. 2017; 12: 10.1111/cla.12178

Zika Virus: Medical Countermeasure Development Challenges. Malone RW, et al. *PLoS Negl Trop Dis*. 2016;10(3):e0004530. **Citations: 212 articles.**

Zika Fetal Neuropathogenesis: Etiology of a Viral Syndrome. Klase ZA, Khakhina S, Schneider Ade B, Callahan MV, Glasspool-Malone J, Malone R. *PLoS Negl Trop Dis*. 2016;10(8):e0004877. **Citations: 97 articles.**

Antibody mediated epitope mimicry in the pathogenesis of Zika virus related disease. Homan J, Malone RW, et al. *BioRxiv*. 2016.

Making vaccines "on demand": a potential solution for emerging pathogens and biodefense? De Groot AS, Einck L, Moise L, Chambers M, Ballantyne J, Malone RW *Hum Vaccin Immunother*. 2013;9(9):1877-84.

Electroporation enhances transfection efficiency in murine cutaneous wounds. Byrnes CK, Malone RW, et al. *Wound Repair Regen*. 2004;12(4):397-403.

DNA transfection of macaque and murine respiratory tissue is greatly enhanced by use of a nuclease inhibitor. Glasspool-Malone J, ..., Malone RW. *J Gene Med*. 2002;4(3):323-2.

Marked enhancement of macaque respiratory tissue transfection by aurintricarboxylic acid. Glasspool-Malone J, ..., Malone RW. *Gene Med*. 2002;4(3):323-2.

Enhancing direct in vivo transfection with nuclease inhibitors and pulsed electrical fields. Glasspool-Malone J, Malone RW. In *Gene Therapy Methods: Methods Enzymol*. 2002;346:72-91

- Cutaneous transfection and immune responses to intradermal nucleic acid vaccination are significantly enhanced by in vivo electroporation. Drabick JJ, Glasspool-Malone J, ..., Malone RW. *Mol Ther.* 2001;3(2):249-55. Citations: 192 articles.
- Theory and in vivo application of electroporative gene delivery. Somiari S, Glasspool-Malone J, ... Malone RW. *Mol Ther.* 2000;2(3):178-87. Citations: 345 articles.
- Nucleic acid vaccination with a single SIV can protect rhesus macaques from oral challenge with pathogenic SIVMAC239. Gary Rhodes, ... Robert Malone, et al. *Journal of Medical Primatology* 29.3-4 (2000).
- Efficient nonviral cutaneous transfection. Glasspool-Malone J, ..., Malone RW. *Mol Ther.* 2000;2(2):140-6. Citations:138 articles.
- Transfer and expression of foreign genes in mammalian cells. Colosimo A, ..., Malone RW, et al. *Biotechniques.* 2000;29(2):314-8, 20-2, 24 passim. Citations: 188 articles.
- Specific inhibition of macrophage TNF-alpha expression by in vivo ribozyme treatment. Kisich KO, Malone RW, ..., Erickson KL. *J Immunol.* 1999;163(4):2008-16. Citations:131 Articles.
- Marked enhancement of direct respiratory tissue transfection by aurintricarboxylic acid. Glasspool-Malone J, Malone RW. *Hum Gene Ther.* 1999;10(10):1703-13
- Developing dendritic cell polynucleotide vaccination for prostate cancer immunotherapy. Berlyn KA, ..., Malone RW *J Biotechnol.* 1999;73(2-3):155-79
- Models of Cationic Liposome Mediated Transfection. *Gene Therapy and Molecular Biology.* Ahearn A, Malone RW. Vol 4. *Gene Therapy and Molecular Biology* 1999;4
- Feline dendritic-like cells: Isolation, culture, and genetic modification using monocytic precursors. Malone, J. G., Watts, T. L., Hale, A., & Malone, R. W. (1998, January). In *JOURNAL OF LEUKOCYTE BIOLOGY* (pp. 63-63): FEDERATION AMER SOC EXP BIOL.
- Mucosal immune responses associated with polynucleotide vaccination. Malone JG, ..., Malone RW. *Behring Inst Mitt.* 1997(98):63-72
- Delivery of exogenous DNA sequences in a mammal. P Felgner, ..., R Malone, D Carson. *Biotechnology Advances.* 1997 15 (3-4), 763-763
- Cationic lipid-mediated gene delivery to murine lung: correlation of lipid hydration with in vivo transfection activity. Bennett MJ, ..., Malone RW, Nantz MH. *J Med Chem.* 1997;40(25):4069-78
- Improved method for the removal of endotoxin from DNA. Montbriand PM, Malone RW. *J Biotechnol.* 1996;44(1-3):43-6. Citations: 43 articles

Toxicity of cationic lipid-ribozyme complexes in human prostate tumor cells can mimic ribozyme activity. Freedland SJ, Malone RW, et al. *Biochem Mol Med*. 1996;59(2):144-53

Considerations for the design of improved cationic amphiphile-based transfection reagents. Bennett MJ, ..., Malone RW. *Journal of Liposome Research* 1996;6(3):545-65

Escherichia coli beta-glucuronidase and Photinus pyralis luciferase reporter. Ayar, S. F., & Malone, R. W. (1996, November). In *CLINICAL CHEMISTRY* (Vol. 42, No. 11, pp. 35-35).

Structural and functional analysis of cationic transfection lipids: the hydrophobic domain. Balasubramaniam RP, ..., Malone RW. *Gene Ther*. 1996;3(2):163-72. Citations: 172 articles.

The counterion influence on cationic lipid-mediated transfection of plasmid DNA. Aberle AM, Bennett MJ, Malone RW, Nantz MH. *Biochim Biophys Acta*. 1996;1299(3):281-3

Direct gene transfer into mouse muscle in vivo. N Shafee, ..., RW Malone, et al. *International Journal of Virology* 2 (1), 33-38

A flexible approach to synthetic lipid ammonium salts for polynucleotide transfection. MJ Bennett, RW Malone, MH Nantz. *Tetrahedron letters* 36 (13), 2207-2210

Tfx-50 Reagent, a new transfection reagent for eukaryotic cells. Schenborn E, ..., Malone RW, et al. 1995

Hepatic gene expression after direct DNA injection. Hickman MA, Malone RW, et al. *Advanced Drug Delivery Reviews*. 1995;17(3):265-71

Ribozyme and messenger-RNA delivery using cationic liposomes RW MALONE 1995/1/5 Conference JOURNAL OF CELLULAR BIOCHEMISTRY Pages 206 Publisher WILEY-LISS

Cholesterol enhances cationic liposome-mediated DNA transfection of human respiratory epithelial cells. Bennett MJ, ..., Malone RW. *Biosci Rep*. 1995;15(1):47-53

Dexamethasone enhancement of gene expression after direct hepatic DNA injection. Malone RW, et al. *J Biol Chem*. 1994;269(47):29903-7

Gene expression following direct injection of DNA into liver. Hickman MA, Malone RW, et al. *Hum Gene Ther*. 1994;5(12):1477-83. Citations: 306 articles.

Cationic liposome-mediated RNA transfection. Dwarki VJ, Malone RW, Verma IM. *Methods Enzymol*. 1993;217:644-54. Citations: 88 articles.

Successful gene transfection of respiratory epithelium invitro using polyamine containing cationic lipids. CB Robinson, RW Malone, J Jessee, G Gebeyehu, R Wu *AMERICAN REVIEW OF RESPIRATORY DISEASE* 147 (4), A546-A546

Direct gene transfer into mouse muscle in vivo. Wolff JA, Malone RW, et al. Science. 1990;247(4949 Pt 1):1465-8. **Citations: 4,695 articles.**

Cationic liposome-mediated RNA transfection. Malone RW, Felgner PL, Verma IM. Proc Natl Acad Sci U S A. 1989;86(16):6077-81. **Citations: 717 articles.**

mRNA Transfection of cultured eukaryotic cells and embryos using cationic liposomes. Malone RW. Focus. 1989;11:61-8

High levels of messenger RNA expression following cationic liposome mediated transfection tissue culture cells. Malone R, Kumar R, Felgner P. NIH Conference: "Self-Cleaving RNA as an Anti-HIV Agent" (Abstract). Washington, DC June 1989.

A novel approach to study packaging of retroviral RNA by RNA transfection (Abstract). RW Malone, P. Felgner, I. Verma. RNA Tumor Viruses, May 17-18, 1988. Cold Spring Harbor

Mammary tumors in feral mice lacking MuMTV DNA. Gardner MB, Malone RW, ..., Cardiff RD, et al. J Exp Pathol. 1985;2(2):93-8

Hyperplastic and neoplastic changes in the mammary glands of feral mice free of endogenous mouse mammary tumor virus provirus. Faulkin LJ, ..., Malone RW, et al. J Natl Cancer Inst. 1984;73(4):971-82.

PUBLISHED ABSTRACTS: Over 50 published

CHAIRPERSON/ORAL PRESENTATIONS BY INVITATION: Over 40 Invitations
(Only the most recent events listed)

- Vaccines R&D, 2021. Keynote Speaker. September, 2021
- International Covid-19 Summit, Keynote speaker and chair. Rome, Italy, September, 2021
- Vaccines R&D, 2019. Keynote Speaker, Panel Moderator: Boston, MA. 18-20 November, 2019.
- Repurposing drugs for Infectious Disease Outbreaks. International Conference on Zika Virus. Washington, DC Feb 22-25, 2017 (Chairperson)
- Accelerated Discovery and Development of re-purposed licensed drugs for Zika virus outbreak antiviral prophylaxis and therapy. International Conference on Zika Virus. Washington, DC Feb 22-25, 2017. (Oral Presentation)
- Zika Virus: Accelerating Development of Medical Countermeasures by Re-purposing Licensed Drugs. Bridging the Sciences: Zika Virus. Emery, Atlanta, GA 1-3 May, 2016. (Oral Presentation)

Robert W. Malone, MD, MS

- Speaker/Round table- Zika virus: Challenges for Medical Countermeasure Development. World Vaccine Conference. Washington, DC. 29-31 March, 2016.
- The World Health Organization (WHO) Consultation for Zika Virus: Research and Development. Presentation of Drug Development TPP. Geneva, Switzerland. 12-14 March, 2016. (Oral Presentation)
- Keynote Speaker: Ebola Vaccine in 12 months, Global Village, and the Need for Speed. Vaccines R&D, Baltimore, MD. 2-4 November, 2015. (Keynote Speaker)
- Current USG contracting Opportunities and Initiatives from the point of View of Vaccine Developers. World Vaccine Conference, Washington, DC. 24-26 March, 2014. (Oral Presentation)
- World Vaccine Conference, Washington, DC. 24-26 March, 2014 Preclinical and Clinical Vaccine Research. (Session Chair)
- PHEMCE Modeling Workshop “Operational Decision Making using Innovative Modeling, Analysis, and Visualization Tools”, Sponsored by Deloitte. 2013 (Conference Co-Organizer and Coordinator/Oral Presentation)
- "Vaccine Production Strategies: Ensuring Alignment and Sustainability" The World Health Organization (WHO) Global Action Plan for Influenza Vaccines. Geneva, Switzerland. 12-14 July 2011 (Oral Presentation)

RECENT STUDY SECTIONS (selected):

- Accelerated COVID-19 Therapeutic Interventions and Vaccines: ACTIV Therapeutics Clinical Working Group, NIH. Invited Participant. June, 2020-present.
- Chairperson, NIH/NIAID/DMID Special Emphasis Panel, Development of Vaccines to Combat Antibiotic Resistant Bacteria September 2019.
- Chairperson, NIH/NIAID Special Emphasis Panel, December 2018.
- Reviewer, NIH/NIAID Special Emphasis Panel, December 2017.
- Chairperson and scientific reviewer for Department of Defense, U.S. Army Medical Research and Materiel Command, for “Congressionally Directed Medical Research Programs (DMRDP), 2012.
- Committee member and reviewer for NIH/NIAID Committee for Development of Technologies that Accelerate the Immune Response to BioDefense Vaccines. 2011
- Chair and reviewer for NIH/NIAID: Partnerships in Biodefense Immunotherapeutics. 2011
- NIH/NIAID Committee member and reviewer for Development of Technologies to Facilitate the Use of, and Response to Biodefense Vaccines,” Special Emphasis panel. 2010
- Chairperson and scientific reviewer for NIH/NIAID Omnibus BAA 2017-1: Research Area 5 (N01) ZAI1-KP- M-C6 (Topic 5: Advanced Development of Vaccine Candidates for Biodefense and Emerging Infectious Diseases), September 2017.
- Scientific reviewer for NIH/NIAID Special Emphasis Panel/Scientific Review Group 2017/08 ZRG1 IMM-R (12) B (Non-HIV Microbial vaccines), June 2017.

Robert W. Malone, MD, MS

- Chairperson and scientific reviewer for Department of Defense, U.S. Army Medical Research and Materiel Command, “CDMRP: Defense Medical Research & Development Program (DMRDP), 2012.
- Chairperson and scientific reviewer for NIH/NIAID Committee on Partnerships in Biodefense Immunotherapeutics, Fall 2011.
- Committee member and reviewer for NIH/ NIAID Committee for Development of Technologies that Accelerate the Immune Response to BioDefense Vaccines, Fall 2011.
- NIH/ NIAID Committee member and reviewer for Development of Technologies to Facilitate the Use of, and Response to Biodefense Vaccines,” Special Emphasis panel, 2010.
- NIH Study Section K01 Breast Cancer Study Section: July 1997
- NIDDK Special Emphasis Panel Review Committee for Competing Continuation Program Project: April 1999 and April 1998
- NIAID Study Section “Innovative Grant Program for Approaches in HIV Vaccine Research”: 1998

BOOKS AND BOOK CHAPTERS

- *Molecular Virology of COVID-19*. Glasspool-Malone, J, Malone RW. In “*COVID-19 for Health Care.*” In press.
- Malone RW. “*Present and Future Status of Gene Therapy.*” Intro Chapter in *Advanced Gene Delivery: From Concepts to Pharmaceutical Products.* Editor: Allain Rolland. Harwood Academic Pub. 1998, republished 2014.
- *Enhancing direct in vivo transfection with nuclease inhibitors and pulsed electrical fields*. Glasspool-Malone J, Malone RW. In *Gene Therapy Methods: Methods Enzymol.* 2002;346:72-91
- Malone RW. “*Toxicology of non-viral gene transfer*”. Editor, Walsh B. In: “*Non-Viral Therapeutics: Advances, Challenges and Applications for Self-Assembling Systems.*” IBC’s Biomedical Library Series. (1996) 4.1

NATIONAL NEWSPAPER ARTICLES

Sorry Facebook, forced universal vaccinations are not the answer

All the science should be considered, not censored

Washington Times, September 1, 2021.

