

**EMERGENCY USE AUTHORIZATION (EUA) REQUEST
FOR**

**PFIZER-BIONTECH COVID-19 VACCINE
USE IN INDIVIDUALS 12-15 YEARS OF AGE**

EUA 27034

**SPONSOR: BioNTech Manufacturing GmbH
AUTHORIZED U.S. AGENT: Pfizer Inc.**

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TABLE OF CONTENTS

| | |
|---|----|
| 1. DESCRIPTION AND INTENDED USE | 7 |
| 1.1. Name of Product..... | 7 |
| 1.2. Description of Product | 7 |
| 1.3. Intended Use..... | 7 |
| 2. UNMET NEED ADDRESSED BY THE EUA..... | 7 |
| 3. APPROVAL/CLEARANCE STATUS | 8 |
| 4. MANUFACTURING SITE/CGMP STATUS | 8 |
| 5. ADEQUATE, APPROVED AND ALTERNATIVE PRODUCTS | 8 |
| 6. SAFETY AND EFFICACY INFORMATION | 8 |
| 6.1. Preclinical Studies | 8 |
| 6.2. Clinical Studies | 8 |
| 6.2.1. Study Design and Endpoints..... | 9 |
| 6.2.1.1. Phase 1/2/3 Registration Study C4591001 | 9 |
| 6.2.2. Phase 3 Results | 17 |
| 6.2.2.1. Safety Results | 17 |
| 6.2.2.2. Efficacy Results..... | 75 |
| 6.2.2.3. Immunogenicity Results..... | 80 |
| 7. POTENTIAL RISKS AND BENEFITS | 94 |
| 7.1. Risk-Benefit Assessment..... | 94 |
| 7.1.1. Risks | 94 |
| 7.1.2. Benefits | 95 |
| 7.1.3. Risk-Benefit Assessment | 96 |
| 7.2. Contraindications | 96 |
| 7.3. Special Populations | 96 |
| 8. CHEMISTRY, MANUFACTURING, AND CONTROLS..... | 96 |
| 9. FACT SHEET FOR VACCINATION PROVIDERS | 97 |
| 10. FACT SHEET FOR RECIPIENTS AND CAREGIVERS..... | 97 |
| 11. PROGRAM SCHEMA | 97 |
| 12. INSTRUCTIONS FOR USE | 97 |
| 13. ADVERSE EVENT AND MEDICATION ERROR MONITORING..... | 97 |
| 14. LABELING..... | 97 |
| 15. RECORD KEEPING, REPORTING, AND RECORD ACCESS BY FDA | 97 |

090177e196b7d611\Approved\Approved On: 07-Apr-2021 01:46 (GMT)

16. REFERENCES97

LIST OF TABLES

| | | |
|-----------|--|----|
| Table 1. | Summary of Clinical Studies Contributing Data to this EUA Amendment..... | 9 |
| Table 2. | Safety Population – Subjects 12 Through 15 and 16 Through 25 Years of Age | 19 |
| Table 3. | Follow-up Time After Dose 2 – Subjects 12 Through 15 Years of Age – Safety Population..... | 20 |
| Table 4. | Disposition of All Randomized Subjects Through 1 Month After Dose 2 – Subjects 12 Through 15 and 16 Through 25 Years of Age | 21 |
| Table 5. | Demographic Characteristics – Subjects 12 Through 15 and 16 Through 25 Years of Age – Safety Population..... | 23 |
| Table 6. | Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through 1 Month After Dose 2 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population..... | 29 |
| Table 7. | Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through Cutoff Date (13MAR2021), Subjects 12 Through 15 Years of Age – Safety Population | 31 |
| Table 8. | Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population..... | 33 |
| Table 9. | Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Subjects 12 Through 15 Years of Age – Safety Population..... | 43 |
| Table 10. | Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population | 48 |
| Table 11. | Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 Through Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Subjects 12 Through 15 Years of Age – Safety Population..... | 50 |
| Table 12. | Number (%) of Subjects Withdrawn Because of Adverse Events From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population..... | 52 |

| | | |
|-----------|--|----|
| Table 13. | Follow-up Time After Dose 2 – Phase 2/3 Subjects 16-55 Years of Age – Safety Population..... | 54 |
| Table 14. | Disposition of All Randomized Subjects – Phase 2/3 Subjects 16-55 Years of Age..... | 55 |
| Table 15. | Demographic Characteristics – Phase 2/3 Subjects 16-55 Years of Age – Safety Population..... | 57 |
| Table 16. | Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 16-55 Years of Age – Safety Population..... | 64 |
| Table 17. | Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date – Phase 2/3 Subjects 16-55 Years of Age – Safety Population..... | 65 |
| Table 18. | 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 Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population..... | 76 |
| Table 19. | 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..... | 77 |
| Table 20. | Vaccine Efficacy – First COVID-19 Occurrence After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age – Dose 1 All-Available Efficacy Population..... | 79 |
| Table 21. | Immunogenicity Populations – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) | 81 |
| Table 22. | Demographic Characteristics – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population..... | 82 |
| Table 23. | Summary of Geometric Mean Ratio – NT50 – Comparison of Subjects 12 Through 15 Years of Age to Subjects 16 Through 25 Years of Age (Immunogenicity Subset) – Subjects Without Evidence of Infection up to 1 Month After Dose 2 – Dose 2 Evaluable Immunogenicity Population..... | 85 |
| Table 24. | Number (%) of Subjects Achieving a ≥ 4 -Fold Rise From Before Vaccination to Each Subsequent Time Point 1 Month After Dose 2 – NT50 – Comparison of Subjects 12 Through 15 Years of Age to Subjects 16 Through 25 Years of Age (Immunogenicity Subset) – Subjects Without Evidence of Infection up to 1 Month After Dose 2 – Dose 2 Evaluable Immunogenicity Population | 86 |

| | | |
|-----------|--|----|
| Table 25. | Summary of Geometric Mean Titers, by Baseline SARS-CoV-2 Status – NT50 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population..... | 91 |
| Table 26. | Summary of Geometric Mean Fold Rise From Before Vaccination to Each Subsequent Time Point, by Baseline SARS-CoV-2 Status – NT50 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population..... | 92 |
| Table 27. | Number (%) of Subjects Achieving a ≥ 4 -Fold Rise From Before Vaccination to Each Subsequent Time Point, by Baseline SARS-CoV-2 Status – NT50 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population..... | 93 |

LIST OF FIGURES

| | | |
|-----------|---|----|
| Figure 1. | Participants Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Reactogenicity Subset for Phase 2/3 Analysis – Safety Population by Age Group: 12-15 Years and 16-25 Years..... | 26 |
| Figure 2. | Participants Reporting Systemic Events, by Maximum Severity, Within 7 Days After Each Dose – Reactogenicity Subset for Phase 2/3 Analysis – Safety Population by Age Group: 12-15 Years and 16-25 Years..... | 28 |
| Figure 3. | Participants Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Reactogenicity Subset for Phase 2/3 Subjects ≥ 16 Years of Age – Safety Population by Age Group: 16-55 Years..... | 61 |
| Figure 4. | Participants Reporting Systemic Events, by Maximum Severity, Within 7 Days After Each Dose – Reactogenicity Subset for Phase 2/3 Subjects ≥ 16 Years of Age – Safety Population by Age Group: 16-55 Years..... | 63 |
| Figure 5. | Geometric Mean Titers: SARS-CoV-2 Neutralization Assay – NT50 – Subjects 12-15 and 16-25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population | 89 |
| Figure 6. | Reverse Cumulative Distribution Curves, SARS-CoV-2 Neutralization Assay – NT50 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population..... | 90 |

LIST OF ABBREVIATIONS

| Abbreviation | Definition |
|---------------------|---|
| 12-15 years of age | adolescent age group in Study C4591001 |
| 16-25 years of age | young age group in Study C4591001, for immunogenicity and safety comparative data |
| 16-55 years of age | Adult age group in Study C4591001, for longer-term safety reference data |
| AE | adverse event |
| AESI | adverse event of special interest |
| BLA | Biologics Licensing Application |
| CDC | Centers for Disease Control and Prevention |
| CI | confidence interval |
| COVID-19 | Coronavirus Disease 2019 |
| CSR | clinical study report |
| e-diary | electronic diary |
| EUA | Emergency Use Application |
| FDA | (US) Food and Drug Administration |
| GMFR | geometric mean fold rise |
| GMR | geometric mean ratio |
| GMT | geometric mean titer |
| IgG | immunoglobulin G |
| IM | intramuscular(ly) |
| IND | Investigational New Drug |
| IR | incidence rate |
| IRC | Internal Review Committee |
| LNP | lipid nanoparticle |
| MedDRA | Medical Dictionary for Regulatory Activities |
| modRNA | nucleoside-modified mRNA |
| NAAT | nucleic acid amplification test |
| PT | Preferred Term |
| PY | person-years |
| RBD | receptor binding domain |
| RNA | ribonucleic acid |
| RT-PCR | reverse transcription–polymerase chain reaction |
| SAE | serious adverse event |
| SARS-CoV-2 | severe acute respiratory syndrome coronavirus 2 |
| SOC | System Organ Class |
| SRC | Safety Review Committee |
| TME | targeted medical event |
| US | United States |
| VE | vaccine efficacy |
| VAE(R)D | Vaccine-associated enhanced (respiratory) disease |

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1. DESCRIPTION AND INTENDED USE

1.1. Name of Product

Pfizer-BioNTech COVID-19 Vaccine

1.2. Description of Product

The Pfizer-BioNTech COVID-19 Vaccine is a prophylactic vaccine developed by BioNTech and Pfizer to prevent Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2 infection.

The Pfizer-BioNTech COVID-19 Vaccine is administered intramuscularly (IM) as a series of two doses (0.3 mL each) three weeks apart.

1.3. Intended Use

The intended use of investigational Pfizer-BioNTech COVID-19 Vaccine under this Emergency Use Authorization (EUA) is to vaccinate individuals ≥ 12 years of age against COVID-19.

Pfizer-BioNTech COVID-19 Vaccine is currently authorized under EUA for individuals ≥ 16 years of age against COVID-19. The data presented in this EUA amendment support the use of Pfizer-BioNTech COVID-19 Vaccine in individuals 12-15 years of age in pivotal Study C4591001 based on noninferiority (NI) of the immune response measured by SARS-CoV-2 neutralizing antibody titers in this adolescent group compared to young adults 16-25 years of age, which serves as immunobridging for adolescents; efficacy data in the 12-15 years of age group; and safety data in approximately 2200 adolescents with a median follow-up time of at least 2 months after Dose 2. Additionally, safety data in adolescents will be compared to the larger data safety data set of individuals 16-55 years of age. These data support that the known and potential benefits of the vaccine outweigh the known and potential risks. The design of the pivotal study in individuals 12-15 years of age was agreed to by the United States (US) Food and Drug Administration (FDA) on 30 September 2020 and implemented as C4591001 Amendment 7 (protocol version 06 October 2020).

2. UNMET NEED ADDRESSED BY THE EUA

Vaccination is the most effective medical countermeasure to decrease risk and mitigate spread of the SARS-CoV-2 virus. Immunization with a safe and effective COVID-19 vaccine is a critical component of the nation's strategy to reduce COVID-19-related illnesses, hospitalizations, and deaths and to help restore societal functioning.

Data from pre-clinical and clinical studies on tolerability, safety, immunogenicity, and efficacy of Pfizer-BioNTech COVID-19 Vaccine have shown the known and potential benefits outweigh the known and potential risks for individuals 16 years of age and older, and formed the basis of authorization of Pfizer-BioNTech COVID-19 Vaccine under the current EUA in the US. The vaccine has also been granted emergency/temporary use authorization or conditional marketing authorization in many countries/regions globally for individuals 16 years of age and older.

