

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 was 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

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Pfizer-BioNTech COVID-19 Vaccine³⁰ 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 alternative³¹ to Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19.³²

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 and Pfizer-BioNTech COVID-19 Vaccine, Bivalent either directly or through authorized distributor(s),³³ to

³⁰ In this section (Section I), references to Pfizer-BioNTech COVID-19 Vaccine also apply to COMIRNATY (COVID-19 Vaccine, mRNA), and Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

³¹ Although COMIRNATY (COVID-19 Vaccine, mRNA) and SPIKEVAX (COVID-19 Vaccine, mRNA) are approved to prevent COVID-19 in certain individuals who fall within the scope of the Pfizer-BioNTech COVID-19 Vaccine authorization, there are not sufficient quantities of 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 a third primary series dose to certain immunocompromised populations described in this EUA or COVID-19 vaccination in certain pediatric populations described in this EUA. In addition, there are no bivalent vaccines that contain or encode the spike protein of the Omicron variant of SARS-CoV-2 that are approved to prevent COVID-19.

³² No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

³³ “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.

For use in individuals who turn from 11 years to 12 years of age between doses in the primary series:

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 doses in the primary series may receive, for any dose in the primary series, either:

- the Pfizer-BioNTech COVID-19 Vaccine authorized for individuals 5 through 11 years of age (each 0.2 mL dose containing 10 mcg modRNA, supplied in multiple dose vials with orange caps and labels with orange borders) covered by this authorization; or
- the Pfizer-BioNTech COVID-19 Vaccine and COMIRNATY (COVID-19 Vaccine, mRNA) formulations provided in one of the presentations for individuals 12 years of age and older (each 0.3 mL dose containing 30 mcg modRNA) covered by this authorization.

This authorization also covers the use of the licensed COMIRNATY (COVID-19 Vaccine, mRNA) product when used 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.

The Pfizer-BioNTech COVID-19 Vaccine that uses PBS buffer and COMIRNATY (COVID-19 Vaccine, mRNA) that uses PBS buffer have the same formulation. Additionally, the Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer and COMIRNATY (COVID-19 Vaccine, mRNA) that uses Tris buffer have the same formulation. 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) that uses PBS buffer can be used interchangeably, and the Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer and COMIRNATY (COVID-19 Vaccine, mRNA) that uses Tris buffer can be used interchangeably, as described above, without presenting any safety or effectiveness concerns. As described below under *Product Description*, the formulations of the Pfizer-BioNTech COVID-19 Vaccine and COMIRNATY (COVID-19 Vaccine, mRNA) that use Tris and PBS buffers, which are covered by this authorization 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 of the Pfizer-BioNTech COVID-19 Vaccine and COMIRNATY (COVID-19 Vaccine, mRNA) differ with respect to certain inactive ingredients only and have been shown to be analytically comparable.³⁶ Accordingly, under this EUA, for individuals 12 years of age and older, the two formulations of COMIRNATY (COVID-19 Vaccine, mRNA) and the two formulations of the Pfizer-BioNTech COVID-19 Vaccine, when prepared according to their respective instructions for use and authorized uses, can be used interchangeably without presenting any safety or effectiveness concerns.

³⁶ 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 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. Release and characterization tests include tests for purity, composition, and critical attributes of mRNA 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.

Therefore, for individuals 12 years of age and older, COMIRNATY (COVID-19 Vaccine, mRNA) is authorized to complete the primary series for individuals who received their initial primary dose(s) with the Pfizer-BioNTech COVID-19 Vaccine, and the Pfizer-BioNTech COVID-19 Vaccine is authorized to complete the primary series for individuals who received their initial primary dose(s) with COMIRNATY (COVID-19 Vaccine, mRNA).

Product Description³⁷

The Pfizer-BioNTech COVID-19 Vaccine, supplied in two formulations, is provided in four different color-coded multiple dose vial presentations:

Table 4: Pfizer-BioNTech COVID-19 Vaccine Vial Presentations

Presentation	Authorized age	Dose Volume and Quantity of modRNA	Buffer used	Dilution
Multiple-Dose Vials with Maroon Caps and Labels with Maroon Borders	6 months through 4 years of age	0.2 mL dose (each containing 3 mcg modRNA)	Tris	Dilute with 2.2 mL of sterile 0.9% Sodium Chloride Injection, USP
Multiple-Dose Vials with Orange Caps and Labels with Orange Borders	5 through 11 years of age	0.2 mL dose (each containing 10 mcg modRNA)	Tris	Dilute with 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP
Multiple-Dose Vials with Gray Caps and Labels with Gray Borders	12 years of age and older	0.3 mL dose (each containing 30 mcg modRNA)	Tris	Not to be diluted
Multiple-Dose Vials with Purple Caps	12 years of age and older	0.3 mL dose (each containing 30 mcg modRNA)	PBS	Dilute with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP

[^] The vial labels may state “Age 2y to < 5y” or “Age 6m to < 5y” and carton labels may state “For age 2 years to < 5 years” or “For age 6 months to < 5 years”. Vials with either printed age range can be used for individuals 6 months through 4 years of age.

³⁷ For COMIRNATY (COVID-19 Vaccine, mRNA) that uses the PBS buffer product description, please see the COMIRNATY (COVID-19 Vaccine, mRNA) prescribing information, found here: <https://www.fda.gov/media/151707/download>; for COMIRNATY (COVID-19 Vaccine, mRNA) that uses the Tris buffer product description, please see the COMIRNATY (COVID-19 Vaccine, mRNA) prescribing information, found here: <https://www.fda.gov/media/154834/download>.

Pfizer Inc. and Authorized Distributor(s)

- A. Pfizer Inc. and authorized distributor(s) will ensure that the authorized Pfizer-BioNTech COVID-19 Vaccine and Pfizer-BioNTech COVID-19 Vaccine, Bivalent are 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 and Pfizer-BioNTech COVID-19 Vaccine, Bivalent. 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 Pfizer-BioNTech COVID-19 Vaccine and Pfizer-BioNTech COVID-19 Vaccine, Bivalent 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 vaccines. 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.³⁹
- F. Pfizer Inc. will report to Vaccine Adverse Event Reporting System (VAERS):
 - Serious adverse events (irrespective of attribution to vaccination);
 - Cases of myocarditis;

³⁹ 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. All changes to the authorization require review and concurrence from OVR. 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).

- S. Vaccination providers will provide the Vaccine Information Fact Sheet for Recipients and Caregivers or 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 of the primary series.
- T. Vaccination providers administering the vaccines must report the following information associated with the administration of the vaccines 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 myocarditis
 - Cases of pericarditis
 - 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” or “Pfizer-BioNTech COVID-19 Vaccine, Bivalent”, as appropriate, 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 and Pfizer-BioNTech COVID-19 Vaccine, Bivalent 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.