By: Dr. Robert Malone and Peter Navarro

<https://www.washingtontimes.com/news/2021/sep/1/sorry-facebook-forced-universal-vaccinations-are-n/>

Biden team’s misguided and deadly COVID-19 vaccine strategy

Vaccination 'arms race' could prove dangerous to the American public

Dr. Robert Malone and Peter Navarro,

Washington Times, August 5, 2021.

<https://www.washingtontimes.com/news/2021/aug/5/biden-teams-misguided-and-deadly-covid-19-vaccine/>

Online and print editions

NATIONAL PODCASTS AND DOCUMENTARIES

Dr. Malone has been featured on many TV shows and podcasts, including Fox News with Tucker Carlson, the War Room with Steve Bannon, Mercola, Glen Beck, Laura Ingraham, News Max, Russia Times, The Dark Horse Studio and dozens more. Please search Spotify or Apple Podcasts (“Robert Malone”) for listings.



EXHIBIT B

September 22, 2021

Pfizer Inc.
Attention: Mr. Amit Patel
235 East 42nd St
New York, NY 10017

Dear Mr. Patel:

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act or the Act), the Secretary of the Department of Health and Human Services (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 citizens living abroad, and that involves the virus that causes Coronavirus Disease 2019 (COVID-19).¹ On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Act (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.²

On December 11, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 for individuals 16 years of age and older pursuant to Section 564 of the Act. FDA reissued the letter of authorization on: December 23, 2020,³ February 25, 2021,⁴ May

¹ U.S. Department of Health and Human Services, Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the FD&C Act, 21 U.S.C. § 360bbb-3, February 4, 2020.

² U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 18250 (April 1, 2020).

³ In the December 23, 2020 revision, FDA removed reference to the number of doses per vial after dilution from the letter of authorization, clarified the instructions for vaccination providers reporting to VAERS, and made other technical corrections. FDA also revised the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) to clarify the number of doses of vaccine per vial after dilution and the instructions for reporting to VAERS. In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and the Fact Sheet for Recipients and Caregivers were revised to include additional information on safety monitoring and to clarify information about the availability of other COVID-19 vaccines.

⁴ In the February 25, 2021 revision, FDA allowed flexibility on the date of submission of monthly periodic safety reports and revised the requirements for reporting of vaccine administration errors by Pfizer Inc. The Fact Sheet for Health Care Providers Administering Vaccine (Vaccination Providers) was revised to provide an update to the storage and transportation temperature for frozen vials, direct the provider to the correct CDC website for information on monitoring vaccine recipients for the occurrence of immediate adverse reactions, to include data from a developmental toxicity study, and add adverse reactions that have been identified during post authorization use. The Fact Sheet for Recipients and Caregivers was revised to add adverse reactions that have been identified during post authorization use.

Page 2 – Pfizer Inc.

10, 2021,⁵ June 25, 2021,⁶ August 12, 2021,⁷ and on August 23, 2021, FDA approved COMIRNATY (COVID-19 Vaccine, mRNA)⁸ and reissued the letter in its entirety for both Pfizer-BioNTech COVID-19 Vaccine and certain uses of COMIRNATY (COVID-19 Vaccine, mRNA).⁹

On September, 22 2021, having concluded that revising this EUA is appropriate to protect the public health or safety under section 564(g)(2) of the Act, FDA is reissuing the August 23, 2021 letter of authorization in its entirety with revisions incorporated to authorize for emergency use the administration of a single booster dose of COMIRNATY (COVID-19 Vaccine, mRNA) or Pfizer-BioNTech COVID-19 Vaccine at least 6 months after completing the primary series of this vaccine in individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

⁵ In the May 10, 2021 revision, FDA authorized Pfizer-BioNTech Vaccine for the prevention of COVID-19 in individuals 12 through 15 years of age, as well as for individuals 16 years of age and older. In addition, FDA revised the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) to include the following Warning: “Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting.” In addition, the Fact Sheet for Recipients and Caregivers was revised to instruct vaccine recipients or their caregivers to tell the vaccination provider about fainting in association with a previous injection.

⁶ In the June 25, 2021 revision, FDA clarified terms and conditions that relate to export of Pfizer-BioNTech COVID-19 Vaccine from the United States. In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was revised to include a Warning about myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine. The Fact Sheet for Recipients and Caregivers was updated to include information about myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine.

⁷ In the August 12, 2021 revision, FDA authorized a third dose of the Pfizer-BioNTech COVID-19 Vaccine administered at least 28 days following the two dose regimen of this vaccine in individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

⁸ COMIRNATY (COVID-19 Vaccine, mRNA) was approved for active immunization to prevent COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

⁹ In the August 23, 2021 revision, FDA clarified that, subsequent to the FDA approval of COMIRNATY (COVID-19 Vaccine, mRNA) for the prevention of COVID-19 for individuals 16 years of age and older, this EUA would remain in place for the Pfizer-BioNTech COVID-19 vaccine for the previously-authorized indication and uses. It also authorized COMIRNATY (COVID-19 Vaccine, mRNA) under this EUA for certain uses that are not included in the approved biologics license application (BLA). In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was revised to provide updates on expiration dating of the authorized Pfizer-BioNTech COVID-19 Vaccine and updated language regarding warnings and precautions related to myocarditis and pericarditis. The Fact Sheet for Recipients and Caregivers was updated as the Vaccine Information Fact Sheet for Recipients and Caregivers, which comprises the Fact Sheet for the authorized Pfizer-BioNTech COVID-19 Vaccine and information about the FDA-licensed vaccine, COMIRNATY (COVID-19 Vaccine, mRNA).

COMIRNATY (COVID-19 Vaccine, mRNA) is the same formulation as the Pfizer-BioNTech COVID-19 Vaccine and can be used interchangeably with the Pfizer-BioNTech COVID-19 Vaccine to provide the COVID-19 vaccination series.¹⁰

For the December 11, 2020 authorization for individuals 16 years of age and older, FDA reviewed safety and efficacy data from an ongoing Phase 1/2/3 trial in approximately 44,000 participants randomized 1:1 to receive Pfizer-BioNTech COVID-19 Vaccine or saline control. The trial has enrolled participants 12 years of age and older. FDA's review at that time considered the safety and effectiveness data as they relate to the request for emergency use authorization in individuals 16 years of age and older. FDA's review of the available safety data from 37,586 of the participants 16 years of age and older, who were followed for a median of two months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. FDA's analysis of the available efficacy data from 36,523 participants 12 years of age and older without evidence of SARS-CoV-2 infection prior to 7 days after dose 2 confirmed that the vaccine was 95% effective (95% credible interval 90.3, 97.6) in preventing COVID-19 occurring at least 7 days after the second dose (with 8 COVID-19 cases in the vaccine group compared to 162 COVID-19 cases in the placebo group). Based on these data, and review of manufacturing information regarding product quality and consistency, FDA concluded that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 16 years of age and older. Finally, on December 10, 2020, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion.

For the May 10, 2021 authorization for individuals 12 through 15 years of age, FDA reviewed safety and effectiveness data from the above-referenced, ongoing Phase 1/2/3 trial that has enrolled approximately 46,000 participants, including 2,260 participants 12 through 15 years of age. Trial participants were randomized 1:1 to receive Pfizer-BioNTech COVID-19 Vaccine or saline control. FDA's review of the available safety data from 2,260 participants 12 through 15 years of age, who were followed for a median of 2 months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. FDA's analysis of SARS-CoV-2 50% neutralizing antibody titers 1 month after the second dose of Pfizer-BioNTech COVID-19 Vaccine in a subset of participants who had no serological or virological evidence of past SARS-CoV-2 infection confirm that the geometric mean antibody titer in participants 12 through 15 years of age was non-inferior to the geometric mean antibody titer in participants 16 through 25 years of age. FDA's analysis of available descriptive efficacy data from 1,983 participants 12 through 15 years of age without evidence of SARS-CoV-2 infection prior to 7 days after dose 2 confirm that the vaccine was 100% effective (95% confidence interval 75.3, 100.0) in preventing COVID-19 occurring at least 7 days after the second dose

¹⁰ The licensed vaccine has the same formulation as the EUA-authorized vaccine and the products can be used interchangeably to provide the vaccination series without presenting any safety or effectiveness concerns. The products are legally distinct with certain differences that do not impact safety or effectiveness.

(with no COVID-19 cases in the vaccine group compared to 16 COVID-19 cases in the placebo group). Based on these data, FDA concluded that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in individuals 12 through 15 years of age. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 12 through 15 years of age.

For the August 12, 2021 authorization of a third dose of the Pfizer-BioNTech COVID-19 Vaccine in individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise, FDA reviewed safety and effectiveness data reported in two manuscripts on solid organ transplant recipients. The first study was a single arm study conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) a median of 97±8 months earlier. A third dose of the Pfizer-BioNTech COVID-19 Vaccine was administered to 99 of these individuals approximately 2 months after they had received a second dose. Levels of total SARS-CoV-2 binding antibodies meeting the pre-specified criteria for success occurred four weeks after the third dose in 26/59 (44.0%) of those who were initially considered to be seronegative and received a third dose of the Pfizer-BioNTech COVID-19 Vaccine; 67/99 (68%) of the entire group receiving a third vaccination were subsequently considered to have levels of antibodies indicative of a significant response. In those who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported. A supportive secondary study describes a double-blind, randomized-controlled study conducted in 120 individuals who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years earlier (range 1.99-6.75 years). A third dose of a similar mRNA vaccine (the Moderna COVID-19 vaccine) was administered to 60 individuals approximately 2 months after they had received a second dose (i.e., doses at 0, 1 and 3 months); saline placebo was given to 60 individuals for comparison. The primary outcome was anti-RBD antibody at 4 months greater than 100 U/mL. This titer was selected based on NHP challenge studies as well as a large clinical cohort study to indicate this antibody titer was protective. Secondary outcomes were based on a virus neutralization assay and polyfunctional T cell responses. Baseline characteristics were comparable between the two study arms as were pre-intervention anti-RBD titer and neutralizing antibodies. Levels of total SARS-CoV-2 binding antibodies indicative of a significant response occurred four weeks after the third dose in 33/60 (55.0%) of the Moderna COVID-19 vaccinated group and 10/57 (17.5%) of the placebo individuals. In the 60 individuals who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 adverse events were reported. Despite the moderate enhancement in antibody titers, the totality of data (i.e., supportive paper by Hall et al. demonstrated efficacy of the product in the elderly and persons with co-morbidities) supports the conclusion that a third dose of the Pfizer-BioNTech COVID-19 Vaccine may be effective in this population, and that the known and potential benefits of a third dose of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine for immunocompromised individuals at least 12 years of age who have received two doses of the Pfizer-BioNTech COVID-19 Vaccine and who have undergone solid organ

transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

For the September 22, 2021 authorization of a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine administered at least 6 months after completing the primary series in individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19, FDA reviewed safety and effectiveness data from the above-referenced, ongoing Phase 1/2/3 trial in which 329 participants 18 through 75 years of age received a booster dose of the Pfizer-BioNTech COVID-19 Vaccine approximately 6 months (range 4.8 to 8.8 months) after completion of the primary series. FDA's review of the available safety data from 329 participants 18 through 75 years of age, who had been followed for a median of 2.6 months after receiving the booster dose, did not identify specific safety concerns that would preclude issuance of an EUA. The effectiveness of the booster dose of the Pfizer-BioNTech COVID-19 Vaccine is based on an assessment of 50% neutralizing antibody titers (NT50) against SARS-CoV-2 (USA_WA1/2020). FDA's analysis of SARS-CoV-2 NT50 one month after the booster dose compared to 1 month after the primary series in study participants 18 through 55 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster dose confirmed noninferiority for both geometric mean ratio and difference in seroresponse rates. Based on the totality of the scientific evidence available, including data from the above-referenced clinical trial, FDA concluded that a booster dose the Pfizer-BioNTech COVID-19 Vaccine may be effective, and that the known and potential benefits of a single booster dose at least 6 months after completing the primary series outweigh the known and potential risks for individuals 65 years of age and older; individuals 18 through 64 years of age at high risk of severe COVID-19; and individuals 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19, as described in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization. Additionally, as specified in subsection III.BB, I am authorizing use of Pfizer-BioNTech COVID-19 Vaccine and of COMIRNATY (COVID-19 Vaccine, mRNA) under this EUA when used to provide: a two-dose regimen for individuals aged 12 through 15 years; a third dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise; or a single booster dose at least 6 months after completing the primary series to individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Pfizer-BioNTech COVID-19 Vaccine¹¹ for the prevention of COVID-19 when administered as described in the Scope of Authorization (Section II) meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

- A. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
- B. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine when used to prevent COVID-19 outweigh its known and potential risks; and
- C. There is no adequate, approved, and available alternative¹² Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19.¹³

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Pfizer Inc. will supply Pfizer-BioNTech COVID-19 Vaccine either directly or through authorized distributor(s),¹⁴ to emergency response stakeholders¹⁵ as directed by the U.S.

¹¹ In this section (Section I), references to Pfizer-BioNTech COVID-19 Vaccine also apply to COMIRNATY (COVID-19 Vaccine, mRNA).

¹² Although COMIRNATY (COVID-19 Vaccine, mRNA) is approved to prevent COVID-19 in individuals 16 years of age and older, there is not sufficient approved vaccine available for distribution to this population in its entirety at the time of reissuance of this EUA. Additionally, there are no products that are approved to prevent COVID-19 in individuals age 12 through 15, or to provide: an additional dose to the immunocompromised population, or a booster dose to the authorized population described in this EUA.

¹³ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

¹⁴ “Authorized Distributor(s)” are identified by Pfizer Inc. or, if applicable, by a U.S. government entity, such as the Centers for Disease Control and Prevention (CDC) and/or other designee, as an entity or entities allowed to distribute authorized Pfizer-BioNTech COVID-19 Vaccine.