Authorizing Pfizer-BioNTech COVID-19 Vaccine for use in individuals 12-15 years of age at this time addresses an urgent public health need. These adolescents have experienced unprecedented prolonged disruption to education and social development for over a year during the SARS-CoV-2 pandemic, due to infection risk in congregate settings; this in turn creates

significant challenges for families and communities, in particular where the pandemic has exacerbated pre-existing socio-economic disparities.^{1,2} Education is a key determinant of health and a driver of economic opportunity. Expanding COVID-19 vaccination eligibility to include adolescents, in addition to individuals 16 years of age and older, would further protect communities (eg, support a safe return to in-person learning for schools). Amendment of the current EUA to include use of Pfizer-BioNTech COVID-19 Vaccine in individuals 12-15 years of age, based on demonstrated effectiveness (via immunobridging), efficacy, and safety data from approximately 2200 individuals in this age group in pivotal Study C4591001, would address critical and dual unmet needs for public health and education.

3. APPROVAL/CLEARANCE STATUS

Pfizer-BioNTech COVID-19 Vaccine is in Phase 3 clinical development under US Investigational New Drug (IND) application, BB-IND 19,736. As of March 2021, this vaccine has received temporary authorization for emergency supply in 28 countries and conditional marketing authorization approval in 39 countries globally. The name of the product supplied under emergency/temporary use authorization for all applicable regions is Pfizer-BioNTech COVID-19 Vaccine. The name of the product supplied under conditional marketing authorization for all applicable regions is COMIRNATY [COVID-19 mRNA Vaccine (nucleoside modified)].

Pfizer-BioNTech COVID-19 Vaccine was authorized for emergency use in the US on 11 December 2020 for individuals 16 years of age and older (EUA 27034).

A Biologics Licensing Application (BLA) is planned to be submitted to US FDA in second quarter of 2021.

4. MANUFACTURING SITE/CGMP STATUS

There are no updates to manufacturing sites or CGMP status related to this amendment.

5. ADEQUATE, APPROVED AND ALTERNATIVE PRODUCTS

While care for individuals who have COVID-19 has improved with clinical experience,³ there remains an urgent and unmet public health need for prophylactic vaccines during the ongoing pandemic. Pfizer-BioNTech COVID-19 Vaccine is currently authorized for emergency use for individuals 16 years of age and older, and at present is the only COVID-19 vaccine with authorization or conditional approval in any market for individuals under 18 years of age. There are no vaccines currently authorized for use in individuals 12-15 years of age.

6. SAFETY AND EFFICACY INFORMATION

6.1. Preclinical Studies

There are no updates to preclinical studies related to this amendment.

6.2. Clinical Studies

Pfizer and BioNTech have developed an investigational vaccine that targets SARS-CoV-2, intended to prevent COVID-19, for which BioNTech initiated a first-in-human study in April 2020 in Germany (BNT162-01) and Pfizer initiated a Phase 1/2/3 study (C4591001)

shortly afterwards in the US; the study expanded to include global sites upon initiation of the Phase 2/3 part of the study. Clinical data that were available as of 14 November 2020 from Phase 1 of Study BNT162-01 and Phases 1, 2, and 3 of Study C4591001 were submitted to support the current EUA for individuals 16 years of age and older.

This EUA amendment presents new clinical data from Phase 3 of ongoing Study C4591001 for adolescents 12-15 years of age up to the data cutoff date (13 March 2021). Data are included from young adults 16-25 years of age for comparison. Longer-term reference safety data are also presented from the protocol specified adult 16-55 years of age stratum up to the date of participant unblinding. No data from Study BNT162-01 are relevant to this EUA amendment; therefore, this study is not discussed further. A summary of Study C4591001, which contributes clinical data to this EUA amendment, is provided in Table 1.

Table 1. Summary of Clinical Studies Contributing Data to this EUA Amendment

| Sponsor | Study Number (Status) | Phase/Study Design | Test Product (Dose) | Number of Subjects | Type of Subjects (Age) |
|-------------------|-----------------------|---|--|---|---|
| BioNTech (Pfizer) | C4591001 (ongoing) | Phase 1/2/3 randomized, observer-blind, placebo-control | Phase 1: BNT162b2 (10, 20, 30 µg) Placebo | Phase 1: 90 randomized 4:1 (within each dose/age group) | Phase 1: Adults (18-55 years of age, 65-85 years of age) |
| | | | Phase 2: BNT162b2 (30 µg) Placebo | Phase 2: 360 randomized 1:1 | Phase 2: Adults (18-55 years of age, 56-85 years of age) |
| | | | Phase 3: BNT162b2 (30 µg) Placebo | Phase 3: ~46,000 randomized 1:1 (includes 360 in Phase 2) | Phase 3: Adolescents, Adults (12-15 years of age, 16-55 years of age, >55 years of age) |

Note: study information relevant to the scope of data presented in the current EUA are summarized in the table.

6.2.1. Study Design and Endpoints

6.2.1.1. Phase 1/2/3 Registration Study C4591001

Study C4591001 is the ongoing, randomized, placebo-controlled, Phase 1/2/3 registration study. It was started as a Phase 1/2 study in adults in the US, was then amended to expand the study to a global Phase 2/3 study enrolling up to approximately 46,000 participants to accrue sufficient COVID-19 cases to conduct a timely efficacy assessment; amended to include older adolescents 16-17 years of age, then later amended (Amendment 7) to include younger adolescents 12-15 years of age (which was approved by FDA prior to implementation).

In Phase 1, two adult age groups were studied separately, younger participants (18-55 years of age) and older participants (65-85 years of age). The study population includes male and female participants deemed healthy as determined by medical history, physical examination (if required), and clinical judgment of the investigator to be eligible for inclusion in the study. Exclusions included screened individuals with high risk of exposure to SARS-CoV-2 infection

due to exposure in the workplace and/or medical conditions that represent risk factors, clinically important prior illness or laboratory abnormalities, serological evidence of prior SARS-CoV-2 infection or current SARS-CoV-2 infection as measured by polymerase chain reaction (PCR).

In Phase 2/3, participants were enrolled with stratification of younger adults (18-55 years of age) and older adults (>55 years of age) to achieve approximately 40% enrollment in the older group. Adolescents were added later by a protocol amendment: participants 16-17 years of age are included in the younger adult stratum, and participants 12-15 years of age were added as a separate adolescent age stratum. Eligibility in Phase 2/3 included higher risk for acquiring COVID-19 in the investigator's judgment, due to medical conditions or exposure, such as:

- Chronic condition (eg, hypertension; diabetes; asthma; pulmonary, liver, or kidney disease)
- Autoimmune disease requiring therapeutic intervention (or history of)
- Chronic HIV, HCV, or HBV infection that is stable and controlled
- Vaping or smoking (or history of smoking within the prior year)
- Resident in a long-term facility
- Occupation with high risk of SARS-CoV-2 exposure (eg, healthcare, emergency response)

Phase 1 of Study C4591001 was conducted in the US. For each of the two vaccine candidates evaluated, younger participants received escalating dose levels (N=15 per dose level, 4:1 randomization ratio between vaccine and placebo) with progression to subsequent dose levels and the older age group (N=15 per dose level, 4:1 randomization ratio between vaccine and placebo) based on recommendation from an Internal Review Committee (IRC). The Pfizer/BioNTech study team was not blinded in this part of the study. Participants who enrolled in Phase 1 are followed for cases of COVID-19 but do not contribute to the efficacy assessment. Safety follow-up will continue for at least 2 years and/or end of study. Based upon review of safety and immunogenicity from the Phase 1 part of the study, the final candidate and dose level was selected as BNT162b2 at 30 µg given twice 21 days apart.

Phase 2/3 of Study C4591001 commenced with the selected vaccine candidate and dose level administered to participants who were randomized 1:1 to receive vaccine or placebo.

Phase 2 was conducted in the US. The Phase 2 portion of the study evaluated reactogenicity and immunogenicity for 360 participants enrolled into the study when the Phase 2/3 part commenced, balancing younger and older adult age strata within each group. Phase 2 participants in this blinded part of the study also contributed to the overall efficacy and safety assessments in the Phase 3 portion of the study.

Phase 3 (which is ongoing) included planned interim analyses of the first primary efficacy endpoint, ongoing efficacy and safety evaluations including reactogenicity assessment in a subset of participants, and exploratory vaccine immunogenicity evaluation in a subset of participants. Phase 3 is being conducted at sites in the US, Brazil, Argentina, Turkey, South Africa, and Germany. Participants were stratified by age group. Participants in the 12-15 years of age group were all enrolled at sites in the US.

The protocol specified interim analysis of efficacy was conducted on an accrued 94 COVID-19 cases (data cutoff date: 04 November 2020) and the protocol specified final analysis of efficacy

was conducted on an accrued 170 cases (data cutoff date: 14 November 2020). Results of both analyses demonstrated 95% vaccine efficacy (VE) against COVID-19 and were submitted in support of the current EUA. Safety and long-term persistence of efficacy follow-up will continue for at least 2 years and/or end of study.

Starting 14 December 2020, individuals 16 years of age and older have been progressively unblinded in the study to receive BNT162b2 vaccination when eligible per protocol (including under EUA, as discussed in [Section 6.2.1.1.2](#)). However, adolescents 12-15 years of age remain blinded in this study, as BNT162b2 vaccination eligibility in all markets/regions is currently for 16 years of age and older (note that a few participants in the 12-15 years of age group turned 16 years of age after study enrollment and thus became eligible for unblinding to treatment assignment and vaccination under emergency use or conditional marketing authorization). Sponsor and site personnel responsible for the ongoing conduct of the study remain blinded to individual participants' randomization for any who have not been unblinded. Safety evaluation for such participants by the study team remains blinded until a decision is made to unblind the entire study. A separate (from study conduct) unblinded submissions team is responsible for regulatory submissions including this EUA amendment.

Phase 3 clinical endpoints and analyses (described in [Section 6.2.1.1.1](#)) presented in this EUA amendment are provided for the following participant age groups:

- Adolescents: 12-15 years of age, immunobridging and safety (median ≥ 2 months follow-up)
- Young adults: 16-25 years of age, reference group for 12-15 years of age group immunogenicity and descriptive safety analysis comparisons
- Adults: 16-55 years of age, per protocol specified 'younger adult' age stratum, to provide reference safety data from analyses of participants with longer-term follow-up. Note that these data are for comparative purposes and do not include a full independent safety evaluation.

6.2.1.1.1. Study C4591001 Endpoints and Analysis Methods

6.2.1.1.1.1. Safety

Safety Endpoints

All participants 12-15 years of age and a subset of participants ≥ 16 years of age (young adults 16-25 years of age and adults 16-55 years of age), were asked to record reactogenicity (referred as reactogenicity subset):⁴ local reactions (pain, redness and swelling at the injection site), systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain), and antipyretic/pain medication usage for 7 days, each evening following administration of study intervention using prompts from an electronic diary (e-diary). This allowed recording of these assessments only within a fixed time window and provided an accurate representation of the participant's experience at that time. Participants were asked to assess local reactions and systemic events from Day 1 through Day 7 after each dose.

Adverse events (AEs) were recorded for up to 1 month after Dose 2 and categorized by frequency, maximum severity, seriousness, and relationship to study intervention using SOC and

PT according to MedDRA. Serious AEs (SAEs) will be recorded up to 6 months after Dose 2. Deaths are recorded to the end of study.

AEs of special interest (AESIs) were not prespecified in the protocol; instead, Pfizer utilizes a safety review as part of the signal detection processes that highlights specified targeted medical events (TMEs) of clinical interest. These are a dynamic list of specific AE terms reviewed on an ongoing basis by routine safety data review procedures throughout the clinical study, based on review of known pharmacology, toxicology findings, possible class effects, published literature, and potential signals arising from safety data assessments. For this study, the list of TMEs includes events of interest due to their association with COVID-19 and terms of interest for vaccines in general. If the events of interest were identified in the adolescent (12-15 years of age) group, they were further analyzed and characterized. This review also takes into consideration the CDC list of AESIs for COVID-19 that include events potentially indicative of severe COVID-19 or autoimmune and neuroinflammatory disorders.

