Our STN: BL 125742/276 **SUPPLEMENT APPROVAL**

BioNTech Manufacturing GmbH
Attention: Leslie Sands
Pfizer, Inc.
66 Hudson Boulevard East
New York, NY 10001

December 6, 2023

Dear Ms. Sands:

Please refer to your supplement to your Biologics License Application (BLA) received February 23, 2023, submitted under section 351(a) of the Public Health Service Act (PHS Act) for COVID-19 Vaccine, mRNA (COMIRNATY).

We also refer to our Supplement Approval letter dated September 11, 2023, which contained the following error:

> The two required deferred pediatric studies were incorrectly described in the following statements:
>
> 1. Deferred pediatric study (C4591048 Substudy A) to evaluate immunogenicity and safety of COMIRNATY in infants and children 6 months through 4 years of age.
>
>   Final Protocol Submission: September 1, 2023 (Submitted)
>   Study Completion: May 31, 2026
>   Final Report Submission: September 30, 2026
>
> 2. Deferred pediatric study (C4591048 Substudy E) to evaluate immunogenicity and safety of a single dose of COMIRNATY in infants and children 2 years to <12 years of age.
>
>   Final Protocol Submission: September 1, 2023 (Submitted)
>   Study Completion: December 31, 2024
>   Final Report Submission: April 30, 2025

This replacement approval letter incorporates the correction of the error. The effective approval date will remain September 11, 2023, the date of the original supplement approval letter.

We have approved your request received February 23, 2023, to supplement your Biologics License Application (BLA) submitted under section 351(a) of the Public Health

Service Act for COVID-19 Vaccine, mRNA (COMIRNATY), manufactured at the Pfizer Manufacturing Belgium NV (Puurs, Belgium) and Pharmacia and Upjohn Company LLC (Kalamazoo, Michigan) facilities, to include: use as a single dose for individuals 12 years of age and older, the 2023-2024 Formula, and all associated labeling revisions.

The review of this supplement was associated with the following National Clinical Trial (NCT) numbers: NCT04368728, NCT04955626, NCT05472038 and NCT05004181.

LABELING

We hereby approve the draft content of labeling: Package Insert submitted to CBER via an email on September 10, 2023, and the draft carton and container labels for the single dose vials and single dose prefilled syringes submitted under amendment 16, dated June 23, 2023.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert submitted to CBER via email on September 10, 2023. Information on submitting SPL files using eLIST may be found in the guidance for industry SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELS

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on June 23, 2023, according to the guidance for industry Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications.

All final labeling should be submitted as Product Correspondence to this BLA STN BL 125742 at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71–G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

Please submit an amendment to all pending supplemental applications for this BLA that include revised labeling incorporating a revised content of labeling that includes these changes.

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for infants less than 6 months of age because there is evidence strongly suggesting that a single dose of COMIRNATY would be ineffective in this pediatric group. Seroprevalence data suggest that a significant proportion of the population younger than 6 months of age are naïve to SARS-CoV-2. Data from clinical studies in individuals 6 months through 4 years of age strongly suggest that a single dose of COMIRNATY would be ineffective in individuals younger than 6 months of age.

We are deferring submission of your pediatric studies for individuals 6 months through 11 years of age for this application because this product is ready for approval for use in individuals 12 years of age and older and the pediatric studies have not been completed.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) are required postmarketing studies. The status of these postmarketing studies must be reported according to 21 CFR 601.28 and section 505B(a)(3)(B) of the FDCA. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

Label your annual report as an **Annual Status Report of Postmarketing Study Requirement/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of the approval of BLA STN BL 125742 until all requirements and commitments subject to the reporting requirements under section 506B of the FDCA are released or fulfilled. These required studies are listed below:

1. Deferred Study C4591048 Substudy A to evaluate the safety and effectiveness of a single dose of COMIRNATY in children 6 months through 4 years of age.

   Final Protocol Submission: September 1, 2023 (Submitted)

   Study Completion: May 31, 2026
   Final Report Submission: September 30, 2026

2. Deferred pediatric Study C4591048 Substudy E to evaluate the safety and effectiveness of a single dose of COMIRNATY in children 2 through 11 years of age.

   Final Protocol Submission: September 1, 2023 (Submitted)

   Study Completion: December 31, 2024

   Final Report Submission: April 30, 2025

Submit the protocols to your IND 19736, with a cross-reference letter to BLA STN BL 125742 explaining that the protocol was submitted to the IND.

Submit final study reports to this BLA STN BL 125742. In order for your PREA PMRs to be considered fulfilled, you must submit and receive approval of either an efficacy or a labeling supplement. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated as:

- **Required Pediatric Assessments**

This product is appropriately labeled for use in ages 12 to 17 years for this indication. Therefore, no additional studies are needed in this pediatric group.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We acknowledge your written commitment, as described in your correspondence of August 23, 2023, to conduct the study as outlined below:

3. Study C4591054, Substudy B, to evaluate immune responses following a single dose of COMIRNATY (2023-2024 Formula) in individuals 12 years and older who are not previously vaccinated with a COVID-19 vaccine.

   Final Protocol Submission: July 21, 2023 (Submitted)

   Study Completion: June 30, 2024

Final Report Submission: December 31, 2024

Please submit the clinical protocol to your IND 19736, and a cross-reference letter to BLA STN BL 125742 explaining that this protocol was submitted to the IND.

If the information in the final study report supports a change in the labeling, the final study report must be submitted as a supplement. Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Correspondence Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment Final Study Report**

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of the approval of BLA STN BL 125742 until all requirements and commitments subject to the reporting requirements of section 506B of the Federal Food, Drug, and Cosmetic Act (FDCA) are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing commitment;
- the original schedule for the commitment;
- the status of the commitment (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

We will include information contained in the above-referenced supplement in your BLA file.

Sincerely,

For David C. Kaslow, M.D.
Acting Deputy Director - Clinical
Division of Vaccines and
Related Products Applications
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research