¹⁵ For purposes of this letter, “emergency response stakeholder” refers to a public health agency and its delegates that have legal responsibility and authority for responding to an incident, based on political or geographical boundary lines (e.g., city, county, tribal, territorial, State, or Federal), or functional (e.g., law enforcement or public health range) or sphere of authority to administer, deliver, or distribute vaccine in an emergency situation. In some cases (e.g., depending on a state or local jurisdiction’s COVID-19 vaccination response organization and plans), there might be overlapping roles and responsibilities among “emergency response stakeholders” and “vaccination providers” (e.g., if a local health department is administering COVID-19 vaccines; if a pharmacy is acting in an official capacity under the authority of the state health department to administer COVID-19 vaccines). In such cases, it is expected that the conditions of authorization that apply to emergency response stakeholders and vaccination providers will all be met.

government, including the Centers for Disease Control and Prevention (CDC) and/or other designee, for use consistent with the terms and conditions of this EUA;

- The Pfizer-BioNTech COVID-19 Vaccine covered by this authorization will be administered by vaccination providers¹⁶ and used only to prevent COVID-19 in individuals ages 12 and older with a two-dose regimen, to provide a third dose to individuals 12 years of age or older who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise, and to provide a single booster dose at least 6 months after completing the primary series of the vaccine to individuals: 65 years of age or older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19; and
- Pfizer-BioNTech COVID-19 Vaccine may be administered by a vaccination provider without an individual prescription for each vaccine recipient.

This authorization also covers the use of the licensed COMIRNATY (COVID-19 Vaccine, mRNA) product when used to provide: a two-dose regimen for individuals aged 12 through 15 years; a third dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise; or a single booster dose at least 6 months after completing the primary series to individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

Product Description¹⁷

The Pfizer-BioNTech COVID-19 Vaccine is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. The Pfizer-BioNTech COVID-19 Vaccine does not contain a preservative.

¹⁶ For purposes of this letter, “vaccination provider” refers to the facility, organization, or healthcare provider licensed or otherwise authorized by the emergency response stakeholder (e.g., non-physician healthcare professionals, such as nurses and pharmacists pursuant to state law under a standing order issued by the state health officer) to administer or provide vaccination services in accordance with the applicable emergency response stakeholder’s official COVID-19 vaccination and emergency response plan(s) and who is enrolled in the CDC COVID-19 Vaccination Program. If the vaccine is exported from the United States, a “vaccination provider” is a provider that is authorized to administer this vaccine in accordance with the laws of the country in which it is administered. For purposes of this letter, “healthcare provider” also refers to a person authorized by the U.S. Department of Health and Human Services (e.g., under the PREP Act Declaration for Medical Countermeasures against COVID-19) to administer FDA-authorized COVID-19 vaccine (e.g., qualified pharmacy technicians and State-authorized pharmacy interns acting under the supervision of a qualified pharmacist). See, e.g., HHS. *Fourth Amendment to the Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19 and Republication of the Declaration*. 85 FR 79190 (December 9, 2020).

¹⁷ For COMIRNATY (COVID-19 Vaccine, mRNA) product description, please see the COMIRNATY (COVID-19 Vaccine, mRNA) prescribing information, found here: <https://www.fda.gov/media/151707/download>.

Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine contains 30 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2. Each dose of the Pfizer-BioNTech COVID-19 Vaccine also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection) contributes an additional 2.16 mg sodium chloride per dose.

The dosing regimen is a primary series of two doses of 0.3 mL each, 3 weeks apart. A third primary series dose may be administered at least 28 days following the second dose to individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise. A single booster dose (0.3 mL) may be administered at least 6 months after completing the primary series to individuals: 65 years of age or older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

The manufacture of the authorized Pfizer-BioNTech COVID-19 Vaccine is limited to those facilities identified and agreed upon in Pfizer's request for authorization.

The Pfizer-BioNTech COVID-19 Vaccine vial label and carton labels are clearly marked for "Emergency Use Authorization." The Pfizer-BioNTech COVID-19 Vaccine is authorized to be distributed, stored, further redistributed, and administered by emergency response stakeholders when packaged in the authorized manufacturer packaging (i.e., vials and cartons), despite the fact that the vial and carton labels may not contain information that otherwise would be required under the FD&C Act.

Pfizer-BioNTech COVID-19 Vaccine is authorized for emergency use with the following product-specific information required to be made available to vaccination providers and recipients, respectively (referred to as "authorized labeling"):

- Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers): Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19)
- Vaccine Information Fact Sheet for Recipients and Caregivers About COMIRNATY (COVID-19 Vaccine, mRNA) and Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease (COVID-19).

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I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine,¹⁸ when used to prevent COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh its known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that Pfizer-BioNTech COVID-19 Vaccine (as described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of Pfizer-BioNTech COVID-19 Vaccine under this EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), Pfizer-BioNTech COVID-19 Vaccine is authorized to prevent COVID-19 in individuals 12 years of age and older as described in the Scope of Authorization (Section II) under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

Pfizer Inc. and Authorized Distributor(s)

- A. Pfizer Inc. and authorized distributor(s) will ensure that the authorized Pfizer-BioNTech COVID-19 Vaccine is distributed, as directed by the U.S. government, including CDC and/or other designee, and the authorized labeling (i.e., Fact Sheets) will be made available to vaccination providers, recipients, and caregivers consistent with the terms of this letter.
- B. Pfizer Inc. and authorized distributor(s) will ensure that appropriate storage and cold chain is maintained until delivered to emergency response stakeholders' receipt sites.
- C. Pfizer Inc. will ensure that the terms of this EUA are made available to all relevant stakeholders (e.g., emergency response stakeholders, authorized distributors, and vaccination providers) involved in distributing or receiving authorized Pfizer-BioNTech COVID-19 Vaccine. Pfizer Inc. will provide to all relevant stakeholders a

¹⁸ The conclusions supporting authorization stated in this Section (Section II) also apply to COMIRNATY (COVID-19 Vaccine, mRNA).

copy of this letter of authorization and communicate any subsequent amendments that might be made to this letter of authorization and its authorized labeling.

- D. Pfizer Inc. may develop and disseminate instructional and educational materials (e.g., video regarding vaccine handling, storage/cold-chain management, preparation, disposal) that are consistent with the authorized emergency use of the vaccine as described in the letter of authorization and authorized labeling, without FDA's review and concurrence, when necessary to meet public health needs during an emergency. Any instructional and educational materials that are inconsistent with the authorized labeling are prohibited.
- E. Pfizer Inc. may request changes to this authorization, including to the authorized Fact Sheets for the vaccine. Any request for changes to this EUA must be submitted to Office of Vaccines Research and Review (OVR)/Center for Biologics Evaluation and Research (CBER). Such changes require appropriate authorization prior to implementation.¹⁹
- F. Pfizer Inc. will report to Vaccine Adverse Event Reporting System (VAERS):
- Serious adverse events (irrespective of attribution to vaccination);
 - Cases of Multisystem Inflammatory Syndrome in children and adults; and
 - Cases of COVID-19 that result in hospitalization or death, that are reported to Pfizer Inc.
- These reports should be submitted to VAERS as soon as possible but no later than 15 calendar days from initial receipt of the information by Pfizer Inc.
- G. Pfizer Inc. must submit to Investigational New Drug application (IND) number 19736 periodic safety reports at monthly intervals in accordance with a due date agreed upon with the Office of Biostatistics and Epidemiology (OBE)/CBER beginning after the first full calendar month after authorization. Each periodic safety report is required to contain descriptive information which includes:
- A narrative summary and analysis of adverse events submitted during the reporting interval, including interval and cumulative counts by age groups, special populations (e.g., pregnant women), and adverse events of special interest;
 - A narrative summary and analysis of vaccine administration errors, whether or not associated with an adverse event, that were identified since the last reporting interval;
 - Newly identified safety concerns in the interval; and

¹⁹ The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), or (7), review and concurrence is required from the Preparedness and Response Team (PREP)/Office of the Center Director (OD)/CBER and the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS).

- Actions taken since the last report because of adverse experiences (for example, changes made to Healthcare Providers Administering Vaccine (Vaccination Providers) Fact Sheet, changes made to studies or studies initiated).
- H. No changes will be implemented to the description of the product, manufacturing process, facilities, or equipment without notification to and concurrence by FDA.
- I. All manufacturing facilities will comply with Current Good Manufacturing Practice requirements.
- J. Pfizer Inc. will submit to the EUA file Certificates of Analysis (CoA) for each drug product lot at least 48 hours prior to vaccine distribution. The CoA will include the established specifications and specific results for each quality control test performed on the final drug product lot.
- K. Pfizer Inc. will submit to the EUA file quarterly manufacturing reports, starting in July 2021, that include a listing of all Drug Substance and Drug Product lots produced after issuance of this authorization. This report must include lot number, manufacturing site, date of manufacture, and lot disposition, including those lots that were quarantined for investigation or those lots that were rejected. Information on the reasons for lot quarantine or rejection must be included in the report.
- L. Pfizer Inc. and authorized distributor(s) will maintain records regarding release of Pfizer-BioNTech COVID-19 Vaccine for distribution (i.e., lot numbers, quantity, release date).
- M. Pfizer Inc. and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.
- N. Pfizer Inc. will conduct post-authorization observational studies to evaluate the association between Pfizer-BioNTech COVID-19 Vaccine and a pre-specified list of adverse events of special interest, including myocarditis and pericarditis, along with deaths and hospitalizations, and severe COVID-19. The study population should include individuals administered the authorized Pfizer-BioNTech COVID-19 Vaccine under this EUA in the general U.S. population (12 years of age and older), individuals that receive a booster dose, populations of interest such as healthcare workers, pregnant women, immunocompromised individuals, subpopulations with specific comorbidities. The studies should be conducted in large scale databases with an active comparator. Pfizer Inc. will provide protocols and status update reports to the IND 19736 with agreed-upon study designs and milestone dates.

Emergency Response Stakeholders

- O. Emergency response stakeholders will identify vaccination sites to receive authorized Pfizer-BioNTech COVID-19 Vaccine and ensure its distribution and administration, consistent with the terms of this letter and CDC's COVID-19 Vaccination Program.

- P. Emergency response stakeholders will ensure that vaccination providers within their jurisdictions are aware of this letter of authorization, and the terms herein and any subsequent amendments that might be made to the letter of authorization, instruct them about the means through which they are to obtain and administer the vaccine under the EUA, and ensure that the authorized labeling [i.e., Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and Vaccine Information Fact Sheet for Recipients and Caregivers] is made available to vaccination providers through appropriate means (e.g., e-mail, website).
- Q. Emergency response stakeholders receiving authorized Pfizer-BioNTech COVID-19 Vaccine will ensure that appropriate storage and cold chain is maintained.

Vaccination Providers

- R. Vaccination providers will administer the vaccine in accordance with the authorization and will participate and comply with the terms and training required by CDC's COVID-19 Vaccination Program.
- S. Vaccination providers will provide the Vaccine Information Fact Sheet for Recipients and Caregivers to each individual receiving vaccination and provide the necessary information for receiving their second dose and/or third dose.
- T. Vaccination providers administering the vaccine must report the following information associated with the administration of the vaccine of which they become aware to VAERS in accordance with the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers):
- Vaccine administration errors whether or not associated with an adverse event
 - Serious adverse events (irrespective of attribution to vaccination)
 - Cases of Multisystem Inflammatory Syndrome in children and adults
 - Cases of COVID-19 that result in hospitalization or death

Complete and submit reports to VAERS online at <https://vaers.hhs.gov/reportevent.html>. The VAERS reports should include the words "Pfizer-BioNTech COVID-19 Vaccine EUA" in the description section of the report. More information is available at vaers.hhs.gov or by calling 1-800-822-7967. To the extent feasible, report to Pfizer Inc. by contacting 1-800-438-1985 or by providing a copy of the VAERS form to Pfizer Inc.; Fax: 1-866-635-8337.

- U. Vaccination providers will conduct any follow-up requested by the U.S government, including CDC, FDA, or other designee, regarding adverse events to the extent feasible given the emergency circumstances.
- V. Vaccination providers will monitor and comply with CDC and/or emergency response stakeholder vaccine management requirements (e.g., requirements

concerning obtaining, tracking, and handling vaccine) and with requirements concerning reporting of vaccine administration data to CDC.

- W. Vaccination providers will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to CDC, and FDA for inspection upon request.

Conditions Related to Printed Matter, Advertising, and Promotion

- X. All descriptive printed matter, advertising, and promotional material, relating to the use of the Pfizer-BioNTech COVID-19 Vaccine shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in section 502(a) and (n) of the FD&C Act and FDA implementing regulations.
- Y. All descriptive printed matter, advertising, and promotional material relating to the use of the Pfizer-BioNTech COVID-19 Vaccine clearly and conspicuously shall state that:
- This product has not been approved or licensed by FDA, but has been authorized for emergency use by FDA, under an EUA to prevent Coronavirus Disease 2019 (COVID-19) for use in individuals 12 years of age and older; and
 - The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of the medical product under Section 564(b)(1) of the FD&C Act unless the declaration is terminated or authorization revoked sooner.

Condition Related to Export

- Z. If the Pfizer-BioNTech COVID-19 Vaccine is exported from the United States, conditions C, D, and O through Y do not apply, but export is permitted only if 1) the regulatory authorities of the country in which the vaccine will be used are fully informed that this vaccine is subject to an EUA and is not approved or licensed by FDA and 2) the intended use of the vaccine will comply in all respects with the laws of the country in which the product will be used. The requirement in this letter that the authorized labeling (i.e., Fact Sheets) be made available to vaccination providers, recipients, and caregivers in condition A will not apply if the authorized labeling (i.e., Fact Sheets) are made available to the regulatory authorities of the country in which the vaccine will be used.

Conditions With Respect to Use of Licensed Product

- AA. COMIRNATY (COVID-19 Vaccine, mRNA) is now licensed for individuals 16 years of age and older. There remains, however, a significant amount of Pfizer-BioNTech COVID-19 Vaccine that was manufactured and labeled in accordance with this emergency use authorization. The authorization remains in place with respect to the Pfizer-BioNTech COVID-19 Vaccine.

