Our Reference: EUA 27034

November 22, 2022

Pfizer, Inc.
Attention: Gosia Mineo, M.S.
1 Pfizer Way 190/004/4405
Pearl River, NY 10965

**Re:** EUA 27034 - Emergency Use Authorization of Pfizer-BioNTech COVID-19 Vaccine and Pfizer-BioNTech COVID-19 Vaccine, Bivalent, Reissued on October 12, 2022, Under Section 564 of the Federal Food, Drug, and Cosmetic Act (FDCA) (21 U.S.C. 360bbb-3);
Request in Amendments received on September 8, 2022, October 11, 2022, October 21, 2022, November 1, 2022, November 2, 2022, and November 4, 2022, to Update the Authorized Fact Sheets for Recipients and Caregivers, the Authorized Vaccine Information Fact Sheet for Recipients and Caregivers, and the Authorized Fact Sheets for Healthcare Providers Administering Vaccine (Vaccination Providers) - (including Full EUA Prescribing Information)

Dear Ms. Mineo:

This letter is to notify you that we have reviewed the requested changes and that your requests to add dizziness to all of the Fact Sheets and to update the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers): Emergency Use Authorization (EUA) Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19), for 6 months through 4 Years of Age Dilute Before Use, as described below, are granted.

We concur with adding 'dizziness' to the EUA Fact Sheets for Recipients and Caregivers and the authorized Vaccine Information Fact Sheet for Recipients and Caregivers in the following section:

**WHAT ARE THE RISKS OF THESE VACCINES?**

Side effects that have been reported with these vaccines include:

We also concur with adding 'dizziness' to the EUA Fact Sheets for Healthcare Providers Administering Vaccine (Vaccination Providers) (Full Prescribing Information) in the following section:

**6.2 Post Authorization Experience**

Nervous System Disorders:

This change was also made to the EUA Fact Sheets for Healthcare Providers Administering Vaccine (Vaccination Providers) (short version) for consistency.

U.S. Food & Drug Administration
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In addition, we concur with the updates to the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers): Emergency Use Authorization (EUA) Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19), for 6 months through 4 Years of Age Dilute Before Use to include the following new information in section **18.2 Effectiveness of a 3-Dose Primary Series in Participants 6 Months Through 4 Years of Age:**

Study 3 is an ongoing Phase 1/2/3 multicenter, randomized, dose finding, open label (Phase 1) and multinational, saline placebo-controlled, observer-blind, immunogenicity and efficacy (Phase 2/3) study to evaluate the safety and effectiveness of Pfizer-BioNTech COVID-19 Vaccine in individuals 6 months through 11 years of age. Randomization was stratified by age: 6 through 23 months of age, 2 through 4 years of age, or 5 through 11 years of age. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Results from participants 6 months through 4 years of age are presented in this subsection. In Phase 2/3, a total of 1,776 participants 6 through 23 months of age and 2,750 participants 2 through 4 years of age were randomized 2:1 and received 3 doses of the Pfizer-BioNTech COVID-19 Vaccine or saline placebo.

Efficacy in Participants 6 Months Through 4 Years of Age After a 3-Dose Primary Series

A descriptive efficacy analysis of Study 3 was performed across the combined population of participants 6 months through 4 years of age based on PCR-confirmed COVID-19 cases among 873 participants in the Pfizer-BioNTech COVID-19 Vaccine group and 381 participants in the placebo group (2:1 randomization) who received 3 doses of study intervention during the blinded follow-up period when the Omicron variant of SARS-CoV-2 (BA.2) was the predominant variant in circulation (data cutoff date of June 17, 2022).

The evaluable efficacy population without prior evidence of SARS-CoV-2 infection up to 7 days after Dose 3 of Pfizer-BioNTech COVID-19 Vaccine was comprised of 873 vaccine recipients and 381 placebo recipients 6 months through 4 years of age. Most vaccine recipients in this analysis population were White (76.3%), with 3.4% Black or African American participants, 10.0% Asian participants, and 10.1% who identified as multiracial, other or not reported. There were 11.2% Hispanic/Latino vaccine recipients. Among the vaccine recipients, 51.1% were female. The median age was 16.0 months in vaccine recipients 6 through 23 months of age and the median age was 3.0 years in vaccine recipients 2 through 4 years of age. In the evaluable efficacy population, 8.7% of vaccine recipients had one or more comorbidities that increase the risk of severe COVID-19 as described in the Morbidity and Mortality Weekly Report (MMWR) 69(32);1081-8 and/or obesity (BMI $\geq 95^{th}$ percentile) for participants 2 through 4 years of age. Between participants who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo, there were no notable differences in demographics.

