



**BNT162b2 (COMIRNATY)**

**BLA STN 125742/0**

**Response to CBER 21 August 2021 Information Request Regarding  
Postmarketing Requirement/Postmarketing Commitment Studies**

**21 August 2021**

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## 1. INTRODUCTION

Reference is made to BLA STN 125742/0 for COVID-19 mRNA Vaccine (COMIRNATY), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals  $\geq 16$  years of age and to CBER's Information Request sent via e-mail at 10:22 AM (original) and then at 10:49 AM (revised) on 21 August 2021.

CBER requests are presented in ***bold italics*** followed by Pfizer-BioNTech response in plain text.

## 2. CBER REQUESTS AND SPONSOR RESPONSES

### 2.1. CBER Request

***There have been numerous information requests and amendments regarding the PMR's and PMC's for this BLA. I have generated the below list of PMR's and PMC's that we have received from you. Please review and submit the list of studies and dates in an amendment to the BLA by COB today containing your commitment to conduct all of these studies in the timeframes noted.***

***Based on our preliminary review, we do not consider the amendment you submitted on August 10, 2021 as adequate for the final protocol for PMC Study C4591007 substudy to evaluate the immunogenicity and safety of lower dose levels of COMIRNATY in individuals 12 through <30 years of age. Therefore, we are using the future date of September 30, 2021 for Final Protocol Submission. In the coming weeks we will provide comments on the amendment submitted on August 10, 2021. Please acknowledge our revision to the Final Protocol Submission date for this PMC (highlighted in yellow below for #11). Please also propose any revisions that you anticipate may be needed for Study Completion Date and Final Report Submission for this PMC.***

### Sponsor Response

Our review of the list of studies and dates is provided below. The [final list of studies and dates](#) is attached. Pfizer/BioNTech acknowledge the revision to the Final Protocol Submission date for PMC Study C4591007 substudy to evaluate the immunogenicity and safety of lower dose levels of COMIRNATY in individuals 12 through <30 years of age. We updated the Study Completion Date and Final Report Submission date for study C4591007 based upon Protocol Amendment 2, however, additional amendments may extend study completion.

### **3. SPONSOR REVIEW OF POSTMARKETING REQUIREMENTS AND POSTMARKETING COMMITMENTS**

#### **3.1. Study C4591001**

*Deferred pediatric Study C4591001 to evaluate the safety and effectiveness of COMIRNATY in children 12 years through 15 years of age.*

*Final Protocol Submission: October 7, 2020*

*Study Completion Date: May 31, 2023*

*Final Report Submission: October 31, 2023*

#### **Sponsor Review**

Pfizer/BioNTech confirm the dates for Study C4591001 are correct.

#### **3.2. Study C4591007**

*Deferred pediatric Study C4591007 to evaluate the safety and effectiveness of COMIRNATY in infants and children 6 months to <12 years of age.*

*Final Protocol Submission: February 8, 2021*

*Study Completion: October 31, 2023*

*Final Report Submission: March 31, 2024*

#### **Sponsor Review**

Pfizer/BioNTech confirm the Final Protocol Submission Date for Study C4591007, 08 February 2021, is correct.

The Study Completion Date and the Final Report Submission Date for Study C4591007 need to be updated. The dates will be revised to 30 November 2023 (Study Completion Date) and 31 May 2024 (Final Report Submission Date) in the next version of the Pharmacovigilance Plan. Submission of the updated Pharmacovigilance Plan is anticipated to be post-approval given our understanding of the imminence of approval of the BLA. The updated dates are based on the Protocol Amendment 2. Additional amendments may extend study completion.

#### **3.3. Study C4591023**

*Deferred pediatric Study C4591023 to evaluate the safety and effectiveness of COMIRNATY in infants <6 months of age.*

*Final Protocol Submission: January 31, 2022*

*Study Completion: July 31, 2024*

***Final Report Submission: October 31, 2024***

**Sponsor Review**

Pfizer/BioNTech confirm the dates for Study C4591023 are correct.

**3.4. Study C4591009**

***Study C4591009, entitled “A Non-Interventional Post-Approval Safety Study of the Pfizer-BioNTech COVID-19 mRNA Vaccine in the United States,” to evaluate the occurrence of myocarditis and pericarditis following administration of COMIRNATY.***

***We acknowledge the timetable you submitted on August 16, 2021, which states that you will conduct this study according to the following schedule:***

***Final Protocol Submission: August 31, 2021***

***Monitoring Report Submission: October 31, 2022***

***Interim Report Submission: October 31, 2023***

***Study Completion Date: June 30, 2025***

***Final Report Submission: October 31, 2025***

**Sponsor Review**

Pfizer/BioNTech confirm the dates for Study C4591009 are correct.