BB. This authorization also covers the use of the licensed COMIRNATY (COVID-19 Vaccine, mRNA) product when used to provide: a two-dose regimen for individuals aged 12 through 15 years; a third dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise; or a single booster dose at least 6 months after completing the primary series to individuals: 65 years of age or older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19. Conditions A through W in this letter apply when COMIRNATY (COVID-19 Vaccine, mRNA) is provided for the uses described in this subsection III.BB, except that product manufactured and labeled in accordance with the approved BLA is deemed to satisfy the manufacturing, labeling, and distribution requirements of this authorization.

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

--S/--

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures



U.S. FOOD & DRUG
ADMINISTRATION

EXHIBIT C

October 20, 2021

Pfizer Inc.
Attention: Mr. Amit Patel
235 East 42nd St
New York, NY 10017

Dear Mr. Patel:

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act or the Act), the Secretary of the Department of Health and Human Services (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 citizens living abroad, and that involves the virus that causes Coronavirus Disease 2019 (COVID-19).¹ On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Act (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.²

On December 11, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 for individuals 16 years of age and older pursuant to Section 564 of the Act. FDA reissued the letter of authorization on: December 23, 2020,³ February 25, 2021,⁴ May

¹ U.S. Department of Health and Human Services, Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the FD&C Act, 21 U.S.C. § 360bbb-3, February 4, 2020.

² U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 18250 (April 1, 2020).

³ In the December 23, 2020 revision, FDA removed reference to the number of doses per vial after dilution from the letter of authorization, clarified the instructions for vaccination providers reporting to VAERS, and made other technical corrections. FDA also revised the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) to clarify the number of doses of vaccine per vial after dilution and the instructions for reporting to VAERS. In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and the Fact Sheet for Recipients and Caregivers were revised to include additional information on safety monitoring and to clarify information about the availability of other COVID-19 vaccines.

⁴ In the February 25, 2021 revision, FDA allowed flexibility on the date of submission of monthly periodic safety reports and revised the requirements for reporting of vaccine administration errors by Pfizer Inc. The Fact Sheet for Health Care Providers Administering Vaccine (Vaccination Providers) was revised to provide an update to the storage and transportation temperature for frozen vials, direct the provider to the correct CDC website for information on monitoring vaccine recipients for the occurrence of immediate adverse reactions, to include data from a developmental toxicity study, and add adverse reactions that have been identified during post authorization use. The Fact Sheet for Recipients and Caregivers was revised to add adverse reactions that have been identified during post authorization use.

10, 2021,⁵ June 25, 2021,⁶ August 12, 2021,⁷ and on August 23, 2021, FDA approved COMIRNATY (COVID-19 Vaccine, mRNA)⁸ and reissued the letter in its entirety for both Pfizer-BioNTech COVID-19 Vaccine and certain uses of COMIRNATY (COVID-19 Vaccine, mRNA).⁹ Subsequently, FDA reissued the letter of authorization on September 22, 2021.¹⁰

On October 20, 2021, having concluded that revising this EUA is appropriate to protect the public health or safety under Section 564(g)(2) of the Act, FDA is reissuing the September 22, 2021 letter of authorization in its entirety with revisions incorporated to clarify eligibility for the booster dose of COMIRNATY (COVID-19 Vaccine, mRNA) or Pfizer-BioNTech COVID-19 Vaccine and to authorize for emergency use the administration of a single booster dose of Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA) as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster

⁵ In the May 10, 2021 revision, FDA authorized Pfizer-BioNTech Vaccine for the prevention of COVID-19 in individuals 12 through 15 years of age, as well as for individuals 16 years of age and older. In addition, FDA revised the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) to include the following Warning: “Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting.” In addition, the Fact Sheet for Recipients and Caregivers was revised to instruct vaccine recipients or their caregivers to tell the vaccination provider about fainting in association with a previous injection.

⁶ In the June 25, 2021 revision, FDA clarified terms and conditions that relate to export of Pfizer-BioNTech COVID-19 Vaccine from the United States. In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was revised to include a Warning about myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine. The Fact Sheet for Recipients and Caregivers was updated to include information about myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine.

⁷ In the August 12, 2021 revision, FDA authorized a third dose of the Pfizer-BioNTech COVID-19 Vaccine administered at least 28 days following the two dose regimen of this vaccine in individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

⁸ COMIRNATY (COVID-19 Vaccine, mRNA) was approved for active immunization to prevent COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

⁹ In the August 23, 2021 revision, FDA clarified that, subsequent to the FDA approval of COMIRNATY (COVID-19 Vaccine, mRNA) for the prevention of COVID-19 for individuals 16 years of age and older, this EUA would remain in place for the Pfizer-BioNTech COVID-19 vaccine for the previously-authorized indication and uses. It also authorized COMIRNATY (COVID-19 Vaccine, mRNA) under this EUA for certain uses that are not included in the approved biologics license application (BLA). In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was revised to provide updates on expiration dating of the authorized Pfizer-BioNTech COVID-19 Vaccine and updated language regarding warnings and precautions related to myocarditis and pericarditis. The Fact Sheet for Recipients and Caregivers was updated as the Vaccine Information Fact Sheet for Recipients and Caregivers, which comprises the Fact Sheet for the authorized Pfizer-BioNTech COVID-19 Vaccine and information about the FDA-licensed vaccine, COMIRNATY (COVID-19 Vaccine, mRNA).

¹⁰ In the September 22, 2021 revision, FDA authorized the administration of a single booster dose of COMIRNATY (COVID-19 Vaccine, mRNA) or Pfizer-BioNTech COVID-19 Vaccine at least 6 months after completing the primary series of this vaccine in individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

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dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

COMIRNATY (COVID-19 Vaccine, mRNA) is the same formulation as the Pfizer-BioNTech COVID-19 Vaccine and can be used interchangeably with the Pfizer-BioNTech COVID-19 Vaccine to provide doses for COVID-19 primary vaccination or a booster dose.¹¹

For the December 11, 2020 authorization for individuals 16 years of age and older, FDA reviewed safety and efficacy data from an ongoing Phase 1/2/3 trial in approximately 44,000 participants randomized 1:1 to receive Pfizer-BioNTech COVID-19 Vaccine or saline control. The trial enrolled participants 12 years of age and older. FDA's review at that time considered the safety and effectiveness data as they relate to the request for emergency use authorization in individuals 16 years of age and older. FDA's review of the available safety data from 37,586 of the participants 16 years of age and older, who were followed for a median of two months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. FDA's analysis of the available efficacy data from 36,523 participants 12 years of age and older without evidence of SARS-CoV-2 infection prior to 7 days after dose 2 confirmed that the vaccine was 95% effective (95% credible interval 90.3, 97.6) in preventing COVID-19 occurring at least 7 days after the second dose (with 8 COVID-19 cases in the vaccine group compared to 162 COVID-19 cases in the placebo group). Based on these data, and review of manufacturing information regarding product quality and consistency, FDA concluded that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 16 years of age and older. Finally, on December 10, 2020, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion.

For the May 10, 2021 authorization for individuals 12 through 15 years of age, FDA reviewed safety and effectiveness data from the above-referenced, ongoing Phase 1/2/3 trial that enrolled approximately 46,000 participants, including 2,260 participants 12 through 15 years of age. Trial participants were randomized 1:1 to receive Pfizer-BioNTech COVID-19 Vaccine or saline control. FDA's review of the available safety data from 2,260 participants 12 through 15 years of age, who were followed for a median of 2 months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. FDA's analysis of SARS-CoV-2 50% neutralizing antibody titers 1 month after the second dose of Pfizer-BioNTech COVID-19 Vaccine in a subset of participants who had no serological or virological evidence of past SARS-CoV-2 infection confirm that the geometric mean antibody titer in participants 12 through 15 years of age was non-inferior to the geometric mean antibody titer in participants 16 through 25 years of age. FDA's analysis of available descriptive efficacy data from 1,983 participants 12 through 15 years of age without evidence of SARS-CoV-2 infection

¹¹ The licensed vaccine has the same formulation as the EUA-authorized vaccine and the products can be used interchangeably to provide doses for primary vaccination or a booster dose without presenting any safety or effectiveness concerns. The products are legally distinct with certain differences that do not impact safety or effectiveness.

prior to 7 days after dose 2 confirm that the vaccine was 100% effective (95% confidence interval 75.3, 100.0) in preventing COVID-19 occurring at least 7 days after the second dose (with no COVID-19 cases in the vaccine group compared to 16 COVID-19 cases in the placebo group). Based on these data, FDA concluded that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in individuals 12 through 15 years of age. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 12 through 15 years of age.

For the August 12, 2021 authorization of a third primary series dose in individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise, FDA reviewed safety and effectiveness data reported in two manuscripts on solid organ transplant recipients. The first study was a single arm study conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) a median of 97±8 months earlier. A third dose of the Pfizer-BioNTech COVID-19 Vaccine was administered to 99 of these individuals approximately 2 months after they had received a second dose. Levels of total SARS-CoV-2 binding antibodies meeting the pre-specified criteria for success occurred four weeks after the third dose in 26/59 (44.0%) of those who were initially considered to be seronegative and received a third dose of the Pfizer-BioNTech COVID-19 Vaccine; 67/99 (68%) of the entire group receiving a third vaccination were subsequently considered to have levels of antibodies indicative of a significant response. In those who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported. A supportive secondary study describes a double-blind, randomized-controlled study conducted in 120 individuals who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years earlier (range 1.99-6.75 years). A third dose of a similar messenger RNA vaccine (the Moderna COVID-19 vaccine) was administered to 60 individuals approximately 2 months after they had received a second dose (i.e., doses at 0, 1 and 3 months); saline placebo was given to 60 individuals for comparison. The primary outcome was anti-RBD antibody at 4 months greater than 100 U/mL. This titer was selected based on NHP challenge studies as well as a large clinical cohort study to indicate this antibody titer was protective. Secondary outcomes were based on a virus neutralization assay and polyfunctional T cell responses. Baseline characteristics were comparable between the two study arms as were pre-intervention anti-RBD titer and neutralizing antibodies. Levels of total SARS-CoV-2 binding antibodies indicative of a significant response occurred four weeks after the third dose in 33/60 (55.0%) of the Moderna COVID-19 vaccinated group and 10/57 (17.5%) of the placebo individuals. In the 60 individuals who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 adverse events were reported. Despite the moderate enhancement in antibody titers, the totality of data (i.e., supportive paper by Hall et al. demonstrated efficacy of the product in the elderly and persons with co-morbidities) supports the conclusion that a third dose of the Pfizer-BioNTech COVID-19 Vaccine may be effective in this population, and that the known and potential benefits of a third dose of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine for immunocompromised individuals at least 12 years of age who have received two

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doses of the Pfizer-BioNTech COVID-19 Vaccine and who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

For the September 22, 2021 authorization of a single booster dose administered at least 6 months after completing the primary series in individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19, FDA reviewed safety and effectiveness data from the above-referenced, ongoing Phase 1/2/3 trial in which 329 participants 18 through 75 years of age received a booster dose of the Pfizer-BioNTech COVID-19 Vaccine approximately 6 months (range 4.8 to 8.8 months) after completion of the primary series. FDA's review of the available safety data from 329 participants 18 through 75 years of age, who had been followed for a median of 2.6 months after receiving the booster dose, did not identify specific safety concerns that would preclude issuance of an EUA. The effectiveness of the booster dose of the Pfizer-BioNTech COVID-19 Vaccine is based on an assessment of 50% neutralizing antibody titers (NT50) against SARS-CoV-2 (USA_WA1/2020). FDA's analysis of SARS-CoV-2 NT50 one month after the booster dose compared to 1 month after the primary series in study participants 18 through 55 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster dose confirmed noninferiority for both geometric mean ratio and difference in seroresponse rates. Based on the totality of the scientific evidence available, including data from the above-referenced clinical trial, FDA concluded that a booster dose the Pfizer-BioNTech COVID-19 Vaccine may be effective, and that the known and potential benefits of a single booster dose at least 6 months after completing the primary series outweigh the known and potential risks for individuals 65 years of age and older; individuals 18 through 64 years of age at high risk of severe COVID-19; and individuals 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

For the October 20, 2021 authorization of a single booster dose as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine, FDA reviewed data from an ongoing Phase 1/2 clinical trial in participants 19-85 years of age. In this trial, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series (N=151) at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine. Adverse events were assessed through 28 days after the booster dose. An overall review of adverse reactions reported following the Pfizer-BioNTech COVID-19 Vaccine heterologous booster dose did not identify any new safety concerns, as compared with adverse reactions reported following Pfizer-BioNTech COVID-19 Vaccine primary series doses or homologous booster dose. Neutralizing antibody titers, as measured by a pseudovirus neutralization assay using a lentivirus expressing the SARS-CoV-2 Spike protein with D614G

mutation, were assessed on Day 1 prior to administration of the booster dose and on Day 15 after the booster dose. A booster response to the Pfizer-BioNTech COVID-19 Vaccine was demonstrated regardless of primary vaccination. Based on the on the totality of the scientific evidence available, including data from the above-referenced clinical trial, FDA concluded that a heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine may be effective, and that the known and potential benefits of a heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine following completion of primary vaccination with another authorized COVID-19 vaccine outweigh the known and potential risks.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19, as described in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization. Additionally, as specified in subsection III.BB, I am authorizing use of COMIRNATY (COVID-19 Vaccine, mRNA) under this EUA when used to provide: (1) a two-dose regimen for individuals aged 12 through 15 years; (2) a third dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise; (3) a single homologous booster dose at least 6 months after completing a primary series to individuals 65 years of age and older, 18 through 64 years of age at high risk of severe COVID-19, and 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2; and (4) a heterologous booster dose to certain individuals who have completed primary vaccination with a different authorized COVID-19 vaccine as described in the Scope of Authorization section of this letter (Section II).

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Pfizer-BioNTech COVID-19 Vaccine¹² for the prevention of COVID-19 when administered as described in the Scope of Authorization (Section II) meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

- A. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
- B. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine when used to prevent COVID-19 outweigh its known and potential risks; and

¹² In this section (Section I), references to Pfizer-BioNTech COVID-19 Vaccine also apply to COMIRNATY (COVID-19 Vaccine, mRNA).

