BNT162b2 (COMIRNATY)

BLA STN 125742/45

Response to CBER Comments Received on 19 January 2022 Regarding Datasets for Adolescents 12 Through 15 Years of Age

02 February 2022

1. INTRODUCTION

On 19 January 2022, Pfizer/BioNTech received the following request from the FDA regarding Study C4591001 submitted to STN125742/45 from Captain Mike Smith, PhD (CBER).

The FDA's request in ***bold italics*** is followed by Pfizer/BioNTech's response below.

2. CBER RESPONSE

The review team has the below information request for STN 125742/45 IR RE the datasets for adolescents 12 through 15 Years of Age

2.1. Item 1

There are 2 subjects (10961068 and 11631062) with AE records that have AEACN = DRUG WITHDRAWN, but they only have COMPLETED records in DS. Please explain.

Sponsor Response

The AEACN = DRUG WITHDRAWN listed for both 10961068 and 11631062 refers to the action taken with the investigational product (IP) following a reported medication error for both subjects. Subject 10961068 received Vax 1 and Vax 2 on 19 August 2020 and 10 September 2020 respectively. They were contacted for revaccination following the initial EUA for administration of BNTb2162b in those aged 16 years and older (12 December 2020) on 21 January 2021 and were confirmed to have received placebo. Therefore, the participant was vaccinated with active BNT162b2 on 26 January 2021 and 26 February 2021, it is on 26 February 2021 that a medication error was reported as the participant was dosed with IP that had a temperature excursion, once identified the IP was permanently discontinued. There were no AEs associated with this medication error and the participant continued the study.

Subject 11631062 received Vax 1 and Vax 2 on 07 August 2020 and 26 August 2020 respectively. A medication error was retrospectively reported as occurring on 13 August 2020 for "unknown study intervention administered (drug therapy)" due to site staff errors in retaining source documentation. The IP prep form for this vaccination was no longer present in source, so the data could not be verified, and this was logged on 25 February 2021. There were no AEs associated with this medication error and the participant continued on the study. They were contacted for revaccination following the initial EUA for administration of BNTb162b2 in those aged 16 years and older (12 December 2020) on 26 February 2021 and were confirmed to have received placebo. Therefore, the participant was vaccinated with active BNT162b2 on 30 March 2021 and 20 April 2021.

The tabulation and analysis package submitted to FDA on 16 December 2021 (Sequence number 0211) included the data to support the review for participants 12-15 years of age. Neither of these subjects (10961068 nor 11631062) are adolescent participants 12 through 15 years of age, therefore, they are appropriately excluded from the dataset.

2.2. Item 2

We have found that subject 11311279 was included in SDTM DM but not ADSL. Please explain

Sponsor Response

Participant 11311279 was 15 years of age at the time of enrollment but turned 16 years of age at the time of vaccination, therefore, this participant was not included in the ASDL. This is also noted in the Analysis Data Reviewer's Guide, (Module 5.3.5.1 Analysis Data Reviewers Guide - 12-15 years 6-Month Follow-Up Sequence number 0211) that was provided to the FDA.

2.3. Items 3a-3e

As previously communicated and discussed under BLA 125742 and other BLAs/INDs reactogenicity events that begin within the prespecified assessment period should have been reported in FACE and summarized with the subject diary data in CE. Since this was not implemented, we request that:

a. reactogenicity events that begin within the prespecified assessment period that are currently reported in the AE dataset be included in FACE, and then be flagged in AE so that we know that it is being included in the FACE dataset.
b. Include all individual supporting assessments (daily e-diary and any unplanned assessments) and the assessor for each finding (identified using FAEVAL=STUDY SUBJECT or INVESTIGATOR) in the FACE domain.
c. Maintain one row per subject/vaccination/symptom in the CE domain, with CE summarizing the duration of the event and maximum severity. Maximum severity (CESEV) should be based on the highest-level severity reported by the subject (via e-diary) or investigator (in the unplanned assessment CRF).
d. Use SUPPCE CESEV1 and CEDIFFRS to show assessment of severity by study subject and reason investigator's assessment of severity differed from study subject as needed for events reported in CE.
e. Update the analysis dataset(s) with records covering the entire event duration (which could go beyond the protocol-defined assessment period) with start/end dates and durations (based on first and last days the symptom was present as recorded in the e-diary and/or Symptom Resolved Dates CRF) derived from both the e-diary and CRF data.

Sponsor Response to Items 3a – 3e:

The tabulation and analysis package submitted to FDA on 06 May 2021 (Sequence number 0001) included the data to support the review for participants 12-15 years of age.

With this response, Pfizer/BioNTech are providing additional documents in Module 5.3.5.1 that address FDA's request 3a to 3e as follows:

- Appendix 1: Roadmap

- Appendix 2: Supplemental Analysis Reviewer Guide
- Appendix 3: Reactogenicity Tables with Tracked Changes
- Appendix 4: Summary of Differences Between CSR and Updated Reactogenicity Data
- Appendix 5: Reactogenicity Supplemental TLFs