Prior SARS-CoV-2 infection was determined by virological testing via nucleic acid amplification test (NAAT) on mid-turbinate swab and serological testing for IgG to the SARS-CoV-2 N-antigen at baseline, and via NAAT at Dose 2. Participants were surveilled for potential COVID-19 illness from Visit 1 onwards.

Pregnancies were reported for participants in any phase of the study.

Narratives for safety events in adolescents (12-15 years of age) are located in Module 5.3.5.1. Narratives for this age group were prepared for participants if they had the following events:

- deaths
- SAEs
- AEs leading to study discontinuation
- AESIs (anaphylaxis, lymphadenopathy, appendicitis, Bell's palsy)
- AEs with numerical imbalance in the vaccine group versus placebo group
- pregnancy exposures
- COVID-19 (participants with a case meeting severe criteria or having >1 episode of COVID-19)

Safety Analysis Methods

Reactogenicity

Descriptive statistics were provided for each reactogenicity endpoint for the reactogenicity subset after each dose for each vaccine group (side-by-side for adolescents 12-15 years of age and young adults 16-25 years of age). Local reactions and systemic events from Day 1 through Day 7 after each vaccination are presented by severity and cumulatively across severity levels. Descriptive summary statistics included counts and percentages of participants with the indicated endpoint and the associated Clopper-Pearson 2-sided 95% confidence intervals (CIs). Missing reactogenicity e-diary data were not imputed.

Adverse Events

AE data were summarized descriptively for the safety population. Descriptive summary statistics including counts, percentages, and associated Clopper-Pearson 2-sided 95% CIs were provided for AEs reported from Dose 1 to 1-month post Dose 2 for each vaccine group (side-by-side for adolescents and young adults). Since all adolescents completed e-diaries for reactogenicity (in addition to AE reporting), the young adult group included in AE summary was comprised of those in the reactogenicity subset. AEs reported from Dose 1 through data cutoff date were summarized by vaccine group for adolescents.

AEs from participants in the protocol specified adult group 16-55 years of age were analyzed through 1 month after Dose 2 and until the date of participant unblinding; the longer-term reference safety data included different individual durations of follow-up time due to unblinding in the study (per protocol) and were summarized as incidence rates (IRs) adjusted with exposure time from each group. IR was calculated as: (number of participants reporting event) / (total exposure time across all participants in the specified group). This accounts for variable exposure since unblinding began for individual participants 16 years of age and older as described in [Section 6.2.1.1.2](#). Two-sided 95% CIs for the IRs were provided based on Poisson distribution.

6.2.1.1.1.2. Efficacy

Study C4591001 is the pivotal efficacy study for BNT162b2. Efficacy was assessed based on confirmed cases of COVID-19 in the efficacy populations. Results from the protocol specified interim analysis conducted on an accrued 94 cases (data cutoff date: 04 November 2020) and the final analysis conducted on an accrued 170 cases (data cutoff date: 14 November 2020) were submitted in support of the current EUA. These analyses included data from all participants in Phase 3 age groups (12-15, 16-55, and >55 years of age) at the time of the analyses. Prespecified primary and secondary efficacy endpoint analyses were completed per protocol as of 14 November 2020. Updated efficacy analyses in this amendment include cases in the 12-15 years of age group accrued in blinded follow-up to a data cutoff date of 13 March 2021.

Efficacy Endpoints

The updated efficacy endpoints analyzed and reported for adolescents 12-15 years of age in this EUA amendment include the following endpoints:

- COVID-19 incidence per 1000 person-years of follow-up in participants either (1) without or (2) with and without serological or virological evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥ 7 days after Dose 2
- Severe COVID-19 incidence per 1000 person-years of follow-up in participants either (1) without or (2) with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥ 7 days after Dose 2.

Efficacy Analysis Methods

Updated efficacy analyses were conducted for efficacy endpoints using statistical methods described in the study statistical analysis plan. The point estimate of VE and associated 2-sided 95% CI derived using the Clopper-Pearson method adjusted for surveillance time were provided as descriptive summary. Updated analyses in the EUA amendment include COVID-19 cases accrued in blinded follow-up in adolescents 12-15 years of age to the data cutoff date (13 March 2021).

COVID-19 Case Definitions

Participants who developed any potential COVID-19 symptoms listed in the protocol were to contact the site immediately and if confirmed to participate in an in-person or telehealth visit as soon as possible (optimally within 3 days of symptom onset, and at the latest 4 days after symptom resolution). At the visit (or prior to the visit, if a participant utilized a self-swab as permitted per protocol), investigators were to collect clinical information and results from local standard-of-care tests sufficient to confirm a COVID-19 diagnosis.

Investigators were to obtain a nasal swab (mid-turbinate) for testing at a central laboratory using a validated reverse transcription–polymerase chain reaction (RT-PCR) test (Cepheid; EUA200047/A001) to detect SARS-CoV-2. If the evaluation was conducted by telehealth, the participant was to self-collect a nasal swab and ship for assessment at the central laboratory. A local NAAT result was only acceptable if it met protocol-specified criteria and if a central laboratory result was not available. Participants with and without evidence of prior infection were determined by virological testing via NAAT on mid-turbinate swab and serological testing for SARS-CoV-2 N-binding antibodies.

COVID-19 cases (defined per FDA guidance)⁵ were based on SARS-CoV-2 positive test result per central laboratory or local testing facility (using an acceptable test per protocol and if no central laboratory result was available) and presence of at least 1 of the following:

- Fever
- New or increased cough
- New or increased shortness of breath
- Chills
- New or increased muscle pain
- New loss of taste or smell
- Sore throat
- Diarrhea
- Vomiting.

Severe COVID-19 cases (defined per FDA guidance)⁵ included presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness:
 - respiratory rate ≥ 30 breaths per minute
 - heart rate ≥ 125 beats per minute
 - $\text{SpO}_2 \leq 93\%$ on room air at sea level or $\text{PaO}_2/\text{FiO}_2 < 300$ mm Hg

- Respiratory failure:
 - needing high-flow oxygen
 - noninvasive ventilation
 - mechanical ventilation
 - ECMO
- Evidence of shock:
 - systolic blood pressure <90 mm Hg
 - diastolic blood pressure <60 mm Hg
 - requiring vasopressors
- Significant acute renal, hepatic, or neurologic dysfunction
- Admission to an intensive care unit
- Death.

In addition to the above specified definition of severe COVID-19, an efficacy analysis for severe COVID-19 cases was conducted using the CDC definition of severe COVID-19 (hospitalization, admission to the ICU, intubation or mechanical ventilation, or death).⁶

6.2.1.1.1.3. Immunogenicity

Immunogenicity Endpoints

In Phase 3, an immunogenicity objective was to demonstrate NI of the immune response to prophylactic BNT162b2 in participants 12-15 years of age compared to participants 16-25 years of age who had no serological or virological evidence of past SARS-CoV-2 infection. This NI analysis of neutralizing titers was performed to provide immunobridging between these younger adolescents and young adults 16-25 years of age. Only a validated SARS-CoV-2 neutralization assay was used.

A random sample of 280 participants who received BNT162b2 and 50 participants who received placebo was selected for each of the two age groups (660 participants total) as an immunogenicity subset for immunogenicity assessment. The placebo participants were selected for serology testing to maintain blinding of the laboratory personnel. This sample size was originally estimated to provide a power of 90.4% to declare NI in the specified analysis.

Due to a testing laboratory supply limitation of the qualified viral lot used during the validation of the assay and clinical testing of samples, immunogenicity analyses were performed on a set of participants who had the required tests completed using the same available viral reagent lot. A blinded review of the samples tested at that time suggested a sufficient sample size properly balanced across age groups to perform the planned NI analysis. It was estimated that if the true geometric mean ratio (GMR) is ≥ 0.88 , there is approximately 90% power to demonstrate NI using the number of samples currently tested, and >99% power if the true GMR is 1. This approached was mutually agreed with the US FDA regarding this analysis approach.

Immunogenicity endpoints were analyzed for SARS-CoV-2 serum neutralizing titers including:

- geometric mean titers (GMT) in each age group and GMR of 12-15 years group to 16-25 years group at 1 month after Dose 2
- geometric mean-fold rise (GMFR) from before vaccination to 1 month after Dose 2 in each age group
- percentage of participants with a ≥ 4 -fold rise in neutralizing titers (seroresponse) from before vaccination to 1 month after Dose 2 in each age group

Immunogenicity Analysis Methods

Immunogenicity analyses of neutralizing titers were conducted with the statistical methods described in the study statistical analysis plan.

NI was assessed based on the GMR of SARS-CoV-2 neutralizing titers at 1 month after Dose 2 using a 1.5-fold margin. The GMR and its 2-sided 95% CI were derived by calculating differences in means and CIs on the natural log scale of titers based on Student's t-distribution, then exponentiating the results. The difference in means on the natural log scale was calculated as: (12-15 years of age) – (16-25 years of age). NI was declared if the lower bound of the 2-sided 95% CI for the GMR was >0.67 .

A supportive analysis was conducted to assess the seroresponse rate, based on the proportions of participants in each age group with a ≥ 4 -fold rise in neutralizing titers from before vaccination to 1 month after Dose 2. The difference in percentages (12-15 years of age – 16-25 years of age) and the associated 2-sided 95% CI calculated using the Miettinen and Nurminen method were provided. GMTs and GMFRs of the neutralizing titers were provided with the associated 2-sided 95% CIs calculated with reference to Student's t-distribution.

The descriptive summary of immunogenicity results was summarized for each age group and by evidence of prior SARS-CoV-2 infection at baseline per NAAT (PCR) or N-binding IgG assay.

The comparative analyses of immunogenicity data between 12-15 years of age and 16-25 years of age were performed for participants without evidence of prior SARS-CoV-2 infection up to 1 month after Dose 2.

6.2.1.1.2. Continuation of Blinded Phase 3 Registration Study Plan if EUA Amendment for Adolescents 12-15 Years of Age is Granted

After discussion with regulatory authorities, C4591001 study participants ≥ 16 years of age have been unblinded according to local eligibility to receive vaccine available under emergency use or conditional marketing authorization in their country/region. Unblinded participants, both those originally randomized to BNT162b2 and those originally randomized to placebo who then received BNT162b2, continue in the study in open-label observational follow-up.

If Pfizer-BioNTech COVID-19 Vaccine becomes available under emergency use or conditional marketing authorization, as applicable per country/region for individuals 12-15 years of age, we plan to proceed in the same manner as for those 16 years of age and older. We intend to collect as much blinded data as possible, while maintaining our ethical obligation to unblind participants to

treatment assignment to be vaccinated if they are eligible. The study team responsible for ongoing study conduct will remain blinded to individual participants' randomization until this time. In all cases, we intend to follow participants in the study up to the original planned 24 months post-vaccination. We anticipate agency collaboration on the statistical considerations and details regarding appropriate protocol language, informed consent, and logistics of this process and on scientifically and statistically sound methods to assess BNT162b2 long-term effectiveness and safety in the pivotal study.

6.2.2. Phase 3 Results

6.2.2.1. Safety Results

6.2.2.1.1. Safety Results – Adolescents 12-15 Years of Age

Safety results are presented for adolescents (12-15 years of age) with accompanying results for young adults (16-25 years of age) who were in the reactogenicity subset, which are the same age groups used for immunobridging analyses ([Section 6.2.2.3](#)).

6.2.2.1.1.1. Study Population Characteristics – Adolescents 12-15 Years of Age

Safety population characteristics for adolescent and young adult groups are summarized below.

Additional study population data including medical history, concomitant vaccines, study vaccine administration, and e-diary transmission are in Module 5.3.5.1.