C. There is no adequate, approved, and available alternative¹³ Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19.¹⁴

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Pfizer Inc. will supply Pfizer-BioNTech COVID-19 Vaccine either directly or through authorized distributor(s),¹⁵ to emergency response stakeholders¹⁶ as directed by the U.S. government, including the Centers for Disease Control and Prevention (CDC) and/or other designee, for use consistent with the terms and conditions of this EUA;
- The Pfizer-BioNTech COVID-19 Vaccine covered by this authorization will be administered by vaccination providers¹⁷ and used only to prevent COVID-19 in individuals ages 12 and older with a two-dose primary regimen and to provide:

¹³ Although COMIRNATY (COVID-19 Vaccine, mRNA) is approved to prevent COVID-19 in individuals 16 years of age and older, there is not sufficient approved vaccine available for distribution to this population in its entirety at the time of reissuance of this EUA. Additionally, there are no COVID-19 vaccines that are approved to provide: COVID-19 vaccination in individuals age 12 through 15; a third primary series dose to certain immunocompromised populations described in this EUA; a homologous booster dose to the authorized population described in this EUA; or a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine.

¹⁴ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

¹⁵ “Authorized Distributor(s)” are identified by Pfizer Inc. or, if applicable, by a U.S. government entity, such as the Centers for Disease Control and Prevention (CDC) and/or other designee, as an entity or entities allowed to distribute authorized Pfizer-BioNTech COVID-19 Vaccine.

¹⁶ For purposes of this letter, “emergency response stakeholder” refers to a public health agency and its delegates that have legal responsibility and authority for responding to an incident, based on political or geographical boundary lines (e.g., city, county, tribal, territorial, State, or Federal), or functional (e.g., law enforcement or public health range) or sphere of authority to administer, deliver, or distribute vaccine in an emergency situation. In some cases (e.g., depending on a state or local jurisdiction’s COVID-19 vaccination response organization and plans), there might be overlapping roles and responsibilities among “emergency response stakeholders” and “vaccination providers” (e.g., if a local health department is administering COVID-19 vaccines; if a pharmacy is acting in an official capacity under the authority of the state health department to administer COVID-19 vaccines). In such cases, it is expected that the conditions of authorization that apply to emergency response stakeholders and vaccination providers will all be met.

¹⁷ For purposes of this letter, “vaccination provider” refers to the facility, organization, or healthcare provider licensed or otherwise authorized by the emergency response stakeholder (e.g., non-physician healthcare professionals, such as nurses and pharmacists pursuant to state law under a standing order issued by the state health officer) to administer or provide vaccination services in accordance with the applicable emergency response stakeholder’s official COVID-19 vaccination and emergency response plan(s) and who is enrolled in the CDC COVID-19 Vaccination Program. If the vaccine is exported from the United States, a “vaccination provider” is a provider that is authorized to administer this vaccine in accordance with the laws of the country in which it is administered. For purposes of this letter, “healthcare provider” also refers to a person authorized by the U.S. Department of Health and Human Services (e.g., under the PREP Act Declaration for Medical Countermeasures against COVID-19) to administer FDA-authorized COVID-19 vaccine (e.g., qualified pharmacy technicians and State-authorized pharmacy interns acting under the supervision of a qualified pharmacist). See, e.g., HHS. *Fourth Amendment to the Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19 and Republication of the Declaration*. 85 FR 79190 (December 9, 2020).

- a third primary series dose to individuals 12 years of age or older who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise;
 - a single booster dose at least 6 months after completion of a primary series of the vaccine to individuals: 65 years of age or older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2; and
 - a single booster dose as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine, where the eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.
- Pfizer-BioNTech COVID-19 Vaccine may be administered by a vaccination provider without an individual prescription for each vaccine recipient.

This authorization also covers the use of the licensed COMIRNATY (COVID-19 Vaccine, mRNA) product when used to provide: (1) a two-dose primary regimen (0.3 mL each, 3 weeks apart) for individuals aged 12 through 15 years; (2) a third primary series dose at least 28 days following the second dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise; (3) a single booster dose (0.3 mL) at least 6 months after completion of the primary series to individuals 65 years of age and older, 18 through 64 years of age at high risk of severe COVID-19, and 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2; and (4) a single booster dose (0.3 mL) as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine, where the eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

Product Description¹⁸

The Pfizer-BioNTech COVID-19 Vaccine is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. The Pfizer-BioNTech COVID-19 Vaccine does not contain a preservative.

Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine contains 30 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2. Each dose of the Pfizer-BioNTech COVID-19 Vaccine also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic

¹⁸ For COMIRNATY (COVID-19 Vaccine, mRNA) product description, please see the COMIRNATY (COVID-19 Vaccine, mRNA) prescribing information, found here: <https://www.fda.gov/media/151707/download>.

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potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection) contributes an additional 2.16 mg sodium chloride per dose.

The manufacture of the authorized Pfizer-BioNTech COVID-19 Vaccine is limited to those facilities identified and agreed upon in Pfizer's request for authorization.

The Pfizer-BioNTech COVID-19 Vaccine vial label and carton labels are clearly marked for "Emergency Use Authorization." The Pfizer-BioNTech COVID-19 Vaccine is authorized to be distributed, stored, further redistributed, and administered by emergency response stakeholders when packaged in the authorized manufacturer packaging (i.e., vials and cartons), despite the fact that the vial and carton labels may not contain information that otherwise would be required under the FD&C Act.

Pfizer-BioNTech COVID-19 Vaccine is authorized for emergency use with the following product-specific information required to be made available to vaccination providers and recipients, respectively (referred to as "authorized labeling"):

- Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers): Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19)
- Vaccine Information Fact Sheet for Recipients and Caregivers About COMIRNATY (COVID-19 Vaccine, mRNA) and Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease (COVID-19)

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine,¹⁹ when used to prevent COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh its known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that Pfizer-BioNTech COVID-19 Vaccine (as described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of Pfizer-BioNTech COVID-19 Vaccine under this EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and

¹⁹ The conclusions supporting authorization stated in this section (Section II) also apply to COMIRNATY (COVID-19 Vaccine, mRNA).

under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), Pfizer-BioNTech COVID-19 Vaccine is authorized to prevent COVID-19 in individuals 12 years of age and older as described in the Scope of Authorization (Section II) under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

Pfizer Inc. and Authorized Distributor(s)

- A. Pfizer Inc. and authorized distributor(s) will ensure that the authorized Pfizer-BioNTech COVID-19 Vaccine is distributed, as directed by the U.S. government, including CDC and/or other designee, and the authorized labeling (i.e., Fact Sheets) will be made available to vaccination providers, recipients, and caregivers consistent with the terms of this letter.
- B. Pfizer Inc. and authorized distributor(s) will ensure that appropriate storage and cold chain is maintained until delivered to emergency response stakeholders' receipt sites.
- C. Pfizer Inc. will ensure that the terms of this EUA are made available to all relevant stakeholders (e.g., emergency response stakeholders, authorized distributors, and vaccination providers) involved in distributing or receiving authorized Pfizer-BioNTech COVID-19 Vaccine. Pfizer Inc. will provide to all relevant stakeholders a copy of this letter of authorization and communicate any subsequent amendments that might be made to this letter of authorization and its authorized labeling.
- D. Pfizer Inc. may develop and disseminate instructional and educational materials (e.g., video regarding vaccine handling, storage/cold-chain management, preparation, disposal) that are consistent with the authorized emergency use of the vaccine as described in the letter of authorization and authorized labeling, without FDA's review and concurrence, when necessary to meet public health needs during an emergency. Any instructional and educational materials that are inconsistent with the authorized labeling are prohibited.
- E. Pfizer Inc. may request changes to this authorization, including to the authorized Fact Sheets for the vaccine. Any request for changes to this EUA must be submitted to Office of Vaccines Research and Review (OVRR)/Center for Biologics Evaluation and Research (CBER). Such changes require appropriate authorization prior to implementation.²⁰

²⁰ The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing

- F. Pfizer Inc. will report to Vaccine Adverse Event Reporting System (VAERS):
- Serious adverse events (irrespective of attribution to vaccination);
 - Cases of Multisystem Inflammatory Syndrome in children and adults; and
 - Cases of COVID-19 that result in hospitalization or death, that are reported to Pfizer Inc.
- These reports should be submitted to VAERS as soon as possible but no later than 15 calendar days from initial receipt of the information by Pfizer Inc.
- G. Pfizer Inc. must submit to Investigational New Drug application (IND) number 19736 periodic safety reports at monthly intervals in accordance with a due date agreed upon with the Office of Biostatistics and Epidemiology (OBE)/CBER beginning after the first full calendar month after authorization. Each periodic safety report is required to contain descriptive information which includes:
- A narrative summary and analysis of adverse events submitted during the reporting interval, including interval and cumulative counts by age groups, special populations (e.g., pregnant women), and adverse events of special interest;
 - A narrative summary and analysis of vaccine administration errors, whether or not associated with an adverse event, that were identified since the last reporting interval;
 - Newly identified safety concerns in the interval; and
 - Actions taken since the last report because of adverse experiences (for example, changes made to Healthcare Providers Administering Vaccine (Vaccination Providers) Fact Sheet, changes made to studies or studies initiated).
- H. No changes will be implemented to the description of the product, manufacturing process, facilities, or equipment without notification to and concurrence by FDA.
- I. All manufacturing facilities will comply with Current Good Manufacturing Practice requirements.
- J. Pfizer Inc. will submit to the EUA file Certificates of Analysis (CoA) for each drug product lot at least 48 hours prior to vaccine distribution. The CoA will include the established specifications and specific results for each quality control test performed on the final drug product lot.
- K. Pfizer Inc. will submit to the EUA file quarterly manufacturing reports, starting in July 2021, that include a listing of all Drug Substance and Drug Product lots produced after issuance of this authorization. This report must include lot number, manufacturing site, date of manufacture, and lot disposition, including those lots that

processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), or (7), review and concurrence is required from the Preparedness and Response Team (PREP)/Office of the Center Director (OD)/CBER and the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS).

were quarantined for investigation or those lots that were rejected. Information on the reasons for lot quarantine or rejection must be included in the report.

- L. Pfizer Inc. and authorized distributor(s) will maintain records regarding release of Pfizer-BioNTech COVID-19 Vaccine for distribution (i.e., lot numbers, quantity, release date).
- M. Pfizer Inc. and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.
- N. Pfizer Inc. will conduct post-authorization observational studies to evaluate the association between Pfizer-BioNTech COVID-19 Vaccine and a pre-specified list of adverse events of special interest, including myocarditis and pericarditis, along with deaths and hospitalizations, and severe COVID-19. The study population should include individuals administered the authorized Pfizer-BioNTech COVID-19 Vaccine under this EUA in the general U.S. population (12 years of age and older), individuals who receive a booster dose, populations of interest such as healthcare workers, pregnant women, immunocompromised individuals, subpopulations with specific comorbidities. The studies should be conducted in large scale databases with an active comparator. Pfizer Inc. will provide protocols and status update reports to the IND 19736 with agreed-upon study designs and milestone dates.

Emergency Response Stakeholders

- O. Emergency response stakeholders will identify vaccination sites to receive authorized Pfizer-BioNTech COVID-19 Vaccine and ensure its distribution and administration, consistent with the terms of this letter and CDC's COVID-19 Vaccination Program.
- P. Emergency response stakeholders will ensure that vaccination providers within their jurisdictions are aware of this letter of authorization, and the terms herein and any subsequent amendments that might be made to the letter of authorization, instruct them about the means through which they are to obtain and administer the vaccine under the EUA, and ensure that the authorized labeling [i.e., Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and Vaccine Information Fact Sheet for Recipients and Caregivers] is made available to vaccination providers through appropriate means (e.g., e-mail, website).
- Q. Emergency response stakeholders receiving authorized Pfizer-BioNTech COVID-19 Vaccine will ensure that appropriate storage and cold chain is maintained.

Vaccination Providers

- R. Vaccination providers will administer the vaccine in accordance with the authorization and will participate and comply with the terms and training required by CDC's COVID-19 Vaccination Program.

- S. Vaccination providers will provide the Vaccine Information Fact Sheet for Recipients and Caregivers to each individual receiving vaccination and provide the necessary information for receiving their second dose and/or third dose.
- T. Vaccination providers administering the vaccine must report the following information associated with the administration of the vaccine of which they become aware to VAERS in accordance with the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers):
- Vaccine administration errors whether or not associated with an adverse event
 - Serious adverse events (irrespective of attribution to vaccination)
 - Cases of Multisystem Inflammatory Syndrome in children and adults
 - Cases of COVID-19 that result in hospitalization or death
- Complete and submit reports to VAERS online at <https://vaers.hhs.gov/reportevent.html>. The VAERS reports should include the words “Pfizer-BioNTech COVID-19 Vaccine EUA” in the description section of the report. More information is available at vaers.hhs.gov or by calling 1-800-822-7967. To the extent feasible, report to Pfizer Inc. by contacting 1-800-438-1985 or by providing a copy of the VAERS form to Pfizer Inc.; Fax: 1-866-635-8337.
- U. Vaccination providers will conduct any follow-up requested by the U.S government, including CDC, FDA, or other designee, regarding adverse events to the extent feasible given the emergency circumstances.
- V. Vaccination providers will monitor and comply with CDC and/or emergency response stakeholder vaccine management requirements (e.g., requirements concerning obtaining, tracking, and handling vaccine) and with requirements concerning reporting of vaccine administration data to CDC.
- W. Vaccination providers will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to CDC, and FDA for inspection upon request.

Conditions Related to Printed Matter, Advertising, and Promotion

- X. All descriptive printed matter, advertising, and promotional material, relating to the use of the Pfizer-BioNTech COVID-19 Vaccine shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in Section 502(a) and (n) of the FD&C Act and FDA implementing regulations.
- Y. All descriptive printed matter, advertising, and promotional material relating to the use of the Pfizer-BioNTech COVID-19 Vaccine clearly and conspicuously shall state that:

- This product has not been approved or licensed by FDA, but has been authorized for emergency use by FDA, under an EUA to prevent Coronavirus Disease 2019 (COVID-19) for use in individuals 12 years of age and older; and
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of the medical product under Section 564(b)(1) of the FD&C Act unless the declaration is terminated or authorization revoked sooner.