The median dose interval between Dose 2 and Dose 3 was 13.4 weeks (range 8 to 33 weeks) among participants 6 through 23 months of age and 10 weeks (range 8 to 34

weeks) among participants 2 through 4 years of age who received Pfizer-BioNTech COVID-19 Vaccine. The median length of blinded follow-up for efficacy after Dose 3 was 1.7 months for participants 6 through 23 months of age and 2.1 months for participants 2 through 4 years of age in the Dose 3 Evaluable Efficacy Population who received Pfizer-BioNTech COVID-19 Vaccine or placebo.

The vaccine efficacy results after Dose 3 in participants 6 months through 4 years of age are presented in Table 11.

**Table 11: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 3 – Blinded Follow-Up Period – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 3 – Phase 2/3 – 6 Months to <5 Years of Age – Evaluable Efficacy (3-Dose) Population**

| First COVID-19 occurrence from 7 days after Dose 3 in participants without evidence of prior SARS-CoV-2 infection* | | | |
|---|---|---|---|
| **Subgroup** | **Pfizer-BioNTech COVID-19 Vaccine 3 mcg/Dose N[a]=873 Cases n1[b] Surveillance Time[c] (n2[d])** | **Placebo N[a]=381 Cases n1[b] Surveillance Time[c] (n2[d])** | **Vaccine Efficacy % (95% CI[e])** |
| 6 months through 4 years[e] | 13<br>0.124 (794) | 21<br>0.054 (351) | 73.2<br>(43.8, 87.6) |
| 2 through 4 years | 9<br>0.081 (498) | 13<br>0.033 (204) | 71.8<br>(28.6, 89.4) |
| 6 through 23 months | 4<br>0.042 (296) | 8<br>0.020 (147) | 75.8<br>(9.7, 94.7) |
| **First COVID-19 occurrence from 7 days after Dose 3 in participants with or without evidence of prior SARS-CoV-2 infection** | | | |
| **Subgroup** | **Pfizer-BioNTech COVID-19 Vaccine 3 mcg/Dose N[a]=1294 Cases n1[b] Surveillance Time[c] (n2[d])** | **Placebo N[a]=612 Cases n1[b] Surveillance Time[c] (n2[d])** | **Vaccine Efficacy % (95% CI[e])** |
| 6 months through 4 years[e] | 14<br>0.149 (981) | 23<br>0.067 (459) | 72.5<br>(44.3, 86.9) |
| 2 through 4 years | 10<br>0.100 (639) | 15<br>0.044 (286) | 70.7<br>(30.3, 88.2) |
| 6 through 23 months | 4<br>0.048 (342) | 8<br>0.023 (173) | 76.2<br>(11.1, 94.8) |

Abbreviations: NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein–binding; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting; inability to eat/poor feeding).

* Participants who had no serological or virological evidence (prior to 7 days after receipt of Dose 3) of past SARS-CoV-2 infection (i.e., negative N-binding antibody [serum] result at Dose 1, 1 month post-Dose 2 (if available), Dose 3 (if available) visits, SARS-CoV-2 not detected by NAAT [nasal swab] at Dose 1, Dose 2, and Dose 3 study visits, and a negative NAAT [nasal swab] result at any unscheduled visit prior to 7 days after receipt of Dose 3) and had no medical history of COVID-19 were included in the analysis.

a. N = number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 3 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Two-sided 95% confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Among participants 6 months through 4 years of age, severe COVID-19 case criteria were fulfilled after Dose 3 in 1 placebo recipient in the 6 through 23-month age group. This case occurred 44 days after Dose 3, based on a single criterion (increased heart rate) and did not require hospitalization. There were no cases of multisystem inflammatory syndrome in children reported through the June 17, 2022 data cutoff date.

This EUA Fact Sheet has also been updated to include other minor editorial changes.

By submitting this amendment for review and concurrence by the Food and Drug Administration (FDA), you have complied with the Conditions of Authorization stated in the October 12, 2022 letter authorizing the emergency use of Pfizer-BioNTech COVID-19 Vaccine and the Pfizer-BioNTech COVID-19 Vaccine, Bivalent .

Sincerely,

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David C. Kaslow, M.D.
Director
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research