Additional data are presented in Module 5.3.5.1:

[Medical History – Subjects 12 Through 15 and 16 Through 25 Years of Age \(Reactogenicity Subset\) – Safety Population](#)

[Concomitant Vaccines Received From After Dose 1 Through 1 Month After Dose 2 – Subjects 12 Through 15 and 16 Through 25 Years of Age \(Reactogenicity Subset\) – Safety Population](#)

[Vaccine as Administered, by Vaccine Group – Subjects 12 Through 15 and 16 Through 25 Years of Age \(Reactogenicity Subset\)](#)

[Vaccine Administration Timing – Subjects 12 Through 15 and 16 Through 25 Years of Age \(Reactogenicity Subset\)](#)

[E-Diary Transmission – Subjects 12 Through 15 and 16 Through 25 Years of Age \(Reactogenicity Subset\) – Safety Population](#)

[16.2.2.1 Listing of Important Protocol Deviations – Subjects 12 Through 25 Years of Age](#)

[16.2.3.2.1 Listing of Subjects Excluded From Safety Population – Subjects 12 Through 25 Years of Age](#)

[16.2.5.2.1 Listing of Medication Errors – Subjects 12 Through 25 Years of Age](#)

[16.1.7.1.1 Listing of Randomization Scheme and Actual Vaccine Received – Subjects 12 Through 25 Years of Age](#)

6.2.2.1.1.1. Safety Population – Adolescents 12-15 Years of Age

The safety populations, including subsets and exclusions, for adolescents (12-15 years of age) and young adults (16-25 years of age) were similar in the corresponding BNT162b2 and placebo groups ([Table 2](#)). Safety analysis results hereafter are presented for adolescent and young adult safety population (including the reactogenicity subset) up to 1 month after Dose 2 and for all available data up to the data cutoff date (13 March 2021).

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Table 2. Safety Population – Subjects 12 Through 15 and 16 Through 25 Years of Age

| | Vaccine Group (as Administered) | | | | | |
|---|------------------------------------|---------------------------|-------------------------|------------------------------------|---------------------------|-------------------------|
| | 12-15 Years | | | 16-25 Years | | |
| | BNT162b2 (30 µg) n ^a | Placebo n ^a | Total n ^a | BNT162b2 (30 µg) n ^a | Placebo n ^a | Total n ^a |
| Randomized ^b | | | 2264 | | | 3788 |
| Vaccinated | 1131 | 1129 | 2260 (99.8) | 1869 | 1906 | 3775 (99.7) |
| Safety population | 1131 | 1129 | 2260 (99.8) | 1867 | 1903 | 3770 (99.5) |
| Reactogenicity subset | 1131 | 1129 | 2260 (99.8) | 537 | 561 | 1098 (29.0) |
| HIV-positive | 0 | 0 | 0 | 1 | 0 | 1 (0.0) |
| Excluded from safety population | | | 4 (0.2) | | | 18 (0.5) |
| Reason for exclusion | | | | | | |
| Subject did not receive study vaccine | | | 4 (0.2) | | | 13 (0.3) |
| Unreliable data due to lack of PI oversight | | | 0 | | | 5 (0.1) |

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but not included in the analyses of the overall study objectives.

a. n = Number of subjects with the specified characteristic, or the total sample.

b. This value is the denominator for the percentage calculations.

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6.2.2.1.1.1.2. Duration of Follow-Up – Adolescents 12-15 Years of Age

The median duration of follow-up for adolescents was >2 months after Dose 2. Almost all (98.3%) of adolescent participants had at least 1 month of follow-up after Dose 2, and 1308 out of 2260 enrolled adolescents (57.9%) had at least 2 months of follow-up after Dose 2 (Table 3).

Table 3. Follow-up Time After Dose 2 – Subjects 12 Through 15 Years of Age – Safety Population

| | Vaccine Group (as Administered) | | |
|---|--|---|---|
| | BNT162b2 (30 µg) (N ^a =1131) n ^b (%) | Placebo (N ^a =1129) n ^b (%) | Total (N ^a =2260) n ^b (%) |
| Subjects (%) with length of follow-up of: | | | |
| Total exposure from Dose 2 to cutoff date | | | |
| <1 Month | 13 (1.1) | 25 (2.2) | 38 (1.7) |
| ≥1 Month to <2 months | 458 (40.5) | 456 (40.4) | 914 (40.4) |
| ≥2 Months to <3 months | 612 (54.1) | 599 (53.1) | 1211 (53.6) |
| ≥3 Months | 48 (4.2) | 49 (4.3) | 97 (4.3) |

Note: Follow-up time was calculated to the cutoff date or the date of unblinding, whichever date was earlier.

a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.

b. n = Number of subjects with the specified characteristic.

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6.2.2.1.1.1.3. Disposition – Adolescents 12-15 Years of Age

The disposition of adolescents (12-15 years of age) and young adults (16-25 years of age) was similar in BNT162b2 and placebo groups through 1 month after Dose 2 (Table 4). Most participants randomized in both age groups (≥97.4%) received Dose 1 and Dose 2. Among adolescents, 7 participants (0.6%) in the BNT162b2 group and 17 participants (1.5%) in the placebo group discontinued from the vaccination period and are continuing in the study for safety follow-up. Most participants across age groups completed the visit at 1 month after Dose 2 (≥94.5%).

Among adolescents who discontinued from vaccination period but continued in the study up to the 1 month post Dose 2 visit, 2 participants discontinued due to AEs, both in the BNT162b2 group (pyrexia considered by the investigator as related to study intervention, and unrelated anxiety/depression; refer to Section 6.2.2.1.1.3.5) and none in the placebo group.

No adolescents in the BNT162b2 and 2 participants in the placebo group withdrew from the study before the 1 month post Dose 2 visit.

A total of 49 adolescent participants withdrew from the vaccination period when they turned 16 years of age after entering the study and became eligible to be unblinded to receive BNT162b2 vaccination; of these, 19/49 received Dose 3 and Dose 4 (BNT162b2). Participants originally randomized to placebo who received Dose 3 of BNT162b2 (per protocol; refer to [Section 6.2.1.1](#)) continued in open-label follow-up in the study, but their data were censored at the time of unblinding with regard to analyses in this submission. Information for these participants are provided for SAEs (refer to [Section 6.2.2.1.3.4](#)) or other significant AEs (refer to [Section 6.2.2.1.3](#)).

Additional data are presented in Module 5.3.5.1:

[16.1.7.2.1 Listing of Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Subjects 12 Through 15 Years of Age – Safety Population](#)

| | Vaccine Group (as Randomized) | | | |
|--|---|---|---|---|
| | BNT162b2 (30 µg) | | Placebo | |
| | 12-15 Years (N ^a =1134) n ^b (%) | 16-25 Years (N ^a =1875) n ^b (%) | 12-15 Years (N ^a =1130) n ^b (%) | 16-25 Years (N ^a =1913) n ^b (%) |
| Randomized | 1134 (100.0) | 1875 (100.0) | 1130 (100.0) | 1913 (100.0) |
| Not vaccinated | 3 (0.3) | 6 (0.3) | 1 (0.1) | 7 (0.4) |
| Vaccinated | | | | |
| Dose 1 | 1131 (99.7) | 1869 (99.7) | 1129 (99.9) | 1906 (99.6) |
| Dose 2 | 1124 (99.1) | 1826 (97.4) | 1117 (98.8) | 1836 (96.0) |
| Completed 1-month post–Dose 2 visit (vaccination period) | 1118 (98.6) | 1803 (96.2) | 1102 (97.5) | 1807 (94.5) |
| Discontinued from vaccination period but continue in the study up to 1-month post–Dose 2 visit | 7 (0.6) | 13 (0.7) | 17 (1.5) | 42 (2.2) |
| Discontinued after Dose 1 and before Dose 2 | 7 (0.6) | 12 (0.6) | 10 (0.9) | 36 (1.9) |
| Discontinued after Dose 2 and before 1-month post–Dose 2 visit | 0 | 1 (0.1) | 7 (0.6) | 6 (0.3) |
| Reason for discontinuation from vaccination period | | | | |
| No longer meets eligibility criteria | 3 (0.3) | 4 (0.2) | 10 (0.9) | 26 (1.4) |
| Withdrawal by subject | 0 | 6 (0.3) | 1 (0.1) | 1 (0.1) |
| Pregnancy | 0 | 1 (0.1) | 0 | 3 (0.2) |
| Adverse event | 2 (0.2) | 1 (0.1) | 0 | 0 |
| Physician decision | 1 (0.1) | 0 | 0 | 2 (0.1) |
| Protocol deviation | 0 | 0 | 1 (0.1) | 2 (0.1) |
| Lost to follow-up | 0 | 0 | 0 | 1 (0.1) |
| Other | 1 (0.1) | 1 (0.1) | 5 (0.4) | 7 (0.4) |
| Withdrawn from the study before 1-month post–Dose 2 visit | 0 | 45 (2.4) | 2 (0.2) | 56 (2.9) |
| Withdrawn after Dose 1 and before Dose 2 | 0 | 25 (1.3) | 1 (0.1) | 34 (1.8) |

Table 4. Disposition of All Randomized Subjects Through 1 Month After Dose 2 – Subjects 12 Through 15 and 16 Through 25 Years of Age

| | Vaccine Group (as Randomized) | | | |
|---|---|---|---|---|
| | BNT162b2 (30 µg) | | Placebo | |
| | 12-15 Years (N ^a =1134) n ^b (%) | 16-25 Years (N ^a =1875) n ^b (%) | 12-15 Years (N ^a =1130) n ^b (%) | 16-25 Years (N ^a =1913) n ^b (%) |
| Withdrawn after Dose 2 and before 1-month post-Dose 2 visit | 0 | 20 (1.1) | 1 (0.1) | 22 (1.2) |
| Reason for withdrawal from the study | | | | |
| Lost to follow-up | 0 | 29 (1.5) | 0 | 32 (1.7) |
| Withdrawal by subject | 0 | 14 (0.7) | 0 | 19 (1.0) |
| Protocol deviation | 0 | 0 | 1 (0.1) | 1 (0.1) |
| Withdrawal by parent/guardian | 0 | 1 (0.1) | 1 (0.1) | 0 |
| Adverse event | 0 | 0 | 0 | 1 (0.1) |
| Physician decision | 0 | 0 | 0 | 1 (0.1) |
| Other | 0 | 1 (0.1) | 0 | 2 (0.1) |

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but not included in the analyses of the overall study objectives.

Note: Subjects randomized but did not sign informed consent or had a significant quality event due to lack of PI oversight are not included in any analysis population.

a. N = number of randomized subjects in the specified group. This value is the denominator for the percentage calculations.

b. n = Number of subjects with the specified characteristic.

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6.2.2.1.1.4. Demographics – Adolescents 12-15 Years of Age

Demographic characteristics for adolescents (12-15 years of age) and young adults (16-25 years of age) were similar in the corresponding BNT162b2 and placebo groups in the safety population (Table 5). Overall, most adolescent participants were White (85.9%), with 4.6% Black participants and 6.4% Asian participants, and other racial groups were <3.0%. There were 11.7% Hispanic/Latino participants. The median age was 14.0 years and 50.1% of adolescents were male. Obese adolescents (based on age- and sex-specific body mass index) made up 11.3% (placebo group) to 12.6% (BNT162b2 group) of this age group in the safety population.

Note that for safety endpoint analyses of adolescents that included comparative data from young adults, the young adult group analyzed was the reactogenicity subset (ie, those participants in the young adult group who completed an e-diary for reactogenicity in addition to AE reporting).