Condition Related to Export

- Z. If the Pfizer-BioNTech COVID-19 Vaccine is exported from the United States, conditions C, D, and O through Y do not apply, but export is permitted only if 1) the regulatory authorities of the country in which the vaccine will be used are fully informed that this vaccine is subject to an EUA and is not approved or licensed by FDA and 2) the intended use of the vaccine will comply in all respects with the laws of the country in which the product will be used. The requirement in this letter that the authorized labeling (i.e., Fact Sheets) be made available to vaccination providers, recipients, and caregivers in condition A will not apply if the authorized labeling (i.e., Fact Sheets) are made available to the regulatory authorities of the country in which the vaccine will be used.

Conditions With Respect to Use of Licensed Product

- AA. COMIRNATY (COVID-19 Vaccine, mRNA) is licensed for individuals 16 years of age and older. There remains, however, a significant amount of Pfizer-BioNTech COVID-19 Vaccine that was manufactured and labeled in accordance with this emergency use authorization. The authorization remains in place with respect to the Pfizer-BioNTech COVID-19 Vaccine for this population.
- BB. This authorization also covers the use of the licensed COMIRNATY (COVID-19 Vaccine, mRNA) product when used to provide: (1) a two-dose primary regimen for individuals aged 12 through 15 years; (2) a third primary series dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise; (3) a single booster dose at least 6 months after completing the primary series to individuals 65 years of age or older, 18 through 64 years of age at high risk of severe COVID-19, and 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2; and (4) a heterologous booster dose to certain individuals who have completed primary vaccination with a different authorized COVID-19 vaccine as described in the Scope of Authorization (Section II) under this EUA. Conditions A through W in this letter apply when COMIRNATY (COVID-19 Vaccine, mRNA) is provided for the uses described in this subsection III.BB., except that product manufactured and labeled in accordance with the approved BLA is deemed to satisfy the manufacturing, labeling, and distribution requirements of this authorization.

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IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

--/S/--

Jacqueline A. O'Shaughnessy, Ph.D.
Acting Chief Scientist
Food and Drug Administration

Enclosures



EXHIBIT D

October 29, 2021

Pfizer Inc.
Attention: Mr. Amit Patel
235 East 42nd St
New York, NY 10017

Dear Mr. Patel:

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act or the Act), the Secretary of the Department of Health and Human Services (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 citizens living abroad, and that involves the virus that causes Coronavirus Disease 2019 (COVID-19).¹ On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Act (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.²

On December 11, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 for individuals 16 years of age and older pursuant to Section 564 of the Act. FDA reissued the letter of authorization on: December 23, 2020,³ February 25, 2021,⁴ May

¹ U.S. Department of Health and Human Services, Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the FD&C Act, 21 U.S.C. § 360bbb-3, February 4, 2020.

² U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act*, 21 U.S.C. § 360bbb-3, 85 FR 18250 (April 1, 2020).

³ In the December 23, 2020 revision, FDA removed reference to the number of doses per vial after dilution from the letter of authorization, clarified the instructions for vaccination providers reporting to VAERS, and made other technical corrections. FDA also revised the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) to clarify the number of doses of vaccine per vial after dilution and the instructions for reporting to VAERS. In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and the Fact Sheet for Recipients and Caregivers were revised to include additional information on safety monitoring and to clarify information about the availability of other COVID-19 vaccines.

⁴ In the February 25, 2021 revision, FDA allowed flexibility on the date of submission of monthly periodic safety reports and revised the requirements for reporting of vaccine administration errors by Pfizer Inc. The Fact Sheet for Health Care Providers Administering Vaccine (Vaccination Providers) was revised to provide an update to the storage and transportation temperature for frozen vials, direct the provider to the correct CDC website for information on monitoring vaccine recipients for the occurrence of immediate adverse reactions, to include data from a developmental toxicity study, and add adverse reactions that have been identified during post authorization use. The Fact Sheet for Recipients and Caregivers was revised to add adverse reactions that have been identified during post authorization use.

10, 2021,⁵ June 25, 2021,⁶ and August 12, 2021.⁷ On August 23, 2021, FDA approved COMIRNATY (COVID-19 Vaccine, mRNA)⁸ and reissued the letter in its entirety for both Pfizer-BioNTech COVID-19 Vaccine and certain uses of COMIRNATY (COVID-19 Vaccine, mRNA).⁹ Subsequently, FDA reissued the letter of authorization on September 22, 2021¹⁰ and October 20, 2021.¹¹

⁵ In the May 10, 2021 revision, FDA authorized Pfizer-BioNTech Vaccine for the prevention of COVID-19 in individuals 12 through 15 years of age, as well as for individuals 16 years of age and older. In addition, FDA revised the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) to include the following Warning: “Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting.” In addition, the Fact Sheet for Recipients and Caregivers was revised to instruct vaccine recipients or their caregivers to tell the vaccination provider about fainting in association with a previous injection.

⁶ In the June 25, 2021 revision, FDA clarified terms and conditions that relate to export of Pfizer-BioNTech COVID-19 Vaccine from the United States. In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was revised to include a Warning about myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine. The Fact Sheet for Recipients and Caregivers was updated to include information about myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine.

⁷ In the August 12, 2021 revision, FDA authorized a third dose of the Pfizer-BioNTech COVID-19 Vaccine administered at least 28 days following the two dose regimen of this vaccine in individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

⁸ COMIRNATY (COVID-19 Vaccine, mRNA) was approved for active immunization to prevent COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

⁹ In the August 23, 2021 revision, FDA clarified that, subsequent to the FDA approval of COMIRNATY (COVID-19 Vaccine, mRNA) for the prevention of COVID-19 for individuals 16 years of age and older, this EUA would remain in place for the Pfizer-BioNTech COVID-19 Vaccine for the previously-authorized indication and uses. It also authorized COMIRNATY (COVID-19 Vaccine, mRNA) under this EUA for certain uses that are not included in the approved biologics license application (BLA). In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was revised to provide updates on expiration dating of the authorized Pfizer-BioNTech COVID-19 Vaccine and updated language regarding warnings and precautions related to myocarditis and pericarditis. The Fact Sheet for Recipients and Caregivers was updated as the Vaccine Information Fact Sheet for Recipients and Caregivers, which comprises the Fact Sheet for the authorized Pfizer-BioNTech COVID-19 Vaccine and information about the FDA-licensed vaccine, COMIRNATY (COVID-19 Vaccine, mRNA).

¹⁰ In the September 22, 2021 revision, FDA authorized the administration of a single booster dose of COMIRNATY (COVID-19 Vaccine, mRNA) or Pfizer-BioNTech COVID-19 Vaccine at least 6 months after completing the primary series of this vaccine in individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

¹¹ In the October 20, 2021 revision, FDA clarified eligibility for the booster dose of COMIRNATY (COVID-19 Vaccine, mRNA) or Pfizer-BioNTech COVID-19 Vaccine and authorized the administration of a single booster dose of Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA) as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

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On October 29, 2021, having concluded that revising this EUA is appropriate to protect the public health or safety under Section 564(g)(2) of the Act, FDA is again reissuing the October 20, 2021 letter of authorization in its entirety with revisions incorporated to:

- 1) authorize the use of Pfizer-BioNTech COVID-19 Vaccine for children 5 through 11 years of age; and
- 2) authorize a manufacturing change to include an additional formulation of the Pfizer-BioNTech COVID-19 Vaccine that uses tromethamine (Tris) buffer instead of phosphate buffered saline (PBS) used in the originally authorized Pfizer-BioNTech COVID-19 Vaccine.

The formulation of the Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer is authorized in two presentations:¹²

- 1) Multiple dose vials, with gray caps and labels with a gray border, formulated to provide, without need for dilution, doses (each 0.3 mL dose containing 30 µg nucleoside-modified messenger RNA (modRNA)) for individuals 12 years of age and older; and
- 2) Multiple dose vials, with orange caps and labels with an orange border, formulated to provide, after dilution, doses (each 0.2 mL dose containing 10 µg modRNA) for individuals 5 through 11 years of age.¹³

The Pfizer-BioNTech COVID-19 Vaccine that uses PBS buffer and COMIRNATY (COVID-19 Vaccine, mRNA) have the same formulation. The products are legally distinct with certain differences that do not impact safety or effectiveness. Accordingly, under this EUA, the Pfizer-BioNTech COVID-19 Vaccine that uses PBS buffer and COMIRNATY (COVID-19 Vaccine, mRNA) can be used interchangeably to provide doses for primary vaccination in individuals 12 years of age and older, or to provide a single booster dose in the adult populations described in Section II of this letter of authorization, without presenting any safety or effectiveness concerns.

The Pfizer-BioNTech COVID-19 Vaccine formulations that use Tris and PBS buffers, and which are authorized for use in individuals 12 years of age and older, contain the same modRNA and lipids, and the same quantity of these ingredients, per 0.3 mL dose. The two formulations differ with respect to certain inactive ingredients only and have been shown to be analytically comparable.¹⁴

¹² The Pfizer-BioNTech COVID-19 Vaccine that uses PBS buffer is available in multiple dose vials with purple caps, and is formulated to provide, after dilution, doses (each 0.3mL containing 30 µg modRNA) for individuals 12 years of age and older. The formulation that uses PBS buffer is not authorized for use in children 5 through 11 years of age.

¹³ The Pfizer-BioNTech COVID-19 Vaccine (0.2 mL dose containing 10 µg modRNA) that uses Tris buffer and is available in multiple dose vials with orange caps and labels with an orange border is the only formulation that is authorized for use in individuals 5 through 11 years of age.

¹⁴ Analytical comparability assessments use laboratory testing to demonstrate that a change in product formulation does not impact a product's safety or effectiveness. For the Pfizer-BioNTech COVID-19 Vaccine, multiple different

Accordingly, under this EUA, for individuals 12 years of age and older, COMIRNATY (COVID-19 Vaccine, mRNA) and these 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.

Therefore, for individuals 12 years of age and older, COMIRNATY (COVID-19 Vaccine, mRNA) is authorized to complete the primary regimen or provide a booster dose for individuals who received their initial primary dose(s) with the Pfizer-BioNTech COVID-19 Vaccine (whether the PBS formulation or Tris formulation), and the Pfizer-BioNTech COVID-19 Vaccine (whether the PBS formulation or Tris formulation) is authorized to complete the primary regimen or provide a booster for individuals who received their initial primary dose(s) with COMIRNATY (COVID-19 Vaccine, mRNA).

For the December 11, 2020 authorization for individuals 16 years of age and older, FDA reviewed safety and effectiveness data from an ongoing Phase 1/2/3 trial in approximately 44,000 participants randomized 1:1 to receive Pfizer-BioNTech COVID-19 Vaccine or saline control. The trial enrolled participants 12 years of age and older. FDA's review at that time considered the safety and effectiveness data as they relate to the request for emergency use authorization in individuals 16 years of age and older. FDA's review of the available safety data from 37,586 of the participants 16 years of age and older, who were followed for a median of two months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. FDA's analysis of the available efficacy data from 36,523 participants 12 years of age and older without evidence of SARS-CoV-2 infection prior to 7 days after dose 2 confirmed that the vaccine was 95% effective (95% credible interval 90.3, 97.6) in preventing COVID-19 occurring at least 7 days after the second dose (with 8 COVID-19 cases in the vaccine group compared to 162 COVID-19 cases in the placebo group). Based on these data, and review of manufacturing information regarding product quality and consistency, FDA concluded that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 16 years of age and older. Finally, on December 10, 2020, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion.

For the May 10, 2021 authorization for individuals 12 through 15 years of age, FDA reviewed safety and effectiveness data from the above-referenced, ongoing Phase 1/2/3 trial that enrolled approximately 46,000 participants, including 2,260 participants 12 through 15 years of age.

release parameters were evaluated to assess the comparability of the modified formulation (the formulation with the Tris buffer) to the originally-authorized formulation (the formulation with the PBS buffer). These release parameters ranged from product appearance to size of the lipid-nanoparticle to the integrity of the modRNA in the product. Additionally, characterization testing was performed to evaluate product composition and purity, including characteristics of the modRNA, as these are characteristics associated with the activity of the vaccine. The combination of release testing and characterization testing demonstrated that the modified formulation is analytically comparable to the original formulation.

Trial participants were randomized 1:1 to receive Pfizer-BioNTech COVID-19 Vaccine or saline control. FDA's review of the available safety data from 2,260 participants 12 through 15 years of age, who were followed for a median of 2 months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. FDA's analysis of SARS-CoV-2 50% neutralizing antibody titers 1 month after the second dose of Pfizer-BioNTech COVID-19 Vaccine in a subset of participants who had no serological or virological evidence of past SARS-CoV-2 infection confirm that the geometric mean antibody titer in participants 12 through 15 years of age was non-inferior to the geometric mean antibody titer in participants 16 through 25 years of age. FDA's analysis of available descriptive efficacy data from 1,983 participants 12 through 15 years of age without evidence of SARS-CoV-2 infection prior to 7 days after dose 2 confirm that the vaccine was 100% effective (95% confidence interval 75.3, 100.0) in preventing COVID-19 occurring at least 7 days after the second dose (with no COVID-19 cases in the vaccine group compared to 16 COVID-19 cases in the placebo group). Based on these data, FDA concluded that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in individuals 12 through 15 years of age. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 12 through 15 years of age.