**3.5. Study C4591021**

***Study C4591021, entitled “Post Conditional Approval Active Surveillance Study Among Individuals in Europe Receiving the Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine,” to evaluate the occurrence of myocarditis and pericarditis following administration of COMIRNATY.***

***We acknowledge the timetable you submitted on August 16, and 19, 2021, which states that you will conduct this study according to the following schedule:***

***Final Protocol Submission: August 11, 2021***

***Progress Report Submission: September 30, 2021***

***Interim Report 1 Submission: March 31, 2022***

***Interim Report 2 Submission: September 30, 2022***

***Interim Report 3 Submission: March 31, 2023***

***Interim Report 4 Submission: September 30, 2023***

***Interim Report 5 Submission: March 31, 2024***

***Study Completion Date: March 31, 2024***

***Final Report Submission: September 30, 2024***

**Sponsor Review**

Pfizer/BioNTech confirm the dates for Study C4591021 are correct.

**3.6. Study C4591021 (Substudy of the natural history of myocarditis and pericarditis)**

***Study C4591021 substudy to describe the natural history of myocarditis and pericarditis following administration of COMIRNATY.***

***We acknowledge the timetable you submitted on August 16, and 19, 2021, which states that you will conduct this study according to the following schedule:***

***Final Protocol Submission: January 31, 2022***

***Study Completion Date: March 31, 2024***

***Final Report Submission: September 30, 2024***

**Sponsor Review**

Pfizer/BioNTech confirm the dates for Study C4591021 are correct.

**3.7. Study C4591036**

***Study C4591036, a prospective cohort study with at least 5 years of follow-up for potential long-term sequelae of myocarditis after vaccination (in collaboration with Pediatric Heart Network).***

***We acknowledge the timetable you submitted on August 16, and 19, 2021, which states that you will conduct this study according to the following schedule:***

***Final Protocol Submission: November 30, 2021***

***Study Completion Date: December 31, 2026***

***Final Report Submission: May 31, 2027***

**Sponsor Review**

Pfizer/BioNTech confirm the dates for Study C4591036 are correct.

### **3.8. Study C4591007 (Substudy of subclinical myocarditis)**

*Study C4591007 substudy to prospectively assess the incidence of subclinical myocarditis following administration of the second dose of COMIRNATY in a subset of participants 5 through 15 years of age.*

*We acknowledge the timetable you submitted on August 18, and 19, 2021, which states that you will conduct this assessment according to the following schedule:*

*Final Protocol Submission: September 30, 2021*

*Study Completion Date: November 30, 2023*

*Final Report Submission: May 31, 2024*

#### **Sponsor Review**

Pfizer/BioNTech confirm the dates for Study C4591007 are correct. These dates are based on Protocol Amendment 2, additional amendments may extend study completion

### **3.9. Study C4591031 (Substudy to prospectively assess the incidence of subclinical myocarditis)**

*Study C4591031 substudy to prospectively assess the incidence of subclinical myocarditis following administration of a third dose of COMIRNATY in a subset of participants 16 to 30 years of age.*

*We acknowledge the timetable you submitted on August 16, 2021, which states that you will conduct this study according to the following schedule:*

*Final Protocol Submission: November 30, 2021*

*Study Completion Date: June 30, 2022*

*Final Report Submission: December 31, 2022*

#### **Sponsor Review**

Pfizer/BioNTech confirm the dates for Study C4591031 are correct.

### **3.10. Study C4591022**

*Study C4591022, entitled “Pfizer-BioNTech COVID-19 Vaccine Exposure during Pregnancy: A Non-Interventional Post- Approval Safety Study of Pregnancy and Infant Outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry.”*

*Final Protocol Submission: July 1, 2021*

***Study Completion Date: June 30, 2025***

***Final Report Submission: December 31, 2025***

**Sponsor Review**

Pfizer/BioNTech confirm the dates for Study C4591022 are correct.

**3.11. Study C4591007 (Substudy evaluation of lower doses)**

***Study C4591007 substudy to evaluate the immunogenicity and safety of lower dose levels of COMIRNATY in individuals 12 through <30 years of age in.***

***Final Protocol Submission: September 30, 2021***

***Study Completion Date: November 30, 2023***

***Final Report Submission: May 31, 2024***

**Sponsor Review**

Pfizer/BioNTech acknowledge CBER's comment and will incorporate the Agency's feedback in Protocol Amendment 3 by 30 September 2021.

**3.12. Study C4591012**

***Study C4591012, entitled "Post-emergency Use Authorization Active Safety Surveillance Study Among Individuals in the Veteran's Affairs Health System Receiving Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine."***

***Final Protocol Submission: January 29, 2021***

***Study Completion Date: June 30, 2023***

***Final Report Submission: December 31, 2023***

**Sponsor Review**

Pfizer/BioNTech confirm the dates for Study C4591012 are correct.

**3.13. Study C4591014**

***Study C4591014, entitled "Pfizer-BioNTech COVID-19 BNT162b2 Vaccine Effectiveness Study - Kaiser Permanente Southern California."***

***Final Protocol Submission: March 22, 2021***

***Study Completion Date: December 31, 2022***



***Final Report Submission: June 30, 2023***

**Sponsor Review**

Pfizer/BioNTech confirm the dates for Study C4591014 are correct.

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## Document Approval Record

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