Additional data are presented in Module 5.3.5.1:

Demographic Characteristics – Subjects 12 Through 15 and 16 Through 25 Years of Age
(Reactogenicity Subset) – Safety Population

Table 5. Demographic Characteristics – Subjects 12 Through 15 and 16 Through 25 Years of Age – Safety Population

| | Vaccine Group (as Administered) | | | |
|---|---|---|---|---|
| | BNT162b2 (30 µg) | | Placebo | |
| | 12-15 Years (N ^a =1131) n ^b (%) | 16-25 Years (N ^a =1867) n ^b (%) | 12-15 Years (N ^a =1129) n ^b (%) | 16-25 Years (N ^a =1903) n ^b (%) |
| Sex | | | | |
| Male | 567 (50.1) | 921 (49.3) | 585 (51.8) | 882 (46.3) |
| Female | 564 (49.9) | 946 (50.7) | 544 (48.2) | 1021 (53.7) |
| Race | | | | |
| White | 971 (85.9) | 1443 (77.3) | 962 (85.2) | 1510 (79.3) |
| Black or African American | 52 (4.6) | 189 (10.1) | 57 (5.0) | 179 (9.4) |
| American Indian or Alaska Native | 4 (0.4) | 32 (1.7) | 3 (0.3) | 18 (0.9) |
| Asian | 72 (6.4) | 108 (5.8) | 71 (6.3) | 108 (5.7) |
| Native Hawaiian or other Pacific Islander | 3 (0.3) | 10 (0.5) | 0 | 3 (0.2) |
| Multiracial | 23 (2.0) | 76 (4.1) | 29 (2.6) | 74 (3.9) |
| Not reported | 6 (0.5) | 9 (0.5) | 7 (0.6) | 11 (0.6) |
| Racial designation | | | | |
| Japanese | 5 (0.4) | 3 (0.2) | 2 (0.2) | 6 (0.3) |
| Ethnicity | | | | |
| Hispanic/Latino | 132 (11.7) | 604 (32.4) | 130 (11.5) | 575 (30.2) |
| Non-Hispanic/non-Latino | 997 (88.2) | 1259 (67.4) | 996 (88.2) | 1322 (69.5) |
| Not reported | 2 (0.2) | 4 (0.2) | 3 (0.3) | 6 (0.3) |
| Country | | | | |
| Argentina | 0 | 282 (15.1) | 0 | 287 (15.1) |
| Brazil | 0 | 160 (8.6) | 0 | 142 (7.5) |
| Germany | 0 | 11 (0.6) | 0 | 20 (1.1) |
| South Africa | 0 | 69 (3.7) | 0 | 75 (3.9) |
| Turkey | 0 | 12 (0.6) | 0 | 15 (0.8) |
| USA | 1131 (100.0) | 1333 (71.4) | 1129 (100.0) | 1364 (71.7) |
| Age at vaccination (years) | | | | |
| Mean (SD) | 13.6 (1.11) | 21.0 (2.99) | 13.6 (1.11) | 21.0 (2.98) |
| Median | 14.0 | 22.0 | 14.0 | 21.0 |
| Min, max | (12, 15) | (16, 25) | (12, 15) | (16, 25) |
| Baseline SARS-CoV-2 status | | | | |
| Positive ^c | 46 (4.1) | 100 (5.4) | 47 (4.2) | 104 (5.5) |
| Negative ^d | 1028 (90.9) | 1754 (93.9) | 1023 (90.6) | 1789 (94.0) |
| Missing | 57 (5.0) | 13 (0.7) | 59 (5.2) | 10 (0.5) |
| Body mass index (BMI) Obese ^e | | | | |
| Yes | 143 (12.6) | 353 (18.9) | 128 (11.3) | 385 (20.2) |
| No | 988 (87.4) | 1514 (81.1) | 1001 (88.7) | 1518 (79.8) |

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Table 5. Demographic Characteristics – Subjects 12 Through 15 and 16 Through 25 Years of Age – Safety Population

| Vaccine Group (as Administered) | | | |
|---|---|---|---|
| BNT162b2 (30 µg) | | Placebo | |
| 12-15 Years (N ^a =1131) n ^b (%) | 16-25 Years (N ^a =1867) n ^b (%) | 12-15 Years (N ^a =1129) n ^b (%) | 16-25 Years (N ^a =1903) n ^b (%) |

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately.

a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.

b. n = Number of subjects with the specified characteristic.

c. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.

d. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.

e. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm. For 16 through 25 years age group, obesity is defined as BMI ≥ 30.0 kg/m².

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6.2.2.1.1.2. Reactogenicity – Adolescents 12-15 Years of Age

Reactogenicity (local reactions and systemic events) was assessed via e-diary in all adolescents and a subset of young adult participants up to 7 days after each dose.

Adolescent participants (12-15 years of age) with e-diary data included N=1131 in the BNT162b2 group and N=1129 in the placebo group post Dose 1, and N=1124 in the BNT162b2 group and N=1117 in the placebo group post Dose 2.

Young adult participants (16-25 years of age) in the reactogenicity subset with e-diary data included N=539 in the BNT162b2 group and N=564 in the placebo group post Dose 1, and N=526 in the BNT162b2 group and N=537 in the placebo group post Dose 2.

6.2.2.1.1.2.1. Local Reactions – Adolescents 12-15 Years of Age

In the BNT162b2 group, pain at the injection site was most frequently reported in adolescents and young adults, and frequency was similar after Dose 1 and after Dose 2 of BNT162b2 in adolescents (86.2% vs 78.9%) and in young adults (83.4% vs 77.5%), shown in Figure 1. In the placebo group, pain at the injection site after Doses 1 and 2 was similar in adolescents (23.3% and 17.9%, respectively) and young adults (15.9% and 12.1%, respectively).

In the BNT162b2 group, frequencies of redness and swelling were similar between adolescents and young adults after Doses 1 and 2 (Figure 1). Frequencies of redness were generally low and

unchanged from after Dose 1 compared with Dose 2 of BNT162b2 in adolescents (5.8% vs 5.0%) and in young adults (6.4% vs 5.7%). Frequencies of swelling were similarly low and slightly reduced after Dose 1 compared with Dose 2 of BNT162b2 in adolescents (6.9% vs 4.9%) and in young adults (8.3% vs 6.8%). In the placebo group, redness and swelling were infrequent in the adolescent ($\leq 1.1\%$) and young adult ($\leq 1.1\%$) groups after Doses 1 and 2.

After the first and second dose and in both age groups, most local reactions were mild or moderate in severity. Severe local reactions were reported infrequently and at lower incidence in adolescents ($\leq 1.5\%$) compared with young adults ($\leq 3.4\%$) across the BNT162b2 and placebo groups after any dose. No Grade 4 local reactions were reported in either age group.

Across age groups, median onset for all local reactions after either dose of BNT162b2 was Day 1 to Day 3 (Day 1 was the day of vaccination) and resolved with a median duration of 1-3 days.

Additional data are presented in Module 5.3.5.1:

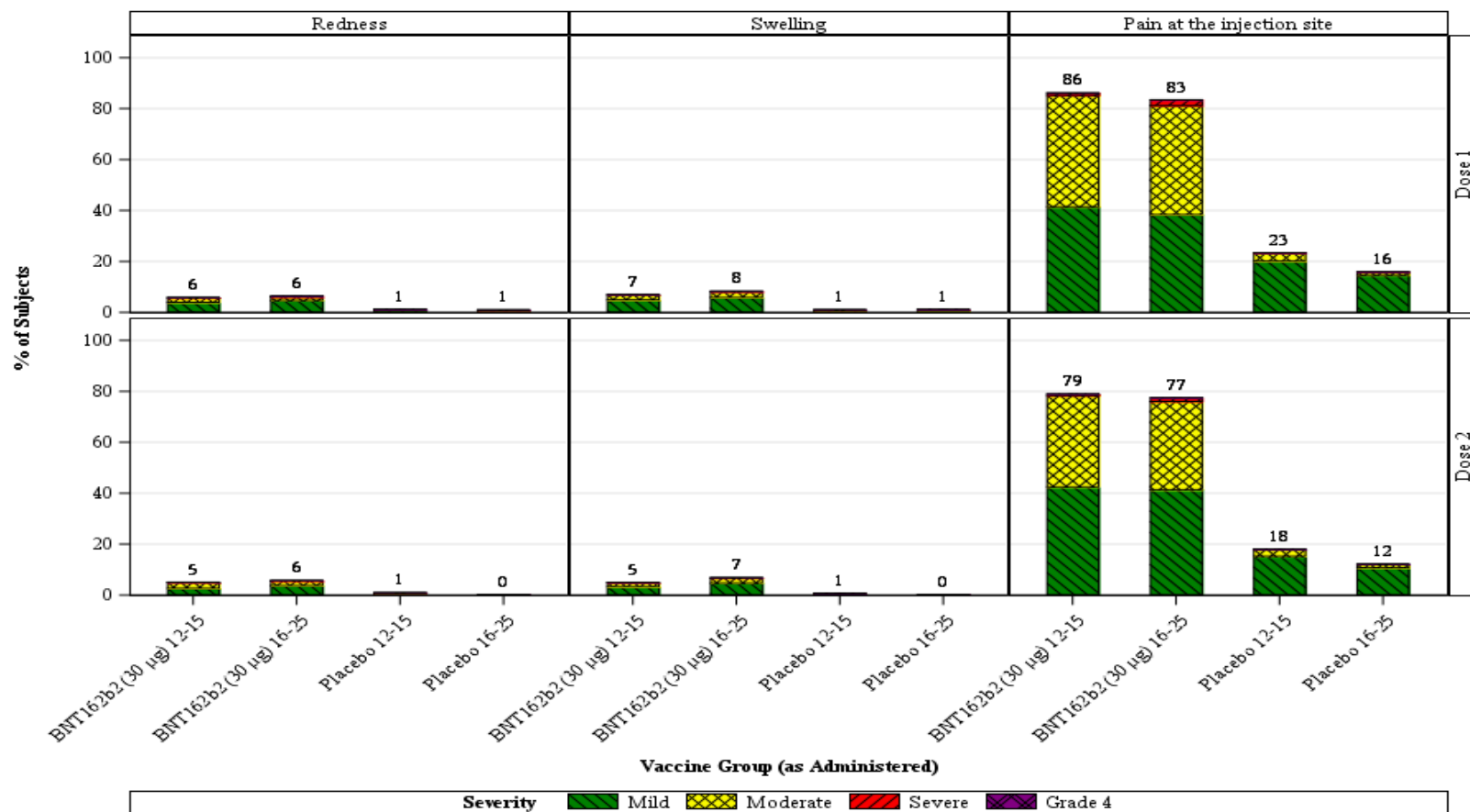
Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

Onset Days for Local Reactions – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

Duration (Days) From First to Last Day of Local Reactions – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

16.2.7.2 Listing of Severe and Grade 4 Local Reactions – Subjects 12 Through 25 Years of Age (Reactogenicity Subset)

Figure 1. Participants Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Reactogenicity Subset for Phase 2/3 Analysis – Safety Population by Age Group: 12-15 Years and 16-25 Years



Note: Number above each bar denotes percentage of subjects reporting the reaction with any severity.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adfacevd Table Generation: 27MAR2021 (01:55)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: /nda2_unblinded/C4591001_BLA/adce_f001_lr_max_ped

6.2.2.1.1.2.2. Systemic Events – Adolescents 12-15 Years of Age

Systemic events were generally similar in frequency and severity in adolescents compared with young adults ([Figure 2](#)), with frequencies and severity increasing with number of doses for most events, with the exceptions of vomiting and diarrhea which were reported infrequently and at similar incidences after each dose, and muscle and joint pain which was reported at higher frequencies in the young adults. Systemic events in the adolescent group compared with the young adult group, in decreasing order of frequency by dose (Dose 1 vs Dose 2), were:

- fatigue: adolescents (60.1% vs 66.2%) compared to young adults (59.9% vs 65.6%)
- headache: adolescents (55.3% vs 64.5%) compared to young adults (53.9% vs 60.9%)
- chills: adolescents (27.6% vs 41.5%) compared to young adults (25.0% vs 40.0%)
- muscle pain: adolescents (24.1% vs 32.4%) compared to young adults (26.9% vs 40.8%)
- joint pain: adolescents (9.7% vs 15.8%) compared to young adults (13.2% vs 21.9%)
- fever: adolescents (10.1% vs 19.6%) compared to young adults (7.3% vs 17.2%)
- vomiting: reported infrequently in both age groups and similar after either dose
- diarrhea: reported infrequently in both age groups and similar after either dose

Systemic events were generally reported less frequently in placebo versus BNT162b2 groups.