For the August 12, 2021 authorization of a third primary series dose in individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise, FDA reviewed safety and effectiveness data reported in two manuscripts on solid organ transplant recipients. The first study was a single arm study conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) a median of 97±8 months earlier. A third dose of the Pfizer-BioNTech COVID-19 Vaccine was administered to 99 of these individuals approximately 2 months after they had received a second dose. Levels of total SARS-CoV-2 binding antibodies meeting the pre-specified criteria for success occurred four weeks after the third dose in 26/59 (44.0%) of those who were initially considered to be seronegative and received a third dose of the Pfizer-BioNTech COVID-19 Vaccine; 67/99 (68%) of the entire group receiving a third vaccination were subsequently considered to have levels of antibodies indicative of a significant response. In those who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported. A supportive secondary study describes a double-blind, randomized-controlled study conducted in 120 individuals who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years earlier (range 1.99-6.75 years). A third dose of a similar messenger RNA vaccine (the Moderna COVID-19 vaccine) was administered to 60 individuals approximately 2 months after they had received a second dose (i.e., doses at 0, 1 and 3 months); saline placebo was given to 60 individuals for comparison. The primary outcome was anti-RBD antibody at 4 months greater than 100 U/mL. This titer was selected based on NHP challenge studies as well as a large clinical cohort study to indicate this antibody titer was protective. Secondary outcomes were based on a virus neutralization assay and polyfunctional T cell responses. Baseline characteristics were comparable between the two study arms as were pre-intervention anti-RBD titer and neutralizing antibodies. Levels of total SARS-CoV-2 binding

antibodies indicative of a significant response occurred four weeks after the third dose in 33/60 (55.0%) of the Moderna COVID-19 vaccinated group and 10/57 (17.5%) of the placebo individuals. In the 60 individuals who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 adverse events were reported. Despite the moderate enhancement in antibody titers, the totality of data (i.e., supportive paper by Hall et al. demonstrated efficacy of the product in the elderly and persons with co-morbidities) supports the conclusion that a third dose of the Pfizer-BioNTech COVID-19 Vaccine may be effective in this population, and that the known and potential benefits of a third dose of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine for immunocompromised individuals at least 12 years of age who have received two doses of the Pfizer-BioNTech COVID-19 Vaccine and who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

For the September 22, 2021 authorization of a single booster dose administered at least 6 months after completing the primary series in individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19, FDA reviewed safety and effectiveness data from the above-referenced, ongoing Phase 1/2/3 trial in which 329 participants 18 through 75 years of age received a booster dose of the Pfizer-BioNTech COVID-19 Vaccine approximately 6 months (range 4.8 to 8.8 months) after completion of the primary series. FDA's review of the available safety data from 329 participants 18 through 75 years of age, who had been followed for a median of 2.6 months after receiving the booster dose, did not identify specific safety concerns that would preclude issuance of an EUA. The effectiveness of the booster dose of the Pfizer-BioNTech COVID-19 Vaccine is based on an assessment of 50% neutralizing antibody titers (NT50) against SARS-CoV-2 (USA_WA1/2020). FDA's analysis of SARS-CoV-2 NT50 one month after the booster dose compared to 1 month after the primary series in study participants 18 through 55 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster dose confirmed noninferiority for both geometric mean ratio and difference in seroresponse rates. Based on the totality of the scientific evidence available, including data from the above-referenced clinical trial, FDA concluded that a booster dose the Pfizer-BioNTech COVID-19 Vaccine may be effective, and that the known and potential benefits of a single booster dose at least 6 months after completing the primary series outweigh the known and potential risks for individuals 65 years of age and older; individuals 18 through 64 years of age at high risk of severe COVID-19; and individuals 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

For the October 20, 2021 authorization of a single booster dose as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine, FDA reviewed data from an ongoing Phase 1/2 clinical trial in participants 19-85 years of age. In this trial, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose

series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series (N=151) at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine. Adverse events were assessed through 28 days after the booster dose. An overall review of adverse reactions reported following the Pfizer-BioNTech COVID-19 Vaccine heterologous booster dose did not identify any new safety concerns, as compared with adverse reactions reported following Pfizer-BioNTech COVID-19 Vaccine primary series doses or homologous booster dose. Neutralizing antibody titers, as measured by a pseudovirus neutralization assay using a lentivirus expressing the SARS-CoV-2 Spike protein with D614G mutation, were assessed on Day 1 prior to administration of the booster dose and on Day 15 after the booster dose. A booster response to the Pfizer-BioNTech COVID-19 Vaccine was demonstrated regardless of primary vaccination. Based on the on the totality of the scientific evidence available, including data from the above-referenced clinical trial, FDA concluded that a heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine may be effective, and that the known and potential benefits of a heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine following completion of primary vaccination with another authorized COVID-19 vaccine outweigh the known and potential risks.

For the October 29, 2021 authorization for the Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer for individuals 5 through 11 years of age, FDA reviewed safety and effectiveness data from an ongoing Phase 1/2/3 trial that has enrolled 4,695 participants 5 through 11 years of age, of whom 3,109 participants received PfizerBioNTech COVID19 Vaccine (containing 10 µg modRNA) formulated using PBS buffer and approximately 1,538 participants received saline control in Phase 2/3. FDA's review of the available safety data from 3,109 participants 5 through 11 years of age who received Pfizer-BioNTech COVID-19 Vaccine (containing 10 µg modRNA), including 1,444 who were followed for at least 2 months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. SARS-CoV-2 50% neutralizing antibody titers 1 month after the second dose were compared between a subset of participants 5 through 11 years of age who received Pfizer-BioNTech COVID-19 Vaccine (containing 10 µg modRNA) and a subset of participants 16 through 25 years of age who received Pfizer-BioNTech COVID-19 Vaccine (containing 30 µg modRNA) in the above-referenced ongoing Phase 1/2/3 trial that enrolled approximately 46,000 participants. Immunobridging analyses included a subset of participants from each study who had no serological or virological evidence of past SARS-CoV-2 infection. FDA's analyses confirm that immunobridging criteria were met for both geometric mean antibody titers and seroresponse rates. FDA's analysis of available descriptive efficacy data from 1,968 participants 5 through 11 years of age without evidence of SARS-CoV-2 infection prior to 7 days after dose 2 confirm that the vaccine was 90.7% effective (95% confidence interval 67.7, 98.3) in preventing COVID-19 occurring at least 7 days after the second dose (with 3 COVID-19 cases in the vaccine group compared to 16 COVID-19 cases in the placebo group). Based on these data, FDA concluded that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in individuals 5 through 11 years of age. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 5 through 11 years of age. Finally, on

October 26, 2021, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion.

For the October 29, 2021 authorization of the manufacturing change to include an additional formulation of the Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer instead of PBS buffer used in the originally authorized Pfizer-BioNTech COVID-19 Vaccine, FDA reviewed data on analytical comparability, which uses laboratory testing to demonstrate that a change in product formulation is not expected to impact safety or effectiveness. In the case of Pfizer-BioNTech COVID-19 Vaccine, multiple different release parameters were evaluated, ranging from product appearance to size of the lipid-nanoparticle to the integrity of the modRNA in the product. Characterization testing included looking at product composition and purity including characteristics of the modRNA, and strength including the lipid-nanoparticle size distribution and shape, as these are characteristics associated with the activity of the vaccine. In this case, analytical comparability to the current PBS formulation of the Pfizer-BioNTech COVID-19 Vaccine was demonstrated for the Tris formulation of the Pfizer-BioNTech COVID-19 Vaccine through a combination of release and characterization testing.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of Pfizer-BioNTech COVID-19 Vaccine¹⁵ for the prevention of COVID-19, as described in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization. Additionally, as specified in subsection III.BB, I am authorizing use of COMIRNATY (COVID-19 Vaccine, mRNA) under this EUA as described in the Scope of Authorization section of this letter (Section II).

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Pfizer-BioNTech COVID-19 Vaccine¹⁶ for the prevention of COVID-19 when administered as described in the Scope of Authorization (Section II) meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

- A. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
- B. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine when used to prevent COVID-19 outweigh its known and potential risks; and

¹⁵ Reference to the Pfizer-BioNTech COVID-19 Vaccine hereinafter refers to both the PBS and Tris formulations, unless specifically delineated otherwise.

¹⁶ In this section (Section I), references to Pfizer-BioNTech COVID-19 Vaccine also apply to COMIRNATY (COVID-19 Vaccine, mRNA).

C. There is no adequate, approved, and available alternative¹⁷ Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19.¹⁸

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Pfizer Inc. will supply Pfizer-BioNTech COVID-19 Vaccine either directly or through authorized distributor(s),¹⁹ to emergency response stakeholders²⁰ as directed by the U.S. government, including the Centers for Disease Control and Prevention (CDC) and/or other designee, for use consistent with the terms and conditions of this EUA;
- Pfizer-BioNTech COVID-19 Vaccine may be administered by a vaccination provider²¹ without an individual prescription for each vaccine recipient.

¹⁷ Although COMIRNATY (COVID-19 Vaccine, mRNA) is approved to prevent COVID-19 in individuals 16 years of age and older, there is not sufficient approved vaccine available for distribution to this population in its entirety at the time of reissuance of this EUA. Additionally, there are no COVID-19 vaccines that are approved to provide: COVID-19 vaccination in individuals 5 through 15 years of age; a third primary series dose to certain immunocompromised populations described in this EUA; a homologous booster dose to the authorized population described in this EUA; or a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine.

¹⁸ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

¹⁹ “Authorized Distributor(s)” are identified by Pfizer Inc. or, if applicable, by a U.S. government entity, such as the Centers for Disease Control and Prevention (CDC) and/or other designee, as an entity or entities allowed to distribute authorized Pfizer-BioNTech COVID-19 Vaccine.

²⁰ For purposes of this letter, “emergency response stakeholder” refers to a public health agency and its delegates that have legal responsibility and authority for responding to an incident, based on political or geographical boundary lines (e.g., city, county, tribal, territorial, State, or Federal), or functional (e.g., law enforcement or public health range) or sphere of authority to administer, deliver, or distribute vaccine in an emergency situation. In some cases (e.g., depending on a state or local jurisdiction’s COVID-19 vaccination response organization and plans), there might be overlapping roles and responsibilities among “emergency response stakeholders” and “vaccination providers” (e.g., if a local health department is administering COVID-19 vaccines; if a pharmacy is acting in an official capacity under the authority of the state health department to administer COVID-19 vaccines). In such cases, it is expected that the conditions of authorization that apply to emergency response stakeholders and vaccination providers will all be met.

²¹ For purposes of this letter, “vaccination provider” refers to the facility, organization, or healthcare provider licensed or otherwise authorized by the emergency response stakeholder (e.g., non-physician healthcare professionals, such as nurses and pharmacists pursuant to state law under a standing order issued by the state health officer) to administer or provide vaccination services in accordance with the applicable emergency response stakeholder’s official COVID-19 vaccination and emergency response plan(s) and who is enrolled in the CDC COVID-19 Vaccination Program. If the vaccine is exported from the United States, a “vaccination provider” is a provider that is authorized to administer this vaccine in accordance with the laws of the country in which it is administered. For purposes of this letter, “healthcare provider” also refers to a person authorized by the U.S. Department of Health and Human Services (e.g., under the PREP Act Declaration for Medical Countermeasures against COVID-19) to administer FDA-authorized COVID-19 vaccine (e.g., qualified pharmacy technicians and State-authorized pharmacy interns acting under the supervision of a qualified pharmacist). See, e.g., HHS. *Fourth Amendment to the Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19 and Republication of the Declaration*. 85 FR 79190 (December 9, 2020).

For use in individuals 12 years of age and older

- The Pfizer-BioNTech COVID-19 Vaccine formulations that use Tris and PBS buffers (each 0.3 mL dose containing 30 µg modRNA) covered by this authorization will be administered by vaccination providers and used only to prevent COVID-19 in individuals 12 years of age and older with a two-dose primary regimen (3 weeks apart) and to provide:
 - a third primary series dose at least 28 days following the second dose to individuals 12 years of age or older who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise;
 - a single booster dose at least 6 months after completion of a primary series of the vaccine to individuals: 65 years of age or older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2;
 - a single booster dose as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine, where the eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination; and

For use in individuals 5 through 11 years of age

- The Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer (each 0.2 mL dose containing 10 µg modRNA) covered by this authorization will be administered by vaccination providers and used only to prevent COVID-19 in individuals 5 through 11 years of age with a two-dose primary regimen (3 weeks apart).

For use in individuals who are 11 years old at the time of the first dose, and turn 12 years old before the second dose:

- Notwithstanding the age limitations for use of the different formulations and presentations described above, individuals who will turn from 11 years to 12 years of age between their first and second dose in the primary regimen may receive, for either dose, either: (1) the Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer (each 0.2 mL dose containing 10 µg modRNA) covered by this authorization; or (2) the Pfizer-BioNTech COVID-19 Vaccine and COMIRNATY formulations provided in one of the presentations for individuals 12 years of age and older (each 0.3 mL dose containing 30 µg modRNA) covered by this authorization.
- The vaccine will be administered by vaccination providers and used only to prevent COVID-19 with a two-dose primary regimen (3 weeks apart).

This authorization also covers the use of the licensed COMIRNATY (COVID-19 Vaccine, mRNA) product when used to provide: (1) a two-dose primary regimen (0.3 mL each, 3 weeks apart) for individuals 12 through 15 years of age; (2) a third primary series dose at least 28 days following the second dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an

equivalent level of immunocompromise; (3) a single booster dose (0.3 mL) at least 6 months after completion of the primary series to individuals 65 years of age and older, 18 through 64 years of age at high risk of severe COVID-19, and 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2; and (4) a single booster dose (0.3 mL) as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine, where the eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

Product Description²²

The Pfizer-BioNTech COVID-19 Vaccine, supplied in two formulations, is provided in three different vials:

For use in individuals 12 years of age and older

- The Pfizer-BioNTech COVID-19 Vaccine that uses PBS buffer is available in multiple dose vials with purple caps. It is formulated to provide, after dilution, 0.3 mL doses (each containing 30 µg modRNA) and can be used for all authorized indications in individuals 12 years of age and older.
- The Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer, and is available in multiple dose vials with gray caps and labels with gray borders, is formulated to provide, after dilution, 0.3 mL doses (each containing 30 µg modRNA) and can be used for all authorized indications in individuals 12 years of age and older.

For use in individuals 5 through 11 years of age

- The Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer, and is available in multiple dose vials with orange caps and labels with orange borders, is formulated to provide, after dilution, 0.2 mL doses (each containing 10 µg modRNA) and can be used for administration to individuals 5 through 11 years of age.

For use in individuals 12 years of age and older

The Pfizer-BioNTech COVID-19 Vaccine that uses PBS buffer (supplied in multiple dose vials with purple caps) is supplied as a frozen suspension; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. The Pfizer-BioNTech COVID-19 Vaccine does not contain a preservative. Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine contains 30 µg of modRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2. Each dose of the Pfizer-BioNTech COVID-19 Vaccine also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylee glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg

²² For COMIRNATY (COVID-19 Vaccine, mRNA) product description, please see the COMIRNATY (COVID-19 Vaccine, mRNA) prescribing information, found here: <https://www.fda.gov/media/151707/download>.

