

Pfizer-BioNTech COVID-19 Vaccine

EUA 27034

**Response to CBER 20 April 2021 Information Request Regarding
Study Data Analysis Programs and Datasets**

April 2021

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1. INTRODUCTION

Reference is made to the EUA 27034 Amendment submitted 09 April 2021 to extend emergency use authorization of the Pfizer-BioNTech COVID-19 vaccine to individuals 12-15 years of age. The purpose of the current document is to respond to CBER's comments communicated from Laura Gottschalk, PhD (CBER), to Neda Aghajani Memar (Pfizer), on 20 April 2021, regarding data analysis programs and datasets.

2. CBER COMMENTS AND PFIZER-BIONTECH'S RESPONSES

2.1. CBER Comment 1

The analysis program for derivation of the ADSL data set entitled "adsl-sas – 12-15 EUA Amendment" is unreadable. Please resubmit this file.

Response

Per Agency request, Pfizer/BioNTech is resubmitting the analysis program for derivation of the ADSL data set entitled: [adsl-sas – 12-15 EUA Amendment](#).

2.2. CBER Comment 2

Please submit the analysis program for Table 19 of the EUA Amendment - 12-15 Years, i.e., vaccine efficacy - First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population.

Response

Per Agency request, Pfizer/BioNTech is submitting the analysis program for Table 19 of the EUA Amendment with file name: [adc19ef-ve-cov-7pd2-peds-eval-sas.txt](#).

2.3. CBER Comment 3

The Analysis Dataset Definition indicates that ADSL.PEDIMMFL is a derived variable. Please clarify the source dataset for deriving this variable.

Response

ADSL.PEDIMMFL variable was derived from an external excel file. Both EXCEL and PDF formats of the source file ([C4591001-subject-list-for-12-25-immuno-analysis-27Jan2021.xlsx](#) and [C4591001-subject-list-for-12-25-immuno-analysis-27Jan2021.pdf](#)) are included in Module 5. There are 660 subjects in total who are based on a random selection of 280 active + 50 placebo from each of the age groups). Below is the SAS code for deriving this variable in ADSL.

```
-----  
*Add PEDIMMFL for pediatric info;  
  
proc import datafile="&expath./C4591001_subject_list_for_12-25_immuno_analysis_27Jan2021.xlsx"  
    out=pop12_25 dbms=xlsx replace;  
    getnames=yes;  
run;  
  
proc sort data=pop12_25;  
    by usubjid;  
run;  
  
data adsl;  
    merge adsl(in=a) pop12_25(in=b);  
    by usubjid subjid;  
    if b then  
        PEDIMMFL='Y';  
    if a;  
    label PEDIMMFL="Pop for Non-inferiority Assessement";  
run;  
-----
```

2.4. CBER Comment 4

We have some questions regarding the derivation of the EV1MD2FL, which determines whether the subjects are included in the immunogenicity non-inferiority (NI) analysis or not, for the following subjects:

a. Subjects 10771292, 11521635, 11521637, 11521655, 11421350, 10571403, and 10441241 were excluded from the NI analysis because EV1MD2FL='N'. However, there do not appear to be any COVID episodes for these subjects; all available PCR tests were negative; and all N-binding assay results were negative. Please clarify why these subjects had 'N' as the value for EV1MD2FL.

b. You included the following subjects in the NI analysis, i.e., EV1MD2FL='Y'. However, we are not able to verify that these subjects do not have evidence of infection prior to 1-month post Dose 2 according to the programming logic:

i. Subject 12041061 had COVID symptoms from 2021-01-03 to 2021-01-12, and the subject had a positive PCR using a local test on 2021-01-04.

ii. Subject 11461316 had COVID symptoms from 2021-01-30 to 2021-01-31, and the subject had no PCR tests available for this COVID episode.

iii. Subjects 10221112 and 10091070 had COVID symptoms from 2021-01-05 to 2021-01-08 and from 2021-01-11 to 2021-01-14, respectively, and their local PCR tests were negative. The local PCR tests were not in the list of NAAT that can be used for case confirmation. Please clarify if all local PCR results, regardless of whether the results can be used for case confirmation, are used to define the NI analysis population.

Responses

a. Subjects need to have a negative N-binding antibody (serum) test at Visit 1, a negative NAAT (nasal swab) at Visits 1 and 2, and a negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 to be considered as “without serological or virological evidence of infection up to 1 month after Dose 2” for the noninferiority analysis. These 7 subjects are missing baseline N-binding antibody test results, baseline NAAT swab results, or NAAT swab results at Dose 2. Subject 10441241 has missing NAAT result at Dose 2 and hence, EV1MPD2FL = N. Subjects 10771292, 11521635, 11521637, 11521655, 11421350, and 10571403 have missing N-binding results at Visit 1, hence EV1MPD2FL = N.

b.i. Subject 12041061 had COVID-19 symptoms from 03 January 2021 to 12 January 2021, and a positive PCR test result from a local test on 04 January 2021. This COVID-19 episode was after the 1-month post Dose 2 visit (26 October 2020), hence, is not being considered in the derivation of EV1MD2FL which captures the infection status up to 1-month post Dose 2.

b.ii. Subject 11461316 had COVID-19 symptoms from 30 January 2021 to 31 January 2021, but there was no PCR test result available for this COVID-19 episode. These symptoms presented after the 1-month post Dose 2 visit date (11 December 2020), and hence, this COVID-19 episode was not considered when deriving this flag (EV1MD2FL).

b.iii Subjects 10221112 and 10091070 had COVID-19 symptoms from 05 January 2021 to 08 January 2021 and from 11 January 2021 to 14 January 2021, respectively, and their local PCR test results were negative. These symptoms presented after the 1-month post Dose 2 visit (22 October 2020 for subject 10221112 and (12 October 2020) for subject 10091070), and hence, these COVID-19 episodes were not considered when deriving this flag (EV1MD2FL). If the symptoms had occurred within the 1-month post Dose 2 visit, the subject would need to have a negative PCR result from a central lab or from one of the acceptable local tests to be considered as “without evidence of infection.” If the test result was missing or was from an unacceptable local test, the subject would not be counted as “without evidence of infection” due to the unconfirmed COVID-19 episode.

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