Following both Dose 1 and Dose 2, use of antipyretic/pain medication was similar in adolescents (36.6% and 50.8%) and in young adults (31.5% and 45.7%), and medication use increased in both age groups after Dose 2 as compared with after Dose 1. Use of antipyretic/pain medication was less frequent in the placebo group than in the BNT162b2 group and was similar after Dose 1 and Dose 2 in the adolescent and young adult placebo groups (ranging from 9.8% to 11.9%).

After the first and second dose and in both age groups, most systemic events were mild or moderate in severity. Severe systemic events were reported infrequently and at lower incidence in adolescents ($\leq 3.5\%$) compared with young adults ($\leq 6.0\%$) across BNT162b2 and placebo groups after any dose. One adolescent in the BNT162b2 group had Grade 4 pyrexia (40.4 °C) on Day 2 after Dose 1, with temperature returning to normal within 2 days; it was also reported as an AE (refer to analysis in [Section 6.2.2.1.1.3.2.1](#), leading to withdrawal in [Section 6.2.2.1.1.3.5](#)).

Across age groups, median onset for all systemic events after either dose of BNT162b2 was Day 1 to Day 4 (Day 1 was the day of vaccination). Systemic events resolved post each dose with a median duration of 1 day, except fatigue and chills which resolved within a median of 1-2 days.

Additional data are presented in Module 5.3.5.1:

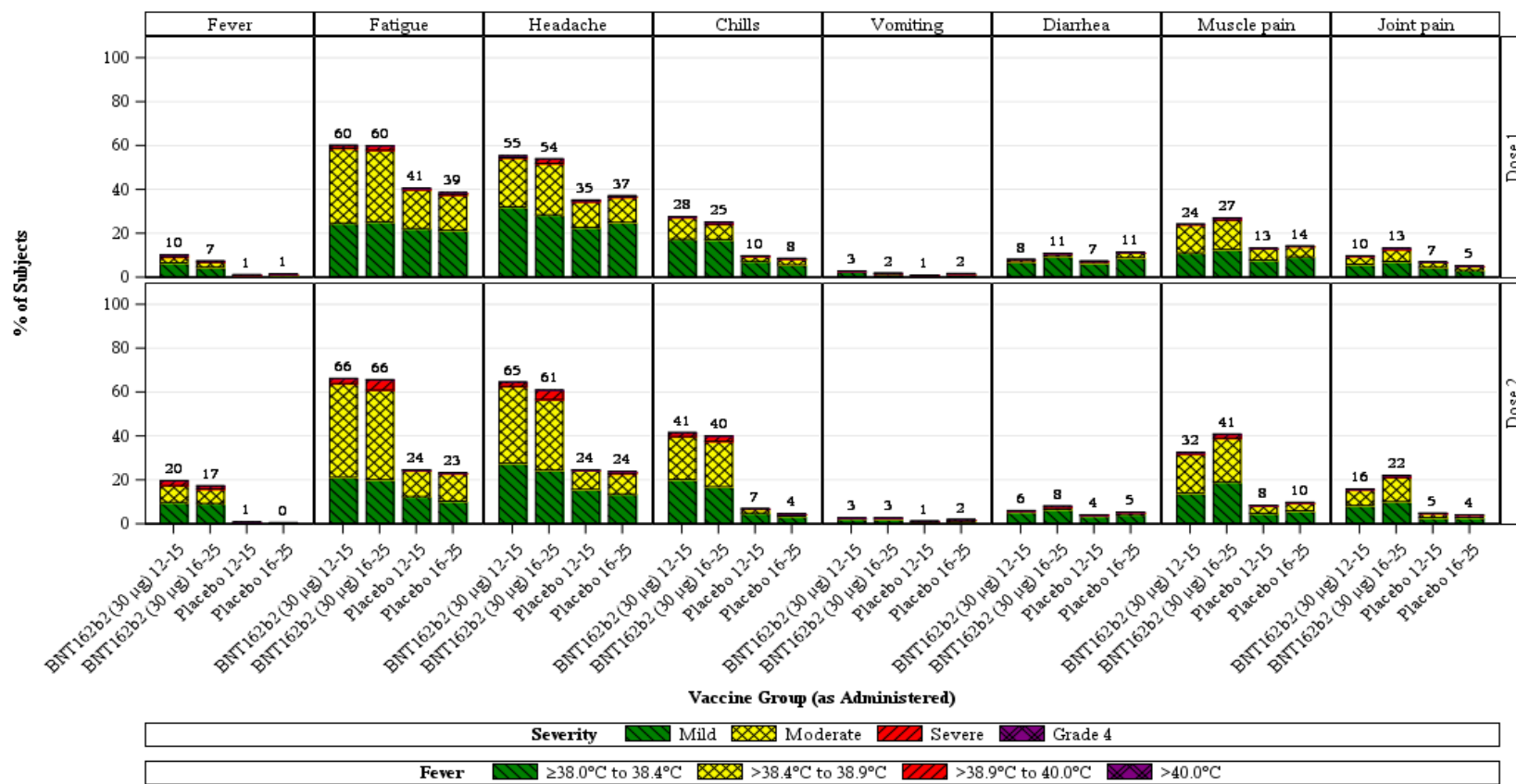
[Systemic Events, by Maximum Severity, Within 7 Days After Each Dose – Subjects 12 Through 15 and 16 Through 25 Years of Age \(Reactogenicity Subset\) – Safety Population](#)

[Onset Days for Systemic Events – Subjects 12 Through 15 and 16 Through 25 Years of Age \(Reactogenicity Subset\) – Safety Population](#)

[Duration \(Days\) From First to Last Day of Systemic Events – Subjects 12 Through 15 and 16 Through 25 Years of Age \(Reactogenicity Subset\) – Safety Population](#)

[16.2.7.3 Listing of Severe and Grade 4 Systemic Events – Subjects 12 Through 25 Years of Age \(Reactogenicity Subset\)](#)

Figure 2. Participants Reporting Systemic Events, by Maximum Severity, Within 7 Days After Each Dose – Reactogenicity Subset for Phase 2/3 Analysis – Safety Population by Age Group: 12-15 Years and 16-25 Years



Note: Number above each bar denotes percentage of subjects reporting the event with any severity.

Note: Subject C4591001 1077 10771278 (13 years of age) experienced systemic events, including a temperature of 40.4°C, on the day of Dose 2. Since these events were recorded as adverse events and not in the electronic diary (e-diary), they do not appear in this output.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adfacevd Table Generation: 27MAR2021 (01:55)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: /nda2_unblinded/C4591001_BLA/adce_f001_se_max_ped

6.2.2.1.1.3. Adverse Events – Adolescents 12-15 Years of Age

6.2.2.1.1.3.1. Overview of Adverse Events – Adolescents 12-15 Years of Age

AE overviews for adolescents and young adults (reactogenicity subset) are reported from Dose 1 to 1 month after Dose 2 (Section 6.2.2.1.1.3.1.1), and from Dose 1 until the data cutoff date (13 March 2021) (Section 6.2.2.1.1.3.1.2).

6.2.2.1.1.3.1.1. Dose 1 to 1 Month After Dose 2 – Adolescents 12-15 Years of Age

An overview of AEs from Dose 1 to 1 month after Dose 2 for adolescents (12-15 years of age) and young adults (16-25 years of age; utilizing the reactogenicity subset) is shown in Table 6. The number of participants with any AE were similar in the BNT162b2 and placebo groups for both age groups. Severe AEs, SAEs, and AEs leading to withdrawal were reported by $\leq 1.7\%$, $\leq 0.4\%$, and $\leq 0.4\%$, respectively, in both groups. No reported SAEs were considered by the investigator as related to study intervention. Withdrawals due to related AEs were reported in 1 adolescent participant in the BNT162b2 group and none in the placebo group; among young adults, withdrawals due to related AEs were reported in 1 participant in the BNT162b2 group and none in the placebo group. Discontinuations due to any AEs were reported in 3 participants in the BNT162b2 group and no participants in the placebo group, across age groups. No study participants 12 through 25 years of age died. Analysis of specific AEs reported from Dose 1 to 1 month after Dose 2 is presented in Section 6.2.2.1.1.3.2.1.

Table 6. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through 1 Month After Dose 2 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

| Adverse Event | Vaccine Group (as Administered) | | | |
|---|---|--|---|--|
| | BNT162b2 (30 µg) | | Placebo | |
| | 12-15 Years (N ^a =1131) n ^b (%) | 16-25 Years (N ^a =536) n ^b (%) | 12-15 Years (N ^a =1129) n ^b (%) | 16-25 Years (N ^a =561) n ^b (%) |
| Any event | 68 (6.0) | 58 (10.8) | 67 (5.9) | 45 (8.0) |
| Related ^c | 33 (2.9) | 33 (6.2) | 21 (1.9) | 12 (2.1) |
| Severe | 7 (0.6) | 9 (1.7) | 2 (0.2) | 3 (0.5) |
| Life-threatening | 1 (0.1) | 0 | 1 (0.1) | 0 |
| Any serious adverse event | 4 (0.4) | 2 (0.4) | 1 (0.1) | 2 (0.4) |
| Related ^c | 0 | 0 | 0 | 0 |
| Severe | 2 (0.2) | 2 (0.4) | 0 | 1 (0.2) |
| Life-threatening | 0 | 0 | 1 (0.1) | 0 |
| Any adverse event leading to withdrawal | 2 (0.2) | 1 (0.2) | 0 | 2 (0.4) |
| Related ^c | 1 (0.1) | 1 (0.2) | 0 | 0 |
| Severe | 1 (0.1) | 1 (0.2) | 0 | 0 |
| Life-threatening | 1 (0.1) | 0 | 0 | 0 |
| Death | 0 | 0 | 0 | 0 |

Table 6. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through 1 Month After Dose 2 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

| Adverse Event | Vaccine Group (as Administered) | | | |
|---------------|---------------------------------------|--------------------------------------|---------------------------------------|--------------------------------------|
| | BNT162b2 (30 µg) | | Placebo | |
| | 12-15 Years (N ^a =1131) | 16-25 Years (N ^a =536) | 12-15 Years (N ^a =1129) | 16-25 Years (N ^a =561) |
| | n ^b (%) | n ^b (%) | n ^b (%) | n ^b (%) |

Note: Adverse events that occurred on the day of or after subjects were unblinded are excluded from this summary.

Note: This table includes all subjects 12 through 15 years of age (all of whom are in the reactogenicity subset) and the subset of subjects 16 through 25 years of age who received an electronic diary (e-diary).

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.

b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.

c. Assessed by the investigator as related to investigational product.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (01:37) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:

./nda2_unblinded/C4591001_BLA/adae_s091_pd2_ped_saf

6.2.2.1.1.3.1.2. Dose 1 to Data Cutoff Date – Adolescents 12-15 Years of Age

An overview of AEs from Dose 1 to the cutoff date for 2260 adolescents (12-15 years of age) during the blinded safety follow-up is presented in [Table 7](#). Data for young adults are not included since they had different follow-up time up to the data cutoff date due to enrollment starting time for the age groups into the study and due to unblinding of individuals ≥ 16 years of age per protocol for vaccination under EUA (unlike the adolescents who remain blinded to treatment assignment; refer to [Section 6.2.1.1](#)).

The number of adolescents with any event was similar in the BNT162b2 and placebo groups. Severe AEs, SAEs, and AEs leading to withdrawal were reported by $\leq 0.8\%$, $\leq 0.4\%$, and $\leq 0.2\%$, respectively, in both groups. No reported SAEs were considered by the investigator as related to study intervention. Discontinuation due to related AEs was reported in 1 participant in the BNT162b2 group and none in the placebo group. As of the data cutoff date, no study participants in the adolescent group died. Analysis of specific AEs reported from Dose 1 to the data cutoff date is presented in [Section 6.2.2.1.1.3.2.2](#).