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dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection) contributes an additional 2.16 mg sodium chloride per dose.

The Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer and that is supplied in multiple dose vials with gray caps is supplied as a frozen suspension and should not be diluted. The Pfizer-BioNTech COVID-19 Vaccine does not contain a preservative. Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine contains 30 µg of a modRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2. Each dose of the Pfizer-BioNTech COVID-19 Vaccine also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.19 mg cholesterol), 0.06 mg tromethamine, 0.4 mg tromethamine hydrochloride, and 31 mg sucrose.

For use in individuals 5 through 11 years of age

The Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer and that is supplied in multiple dose vials with orange caps is supplied as a frozen suspension; each vial must be diluted with 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of the Pfizer-BioNTech COVID-19 Vaccine contains 10 µg of a modRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2. Each dose of the Pfizer-BioNTech COVID-19 Vaccine also includes the following ingredients: lipids (0.14 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.02 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.03 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.06 mg cholesterol), 10.3 mg sucrose, 0.02 mg tromethamine, and 0.13 mg tromethamine hydrochloride. The diluent (0.9% Sodium Chloride Injection, USP) contributes 0.9 mg sodium chloride per dose.

The manufacture of the authorized Pfizer-BioNTech COVID-19 Vaccine is limited to those facilities identified and agreed upon in Pfizer's request for authorization.

The Pfizer-BioNTech COVID-19 Vaccine vial label and carton labels are clearly marked for "Emergency Use Authorization." The Pfizer-BioNTech COVID-19 Vaccine is authorized to be distributed, stored, further redistributed, and administered by emergency response stakeholders when packaged in the authorized manufacturer packaging (i.e., vials and cartons), despite the fact that the vial and carton labels may not contain information that otherwise would be required under the FD&C Act.

Pfizer-BioNTech COVID-19 Vaccine is authorized for emergency use with the following product-specific information required to be made available to vaccination providers and recipients, respectively (referred to as "authorized labeling"):

- Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers): Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) - For 12 Years of Age and Older Dilute Before Use)

- Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers): Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) - For 12 Years of Age and Older Do Not Dilute
- Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers): Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) - For 5 Through 11 Years of Age Dilute Prior To Use
- Vaccine Information Fact Sheet for Recipients and Caregivers About COMIRNATY (COVID-19 Vaccine, mRNA) and Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease (COVID-19) For Use in Individuals 12 Years of Age and Older
- Vaccine Information Fact Sheet for Recipients and Caregivers About the Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease (COVID-19) for Use in Individuals 5 Through 11 Years of Age

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine,²³ when used to prevent COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh its known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that Pfizer-BioNTech COVID-19 Vaccine (as described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of Pfizer-BioNTech COVID-19 Vaccine under this EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), Pfizer-BioNTech COVID-19 Vaccine is authorized to prevent COVID-19 in individuals 5 years of age and older as described in the Scope of Authorization (Section II) under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

²³ The conclusions supporting authorization stated in this section (Section II) also apply to COMIRNATY (COVID-19 Vaccine, mRNA).

Pfizer Inc. and Authorized Distributor(s)

- A. Pfizer Inc. and authorized distributor(s) will ensure that the authorized Pfizer-BioNTech COVID-19 Vaccine is distributed, as directed by the U.S. government, including CDC and/or other designee, and the authorized labeling (i.e., Fact Sheets) will be made available to vaccination providers, recipients, and caregivers consistent with the terms of this letter.
- B. Pfizer Inc. and authorized distributor(s) will ensure that appropriate storage and cold chain is maintained until delivered to emergency response stakeholders' receipt sites.
- C. Pfizer Inc. will ensure that the terms of this EUA are made available to all relevant stakeholders (e.g., emergency response stakeholders, authorized distributors, and vaccination providers) involved in distributing or receiving authorized Pfizer-BioNTech COVID-19 Vaccine. Pfizer Inc. will provide to all relevant stakeholders a copy of this letter of authorization and communicate any subsequent amendments that might be made to this letter of authorization and its authorized labeling.
- D. Pfizer Inc. may develop and disseminate instructional and educational materials (e.g., video regarding vaccine handling, storage/cold-chain management, preparation, disposal) that are consistent with the authorized emergency use of the vaccine as described in the letter of authorization and authorized labeling, without FDA's review and concurrence, when necessary to meet public health needs during an emergency. Any instructional and educational materials that are inconsistent with the authorized labeling are prohibited.
- E. Pfizer Inc. may request changes to this authorization, including to the authorized Fact Sheets for the vaccine. Any request for changes to this EUA must be submitted to Office of Vaccines Research and Review (OVRR)/Center for Biologics Evaluation and Research (CBER). Such changes require appropriate authorization prior to implementation.²⁴
- F. Pfizer Inc. will report to Vaccine Adverse Event Reporting System (VAERS):
 - Serious adverse events (irrespective of attribution to vaccination);
 - Cases of Multisystem Inflammatory Syndrome in children and adults; and
 - Cases of COVID-19 that result in hospitalization or death, that are reported to Pfizer Inc.

²⁴ The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), or (7), review and concurrence is required from the Preparedness and Response Team (PREP)/Office of the Center Director (OD)/CBER and the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS).

These reports should be submitted to VAERS as soon as possible but no later than 15 calendar days from initial receipt of the information by Pfizer Inc.

- G. Pfizer Inc. must submit to Investigational New Drug application (IND) number 19736 periodic safety reports at monthly intervals in accordance with a due date agreed upon with the Office of Biostatistics and Epidemiology (OBE)/CBER beginning after the first full calendar month after authorization. Each periodic safety report is required to contain descriptive information which includes:
- A narrative summary and analysis of adverse events submitted during the reporting interval, including interval and cumulative counts by age groups, special populations (e.g., pregnant women), and adverse events of special interest;
 - A narrative summary and analysis of vaccine administration errors, whether or not associated with an adverse event, that were identified since the last reporting interval;
 - Newly identified safety concerns in the interval; and
 - Actions taken since the last report because of adverse experiences (for example, changes made to Healthcare Providers Administering Vaccine (Vaccination Providers) Fact Sheet, changes made to studies or studies initiated).
- H. No changes will be implemented to the description of the product, manufacturing process, facilities, or equipment without notification to and concurrence by FDA.
- I. All manufacturing facilities will comply with Current Good Manufacturing Practice requirements.
- J. Pfizer Inc. will submit to the EUA file Certificates of Analysis (CoA) for each drug product lot at least 48 hours prior to vaccine distribution. The CoA will include the established specifications and specific results for each quality control test performed on the final drug product lot.
- K. Pfizer Inc. will submit to the EUA file quarterly manufacturing reports, starting in July 2021, that include a listing of all Drug Substance and Drug Product lots produced after issuance of this authorization. This report must include lot number, manufacturing site, date of manufacture, and lot disposition, including those lots that were quarantined for investigation or those lots that were rejected. Information on the reasons for lot quarantine or rejection must be included in the report.
- L. Pfizer Inc. and authorized distributor(s) will maintain records regarding release of Pfizer-BioNTech COVID-19 Vaccine for distribution (i.e., lot numbers, quantity, release date).
- M. Pfizer Inc. and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.
- N. Pfizer Inc. will conduct post-authorization observational studies to evaluate the association between Pfizer-BioNTech COVID-19 Vaccine and a pre-specified list of

adverse events of special interest, including myocarditis and pericarditis, along with deaths and hospitalizations, and severe COVID-19. The study population should include individuals administered the authorized Pfizer-BioNTech COVID-19 Vaccine under this EUA in the general U.S. population (5 years of age and older), individuals who receive a booster dose, populations of interest such as healthcare workers, pregnant women, immunocompromised individuals, subpopulations with specific comorbidities. The studies should be conducted in large scale databases with an active comparator. Pfizer Inc. will provide protocols and status update reports to the IND 19736 with agreed-upon study designs and milestone dates.

Emergency Response Stakeholders

- O. Emergency response stakeholders will identify vaccination sites to receive authorized Pfizer-BioNTech COVID-19 Vaccine and ensure its distribution and administration, consistent with the terms of this letter and CDC's COVID-19 Vaccination Program.
- P. Emergency response stakeholders will ensure that vaccination providers within their jurisdictions are aware of this letter of authorization, and the terms herein and any subsequent amendments that might be made to the letter of authorization, instruct them about the means through which they are to obtain and administer the vaccine under the EUA, and ensure that the authorized labeling [i.e., Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and Vaccine Information Fact Sheet for Recipients and Caregivers] is made available to vaccination providers through appropriate means (e.g., e-mail, website).
- Q. Emergency response stakeholders receiving authorized Pfizer-BioNTech COVID-19 Vaccine will ensure that appropriate storage and cold chain is maintained.

Vaccination Providers

- R. Vaccination providers will administer the vaccine in accordance with the authorization and will participate and comply with the terms and training required by CDC's COVID-19 Vaccination Program.
- S. Vaccination providers will provide the Vaccine Information Fact Sheet for Recipients and Caregivers to each individual receiving vaccination and provide the necessary information for receiving their second dose and/or third dose.
- T. Vaccination providers administering the vaccine must report the following information associated with the administration of the vaccine of which they become aware to VAERS in accordance with the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers):
 - Vaccine administration errors whether or not associated with an adverse event
 - Serious adverse events (irrespective of attribution to vaccination)
 - Cases of Multisystem Inflammatory Syndrome in children and adults
 - Cases of COVID-19 that result in hospitalization or death

Complete and submit reports to VAERS online at <https://vaers.hhs.gov/reportevent.html>. The VAERS reports should include the words “Pfizer-BioNTech COVID-19 Vaccine EUA” in the description section of the report. More information is available at vaers.hhs.gov or by calling 1-800-822-7967. To the extent feasible, report to Pfizer Inc. by contacting 1-800-438-1985 or by providing a copy of the VAERS form to Pfizer Inc.; Fax: 1-866-635-8337.

- U. Vaccination providers will conduct any follow-up requested by the U.S government, including CDC, FDA, or other designee, regarding adverse events to the extent feasible given the emergency circumstances.
- V. Vaccination providers will monitor and comply with CDC and/or emergency response stakeholder vaccine management requirements (e.g., requirements concerning obtaining, tracking, and handling vaccine) and with requirements concerning reporting of vaccine administration data to CDC.
- W. Vaccination providers will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to CDC, and FDA for inspection upon request.

Conditions Related to Printed Matter, Advertising, and Promotion

- X. All descriptive printed matter, advertising, and promotional material, relating to the use of the Pfizer-BioNTech COVID-19 Vaccine shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in Section 502(a) and (n) of the FD&C Act and FDA implementing regulations.
- Y. All descriptive printed matter, advertising, and promotional material relating to the use of the Pfizer-BioNTech COVID-19 Vaccine clearly and conspicuously shall state that:
 - This product has not been approved or licensed by FDA, but has been authorized for emergency use by FDA, under an EUA to prevent Coronavirus Disease 2019 (COVID-19) for use either in individuals 12 years of age and older, or in individuals 5 through 11 years of age, as appropriate; and
 - The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of the medical product under Section 564(b)(1) of the FD&C Act unless the declaration is terminated or authorization revoked sooner.

Condition Related to Export

- Z. If the Pfizer-BioNTech COVID-19 Vaccine is exported from the United States, conditions C, D, and O through Y do not apply, but export is permitted only if 1) the regulatory authorities of the country in which the vaccine will be used are fully

informed that this vaccine is subject to an EUA and is not approved or licensed by FDA and 2) the intended use of the vaccine will comply in all respects with the laws of the country in which the product will be used. The requirement in this letter that the authorized labeling (i.e., Fact Sheets) be made available to vaccination providers, recipients, and caregivers in condition A will not apply if the authorized labeling (i.e., Fact Sheets) are made available to the regulatory authorities of the country in which the vaccine will be used.

Conditions With Respect to Use of Licensed Product

AA. COMIRNATY (COVID-19 Vaccine, mRNA) is licensed for individuals 16 years of age and older. There remains, however, a significant amount of Pfizer-BioNTech COVID-19 Vaccine that was manufactured and labeled in accordance with this emergency use authorization. The authorization remains in place with respect to the Pfizer-BioNTech COVID-19 Vaccine for this population.

BB. This authorization also covers the use of the licensed COMIRNATY (COVID-19 Vaccine, mRNA) product when used to provide: (1) a two-dose primary regimen for individuals 12 through 15 years of age;²⁵ (2) a third primary series dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise; (3) a single booster dose at least 6 months after completing the primary series to individuals 65 years of age or older, 18 through 64 years of age at high risk of severe COVID-19, and 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2; and (4) a heterologous booster dose to certain individuals who have completed primary vaccination with a different authorized COVID-19 vaccine as described in the Scope of Authorization (Section II) under this EUA. Conditions A through W in this letter apply when COMIRNATY (COVID-19 Vaccine, mRNA) is provided for the uses described in this subsection III.BB., except that product manufactured and labeled in accordance with the approved BLA is deemed to satisfy the manufacturing, labeling, and distribution requirements of this authorization.

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

²⁵ As noted above, this includes the first dose of a two-dose primary regimen for individuals who are 11 years old and will turn 12 years of age between their first and second dose in the primary regimen.

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Sincerely,

--/S/--

Jacqueline A. O'Shaughnessy, Ph.D.
Acting Chief Scientist
Food and Drug Administration

Enclosures



EXHIBIT E

COVID-19 Information

x

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NEWS: DailyMed Announcements

SEPTEMBER 13, 2021

Pfizer received FDA BLA license for its COVID-19 vaccine

Pfizer received FDA BLA license on 8/23/2021 for its COVID-19 vaccine for use in individuals 16 and older (COMIRNATY). At that time, the FDA published a BLA package insert that included the approved new COVID-19 vaccine tradename COMIRNATY and listed 2 new NDCs (0069-1000-03, 0069-1000-02) and images of labels with the new tradename.

At present, Pfizer does not plan to produce any product with these new NDCs and labels over the next few months while EUA authorized product is still available and being made available for U.S. distribution. As such, the CDC, AMA, and drug compendia may not publish these new codes until Pfizer has determined when the product will be produced with the BLA labels.

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