DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH
OFFICE OF VACCINES RESEARCH AND REVIEW
DIVISION OF VACCINES AND RELATED PRODUCTS APPLICATIONS

DATE: **September 10, 2021** **PAGES: 4**

TO: **BioNTech RNA Pharmaceuticals GmbH/Pfizer. Inc.**
Attention: Amit Patel
235 East 42nd Street
New York, NY 10017
Phone: 214-918-5262
Fax number: 845-474-3500
E-mail: Amitkumar.Patel@pfizer.com

FROM: **Laura Gottschalk, Ph.D.**
Division of Vaccines and Related Products Applications
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Phone number: 301-796-2640
Fax number: 301-595-1244

Laura B. Gottschalk -S
2021.09.10 14:50:55
-04'00'

CBER Reference: STN 125742/5

Product: COVID-19 Vaccine, mRNA (COMIRNATY)

SUBJECT: CBER Responses to Pfizer/BioNTech's Plan for Reporting Adverse Events

Dear Mr. Patel:

Reference is made to the Product Correspondence (dated September 7, 2021) submitted to your BLA STN 125742/5 that contained a request for comments and advice regarding Pfizer/BioNTech's plan for reporting adverse events. We have the following comments on the scenarios you presented in the Request for Comments and Advice document.

Applicant Comment 1:
Cases where the patient age or age group is reported as less than 16 years, Pfizer will report to the EUA, and if the age or age group is equal to or greater than 16 or is unknown/not reported, Pfizer will report these cases to the BLA.

FDA Response to Comment 1:
You must submit all individual case safety reports (i.e., ICSRs) to the Vaccine Adverse Event Reporting System (VAERS), as per the following adverse event (AE) reporting requirements:

- For reports where the patient age or age group is reported as less than 16 years; or where a third dose is administered to immunocompromised patients, or where the date of vaccine administration is known to be prior to the BLA approval date of August 23, 2021, you must submit 15-day reports as per the reporting requirements described under the EUA 27034 letter of authorization, conditions of authorization – condition F.
    - For the above ICSRs, please reference the EUA number (STN 27034) in field G.k.3.3 "Name of Holder/Applicant" in the following format "[name of applicant] EUA NNNNN." Please omit the authorization number field G.k.3.1. Please see the VAERS Technical Specifications document, "Specifications for Preparing and Submitting Postmarket Individual Case Safety Reports (ICSRs) for Vaccines" and associated Business Rules at: https://www.fda.gov/industry/about-esg/cber-vaccine-icsr-implementation for a full explanation of these data fields in ICSR reports to VAERS.

- For all other reports, submit ICSRs to VAERS in accordance with 21 CFR 600.80, i.e., 15-day reports for serious and unexpected AEs and periodic reports for serious and expected AEs and non-serious AEs. Additionally, FDA is requesting that you submit all U.S. ICSRs for the following AEs as 15-day alert reports in accordance with 21 CFR 600.80(c)(2), regardless of seriousness or expectedness: myocarditis; pericarditis; multisystem inflammatory syndrome in children and adults; and cases of COVID-19 that result in hospitalization.
    - For the above ICSRs, please reference the BLA number (125742) in the authorization number field G.k.3.1.
      Please see the VAERS Technical Specifications document, "Specifications for Preparing and Submitting Postmarket Individual Case Safety Reports (ICSRs) for Vaccines" and associated Business Rules at: https://www.fda.gov/industry/about-esg/cber-vaccine-icsr-implementation, for a full explanation of these data fields in ICSR reports to VAERS.

Applicant Comment 2:
Similarly, cases involving an adverse event where a third dose is administered to immunocompromised patients will be reported to the EUA. If the dose number is not reported or unknown, Pfizer will report those adverse events to the BLA.

FDA Response to Comment 2:
Please see response to Comment 1.

Applicant Comment 3:
Per the BLA reporting requirements, cases reported in association with BLA number will be included in PAER.

FDA Response to Comment 3:
FDA is requesting that you submit periodic safety reports to BLA 125742, at monthly intervals, in accordance with 21 CFR 600.80(c)(2), to include your consolidated aggregate analysis for all postmarketing and post-authorization spontaneous AE reports.
Submit the periodic safety reports to your BLA 125742, with a cross-reference letter to the IND 19736, explaining that the periodic safety report for the monthly reporting interval was submitted to the BLA.

Each periodic safety report is required to contain descriptive information which includes:

- A narrative summary and analysis of AEs 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 the package insert, Healthcare Providers Administering Vaccine (Vaccination Providers) Fact Sheet, changes made to studies or studies initiated).

Additionally, we have noted your inclusion of Appendix 2 and its subsections (“Summary Tabulation by Preferred Term and MedDRA System Organ Class”) in your summary monthly safety reports (SMSRs) to the EUA. For future submissions of your periodic safety reports to the BLA, please only include a cumulative summary such as appendix 2.1; and additional subsections (such as 2.2 – 2.6.1) are not needed.

Applicant Comment 4:
In order to simplify reporting and ensure consistency, if and when additional indications/ populations are authorized under the EUA, Pfizer would propose to use the same EUA number.

FDA Response to Comment 4:
Yes, we agree with using the same EUA number as applicable in the future.

Applicant Comment 5:
Existing and future Pfizer Interventional studies will be reported to the IND, as well as to the BLA or EUA, depending on the population under investigation.

FDA Response to Comment 5:
We agree with your proposal.