Table 7. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through Cutoff Date (13MAR2021), Subjects 12 Through 15 Years of Age – Safety Population

| Adverse Event | Vaccine Group (as Administered) | |
|---|--|-----------------------------------|
| | BNT162b2 (30 µg) (N ^a =1131) | Placebo (N ^a =1129) |
| | n ^b (%) | n ^b (%) |
| Any event | 72 (6.4) | 71 (6.3) |
| Related ^c | 33 (2.9) | 21 (1.9) |
| Severe | 9 (0.8) | 3 (0.3) |
| Life-threatening | 1 (0.1) | 1 (0.1) |
| Any serious adverse event | 5 (0.4) | 2 (0.2) |
| Related ^c | 0 | 0 |
| Severe | 4 (0.4) | 1 (0.1) |
| Life-threatening | 0 | 1 (0.1) |
| Any adverse event leading to withdrawal | 2 (0.2) | 0 |
| Related ^c | 1 (0.1) | 0 |
| Severe | 1 (0.1) | 0 |
| Life-threatening | 1 (0.1) | 0 |
| Death | 0 | 0 |

Note: Adverse events that occurred on the day of or after subjects were unblinded are excluded from this summary.

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.

b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.

c. Assessed by the investigator as related to investigational product.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (01:37)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:

./nda2_unblinded/C4591001_BLA/adae_s091_d1_cut_ped_saf

6.2.2.1.1.3.2. Analysis of Adverse Events – Adolescents 12-15 Years of Age

AE analyses for adolescents and young adults (reactogenicity subset) are reported from Dose 1 to 1 month after Dose 2 (Section 6.2.2.1.1.3.2.1), and from Dose 1 until the data cutoff date (13 March 2021) (Section 6.2.2.1.1.3.2.2).

6.2.2.1.1.3.2.1. Dose 1 to 1 Month After Dose 2 – Adolescents 12-15 Years of Age

Adverse Events by System Organ Class and Preferred Term

AEs reported from Dose 1 to 1 month after Dose 2 for all adolescents and for young adults (in the reactogenicity subset) are presented in Table 8. AEs reported in adolescents were generally similar to young adults within the respective BNT162b2 and placebo groups.

Most of the AEs after Dose 1 up to 1 month after Dose 2 were reactogenicity events reported as AEs (ie, headache, nausea, and diarrhea). In adolescents, AE frequencies in these reactogenicity SOC (BNT162b2 vs placebo) were:

- general disorders and administration site conditions (1.4% vs 1.0%)
- musculoskeletal and connective tissue disorders (0.8% vs 0.7%)
- nervous system disorders (1.1% vs 0.6%)
- gastrointestinal disorders (1.2% vs 0.3%)

In young adults, AE frequencies in these reactogenicity SOC (BNT162b2 vs placebo) were:

- general disorders and administration site conditions (3.9% vs 1.8%)
- musculoskeletal and connective tissue disorders (2.2% vs 1.4%)
- nervous system disorders (2.4% vs 1.2%)
- gastrointestinal disorders (0.9% vs 1.1%)

Overall, AEs reported in adolescents and young adults at 1 month after Dose 2 were largely attributable to reactogenicity events. This observation provides a reasonable explanation for the greater rates of AEs observed overall in the BNT162b2 group compared with the placebo group.

Additional data are presented in Module 5.3.5.1:

[16.2.7.4.1.1 Listing of Adverse Events – Subjects 12 Through 25 Years of Age \(Reactogenicity Subset\)](#)

[16.2.7.1 Adverse Events Legend Page](#)

Table 8. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | | | | | | | |
|--------------------------------------|---------------------------------------|------------------------|--------------------------------------|------------------------|---------------------------------------|------------------------|--------------------------------------|------------------------|
| | BNT162b2 (30 µg) | | | | Placebo | | | |
| | 12-15 Years (N ^a =1131) | | 16-25 Years (N ^a =536) | | 12-15 Years (N ^a =1129) | | 16-25 Years (N ^a =561) | |
| | n ^b (%) | (95% CI ^c) | n ^b (%) | (95% CI ^c) | n ^b (%) | (95% CI ^c) | n ^b (%) | (95% CI ^c) |
| Any event | 68 (6.0) | (4.7, 7.6) | 58 (10.8) | (8.3, 13.8) | 67 (5.9) | (4.6, 7.5) | 45 (8.0) | (5.9, 10.6) |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS | 9 (0.8) | (0.4, 1.5) | 1 (0.2) | (0.0, 1.0) | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) |
| Lymphadenopathy | 9 (0.8) | (0.4, 1.5) | 1 (0.2) | (0.0, 1.0) | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) |
| CARDIAC DISORDERS | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Tachycardia | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| EAR AND LABYRINTH DISORDERS | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) |
| Ear pain | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Cerumen impaction | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| EYE DISORDERS | 1 (0.1) | (0.0, 0.5) | 1 (0.2) | (0.0, 1.0) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Eye pain | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Eyelid rash | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Ocular hyperaemia | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Retinal haemorrhage | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| GASTROINTESTINAL DISORDERS | 14 (1.2) | (0.7, 2.1) | 5 (0.9) | (0.3, 2.2) | 3 (0.3) | (0.1, 0.8) | 6 (1.1) | (0.4, 2.3) |
| Nausea | 5 (0.4) | (0.1, 1.0) | 2 (0.4) | (0.0, 1.3) | 1 (0.1) | (0.0, 0.5) | 2 (0.4) | (0.0, 1.3) |
| Diarrhoea | 3 (0.3) | (0.1, 0.8) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 2 (0.4) | (0.0, 1.3) |
| Abdominal pain | 2 (0.2) | (0.0, 0.6) | 2 (0.4) | (0.0, 1.3) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Aphthous ulcer | 1 (0.1) | (0.0, 0.5) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Lip swelling | 1 (0.1) | (0.0, 0.5) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Vomiting | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |

Table 8. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | | | | | | | |
|--|---------------------------------------|-----------------------|--------------------------------------|-----------------------|---------------------------------------|-----------------------|--------------------------------------|-----------------------|
| | BNT162b2 (30 µg) | | | | Placebo | | | |
| | 12-15 Years (N ^a =1131) | | 16-25 Years (N ^a =536) | | 12-15 Years (N ^a =1129) | | 16-25 Years (N ^a =561) | |
| | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c |
| Gastritis | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Inguinal hernia | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Mouth swelling | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Oral mucosal blistering | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Rectal prolapse | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Toothache | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 16 (1.4) | (0.8, 2.3) | 21 (3.9) | (2.4, 5.9) | 11 (1.0) | (0.5, 1.7) | 10 (1.8) | (0.9, 3.3) |
| Injection site pain | 7 (0.6) | (0.2, 1.3) | 10 (1.9) | (0.9, 3.4) | 7 (0.6) | (0.2, 1.3) | 2 (0.4) | (0.0, 1.3) |
| Fatigue | 7 (0.6) | (0.2, 1.3) | 7 (1.3) | (0.5, 2.7) | 4 (0.4) | (0.1, 0.9) | 3 (0.5) | (0.1, 1.6) |
| Pyrexia | 5 (0.4) | (0.1, 1.0) | 7 (1.3) | (0.5, 2.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Chills | 1 (0.1) | (0.0, 0.5) | 2 (0.4) | (0.0, 1.3) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Injection site erythema | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 2 (0.4) | (0.0, 1.3) |
| Injection site swelling | 1 (0.1) | (0.0, 0.5) | 2 (0.4) | (0.0, 1.3) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Oedema peripheral | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 1 (0.2) | (0.0, 1.0) |
| Pain | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Chest pain | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Injection site bruising | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Injection site discomfort | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Injection site hyperaesthesia | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Nodule | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Peripheral swelling | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Vessel puncture site pain | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |

Table 8. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | | | | | | | |
|--------------------------------------|---------------------------------------|-----------------------|--------------------------------------|-----------------------|---------------------------------------|-----------------------|--------------------------------------|-----------------------|
| | BNT162b2 (30 µg) | | | | Placebo | | | |
| | 12-15 Years (N ^a =1131) | | 16-25 Years (N ^a =536) | | 12-15 Years (N ^a =1129) | | 16-25 Years (N ^a =561) | |
| | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c |
| IMMUNE SYSTEM DISORDERS | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Food allergy | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| INFECTIONS AND INFESTATIONS | 7 (0.6) | (0.2, 1.3) | 5 (0.9) | (0.3, 2.2) | 7 (0.6) | (0.2, 1.3) | 12 (2.1) | (1.1, 3.7) |
| Ear infection | 3 (0.3) | (0.1, 0.8) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Appendicitis | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Conjunctivitis | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) |
| Otitis externa | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Otitis media | 1 (0.1) | (0.0, 0.5) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Sinusitis | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 2 (0.4) | (0.0, 1.3) |
| Tonsillitis | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 2 (0.4) | (0.0, 1.3) |
| Vulvovaginal mycotic infection | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Body tinea | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Candida infection | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Cellulitis | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Cystitis | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Focal peritonitis | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Folliculitis | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Genital herpes | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Genital herpes simplex | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Impetigo | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Infectious mononucleosis | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Oral fungal infection | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Pharyngitis streptococcal | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |

Table 8. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | | | | | | | |
|--|---------------------------------------|-----------------------|--------------------------------------|-----------------------|---------------------------------------|-----------------------|--------------------------------------|-----------------------|
| | BNT162b2 (30 µg) | | | | Placebo | | | |
| | 12-15 Years (N ^a =1131) | | 16-25 Years (N ^a =536) | | 12-15 Years (N ^a =1129) | | 16-25 Years (N ^a =561) | |
| | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c |
| Pilonidal cyst | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Subcutaneous abscess | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Tinea capitis | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Tinea infection | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Urinary tract infection | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Vulval abscess | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| INJURY, POISONING AND PROCEDURAL COMPLICATIONS | 8 (0.7) | (0.3, 1.4) | 3 (0.6) | (0.1, 1.6) | 10 (0.9) | (0.4, 1.6) | 6 (1.1) | (0.4, 2.3) |
| Ligament sprain | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 2 (0.2) | (0.0, 0.6) | 2 (0.4) | (0.0, 1.3) |
| Concussion | 3 (0.3) | (0.1, 0.8) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Accident | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Clavicle fracture | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Contusion | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Exposure during pregnancy | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 2 (0.4) | (0.0, 1.3) |
| Fall | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Muscle strain | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Procedural pain | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) |
| Tooth fracture | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) |
| Fibula fracture | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Flail chest | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Foot fracture | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Hand fracture | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Humerus fracture | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Joint dislocation | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |

Table 8. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | | | | | | | |
|---|---------------------------------------|------------------------|--------------------------------------|------------------------|---------------------------------------|------------------------|--------------------------------------|------------------------|
| | BNT162b2 (30 µg) | | | | Placebo | | | |
| | 12-15 Years (N ^a =1131) | | 16-25 Years (N ^a =536) | | 12-15 Years (N ^a =1129) | | 16-25 Years (N ^a =561) | |
| | n ^b (%) | (95% CI ^c) | n ^b (%) | (95% CI ^c) | n ^b (%) | (95% CI ^c) | n ^b (%) | (95% CI ^c) |
| Lip injury | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Meniscus injury | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Patella fracture | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Radius fracture | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Road traffic accident | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| INVESTIGATIONS | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Electrocardiogram QT prolonged | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| METABOLISM AND NUTRITION DISORDERS | 0 | (0.0, 0.3) | 2 (0.4) | (0.0, 1.3) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Decreased appetite | 0 | (0.0, 0.3) | 2 (0.4) | (0.0, 1.3) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS | 9 (0.8) | (0.4, 1.5) | 12 (2.2) | (1.2, 3.9) | 8 (0.7) | (0.3, 1.4) | 8 (1.4) | (0.6, 2.8) |
| Arthralgia | 2 (0.2) | (0.0, 0.6) | 3 (0.6) | (0.1, 1.6) | 3 (0.3) | (0.1, 0.8) | 4 (0.7) | (0.2, 1.8) |
| Myalgia | 3 (0.3) | (0.1, 0.8) | 6 (1.1) | (0.4, 2.4) | 2 (0.2) | (0.0, 0.6) | 1 (0.2) | (0.0, 1.0) |
| Back pain | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Pain in extremity | 1 (0.1) | (0.0, 0.5) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Arthropathy | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Joint swelling | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Limb mass | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Mobility decreased | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Musculoskeletal chest pain | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Musculoskeletal discomfort | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Neck pain | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Osteochondrosis | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |

Table 8. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | | | | | | | |
|--|---------------------------------------|------------------------|--------------------------------------|------------------------|---------------------------------------|------------------------|--------------------------------------|------------------------|
| | BNT162b2 (30 µg) | | | | Placebo | | | |
| | 12-15 Years (N ^a =1131) | | 16-25 Years (N ^a =536) | | 12-15 Years (N ^a =1129) | | 16-25 Years (N ^a =561) | |
| | n ^b (%) | (95% CI ^c) | n ^b (%) | (95% CI ^c) | n ^b (%) | (95% CI ^c) | n ^b (%) | (95% CI ^c) |
| Plantar fasciitis | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Spinal disorder | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Torticollis | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) |
| Fibroadenoma of breast | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Skin papilloma | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| NERVOUS SYSTEM DISORDERS | 12 (1.1) | (0.5, 1.8) | 13 (2.4) | (1.3, 4.1) | 7 (0.6) | (0.2, 1.3) | 7 (1.2) | (0.5, 2.6) |
| Headache | 5 (0.4) | (0.1, 1.0) | 11 (2.1) | (1.0, 3.6) | 4 (0.4) | (0.1, 0.9) | 5 (0.9) | (0.3, 2.1) |
| Dizziness | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 2 (0.4) | (0.0, 1.3) |
| Migraine | 2 (0.2) | (0.0, 0.6) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Presyncope | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) |
| Burning sensation | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Neuralgia | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Paraesthesia | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| PSYCHIATRIC DISORDERS | 7 (0.6) | (0.2, 1.3) | 5 (0.9) | (0.3, 2.2) | 5 (0.4) | (0.1, 1.0) | 1 (0.2) | (0.0, 1.0) |
| Depression | 3 (0.3) | (0.1, 0.8) | 1 (0.2) | (0.0, 1.0) | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) |
| Anxiety | 1 (0.1) | (0.0, 0.5) | 1 (0.2) | (0.0, 1.0) | 2 (0.2) | (0.0, 0.6) | 1 (0.2) | (0.0, 1.0) |
| Attention deficit hyperactivity disorder | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Depressed mood | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Disorientation | 1 (0.1) | (0.0, 0.5) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Generalised anxiety disorder | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Sleep terror | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |

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| System Organ Class Preferred Term | Vaccine Group (as Administered) | | | | | | | |
|---|---------------------------------------|-----------------------|--------------------------------------|-----------------------|---------------------------------------|-----------------------|--------------------------------------|-----------------------|
| | BNT162b2 (30 µg) | | | | Placebo | | | |
| | 12-15 Years (N ^a =1131) | | 16-25 Years (N ^a =536) | | 12-15 Years (N ^a =1129) | | 16-25 Years (N ^a =561) | |
| | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c |
| Tic | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| REPRODUCTIVE SYSTEM AND BREAST DISORDERS | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Cervical dysplasia | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS | 2 (0.2) | (0.0, 0.6) | 1 (0.2) | (0.0, 1.0) | 4 (0.4) | (0.1, 0.9) | 4 (0.7) | (0.2, 1.8) |
| Rhinorrhoea | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 4 (0.4) | (0.1, 0.9) | 0 | (0.0, 0.7) |
| Oropharyngeal pain | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 3 (0.5) | (0.1, 1.6) |
| Asthma | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Nasal congestion | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Reflux laryngitis | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| SKIN AND SUBCUTANEOUS TISSUE DISORDERS | 6 (0.5) | (0.2, 1.2) | 5 (0.9) | (0.3, 2.2) | 13 (1.2) | (0.6, 2.0) | 2 (0.4) | (0.0, 1.3) |
| Rash | 2 (0.2) | (0.0, 0.6) | 3 (0.6) | (0.1, 1.6) | 4 (0.4) | (0.1, 0.9) | 0 | (0.0, 0.7) |
| Urticaria | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) | 4 (0.4) | (0.1, 0.9) | 0 | (0.0, 0.7) |
| Acne | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 2 (0.2) | (0.0, 0.6) | 0 | (0.0, 0.7) |
| Dermatitis contact | 1 (0.1) | (0.0, 0.5) | 1 (0.2) | (0.0, 1.0) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Macule | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Pityriasis rosea | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Rash erythematous | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Rash maculo-papular | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Seborrhoeic dermatitis | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| SURGICAL AND MEDICAL PROCEDURES | 0 | (0.0, 0.3) | 2 (0.4) | (0.0, 1.3) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Sclerotherapy | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Tooth extraction | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |

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| System Organ Class Preferred Term | Vaccine Group (as Administered) | | | | | | | |
|--------------------------------------|---------------------------------------|-----------------------|--------------------------------------|-----------------------|---------------------------------------|-----------------------|--------------------------------------|-----------------------|
| | BNT162b2 (30 µg) | | | | Placebo | | | |
| | 12-15 Years (N ^a =1131) | | 16-25 Years (N ^a =536) | | 12-15 Years (N ^a =1129) | | 16-25 Years (N ^a =561) | |
| | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c |
| Wisdom teeth removal | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |

Note: MedDRA (v23.1) coding dictionary applied.

Note: Adverse events that occurred on the day of or after subjects were unblinded are excluded from this summary.

Note: This table includes all subjects 12 through 15 years of age (all of whom are in the reactogenicity subset) and the subset of subjects 16 through 25 years of age who received an electronic diary (e-diary).

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.

b. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.

c. Exact 2-sided CI based on the Clopper and Pearson method.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (01:37)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s130_1md2_soc_ped_saf

Related Adverse Events – Dose 1 to 1 Month After Dose 2 – Adolescents 12-15 Years of Age

From Dose 1 to 1 month after Dose 2, AEs assessed as related by the investigator in adolescents and young adults were similar in the BNT162b2 group and in the placebo group (Table 6). Most related AEs were reactogenicity events and in the SOC of general disorders and administration site conditions, reported by 15 adolescents (1.3%) and 19 young adults (3.5%) in the BNT162b2 group compared with 9 adolescents (0.8%) and 9 young adults (1.6%) in the placebo group. Related events of lymphadenopathy were reported in the 7 adolescents in the BNT162b2 group and 1 adolescent in the placebo group, compared with 1 young adult in the BNT162b2 group and none in the placebo group (refer to other significant AEs in Section 6.2.2.1.3).

Additional data are presented in Module 5.3.5.1:

Number (%) of Subjects Reporting at Least 1 Related Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

Immediate Adverse Events – Adolescents 12-15 Years of Age

After Dose 1, adolescents and young adults with immediate AEs were low in frequency ($\leq 0.4\%$) and were reported only in the placebo groups. All immediate AEs after Dose 1 were in the SOC of general disorders and administration site conditions (injection site pain, injection site erythema, and vessel puncture site pain) and nervous system disorders (dizziness and headache).

After Dose 2, adolescents and young adults with immediate AEs were low in frequency ($\leq 0.4\%$) in BNT162b2 and placebo groups. Most immediate AEs after Dose 2 were in the SOC of general disorders and administration site conditions (injection site pain, injection site bruising, injection site hyperesthesia, fatigue, chills; 1-2 participants reporting each). Other immediate AEs after Dose 2 were reported in the SOC of nervous system disorders (dizziness; 1 participant in the BNT162b2 adolescent group) or skin and subcutaneous tissue disorders (rash maculo-papular; 1 participant in the placebo adolescent group).

No allergic AEs were reported after either dose of BNT162b2 within 30 minutes after vaccination.

Additional data are presented in Module 5.3.5.1:

Number (%) of Subjects Reporting at Least 1 Immediate Adverse Event After Dose 1, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

Number (%) of Subjects Reporting at Least 1 Immediate Adverse Event After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

Severe or Life-Threatening Adverse Events – Dose 1 to 1 Month After Dose 2 – Adolescents 12-15 Years of Age

From Dose 1 to 1 month after Dose 2, severe AEs reported in adolescents and young adults were overall low in frequency: 0.6% in the BNT162b2 group versus 0.2% in the placebo group among adolescents, and 1.7% in the BNT162b2 group versus 0.5% in the placebo group among young adults ([Table 6](#)).

Among adolescents, 2 participants (1 each in the BNT162b2 and placebo groups) had at least 1 life-threatening (or Grade 4) AE from Dose 1 to 1 month after Dose 2. These included:

- Focal peritonitis and appendicitis reported in 1 adolescent in the placebo group, occurring concurrently 19 days after Dose 2 with a duration of 2 days, and considered by the investigator as not related to study intervention; both events were reported as SAEs (refer to [Section 6.2.2.1.1.3.4.1](#)), resolved, and the participant continued in the study
- Pyrexia (40.4 °C) reported as Grade 4 in 1 adolescent in the BNT162b2 group, occurred 2 days after Dose 1 with a duration of 3 days (ie, temperature returned to normal within 2 days), and was considered by the investigator as related to study intervention; the event was reported by the investigator as non-serious, resolved, and the participant withdrew from the study (also recorded in the e-diary as reactogenicity systemic event in [Section 6.2.2.1.1.2.2](#))

Additionally, 2 participants in the adolescent age group had life-threatening AEs that occurred after they turned 16 years of age during the study and were unblinded to receive BNT162b2 and were therefore not included in analyses of blinded data (per protocol; refer to [Section 6.2.1.1](#)):

- Anaphylactoid reaction reported in 1 participant originally randomized to the placebo group, 3 days after receiving the first dose of BNT162b2 (Dose 3) with a duration of 1 day, considered by the investigator as related to study intervention; the event was reported as an SAE (refer to [Section 6.2.2.1.1.3.4.2](#), resolved, and the participant withdrew from the study
- Depression reported in 1 participant originally randomized to the placebo group, 7 days after receiving the first dose of BNT162b2 (Dose 3) reported as ongoing at the time of the data cutoff date, considered by the investigator as not related to study intervention; the event was reported as an SAE due to hospitalization (refer to [Section 6.2.2.1.1.3.4.1](#)) and reported as resolving, and the participant continued in the study

Among young adults, there were no life-threatening AEs reported from Dose 1 to 1 month after Dose 2.

Additional data are presented in Module 5.3.5.1:

Number (%) of Subjects Reporting at Least 1 Severe Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

Number (%) of Subjects Reporting at Least 1 Life-Threatening Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

6.2.2.1.1.3.2.2. Dose 1 to Data Cutoff Date – Adolescents 12-15 Years of Age

Adverse Events by System Organ Class and Preferred Term

AEs reported from Dose 1 to the data cutoff date for adolescents (13 March 2021) are presented in Table 9. Data for young adults are not included since they had different follow-up time up to the data cutoff date (due to enrollment starting time into the study and due to unblinding of individuals ≥ 16 years of age per protocol, for vaccination under EUA; refer to [Section 6.2.1.1](#)).

AEs reported in adolescents through the data cutoff date were similar in the BNT162b2 and placebo groups. The most frequently reported AEs in adolescents through the data cutoff date included lymphadenopathy (0.8%), injection site pain (0.6%), fatigue (0.6%), pyrexia (0.4%), nausea (0.4%), and headache (0.4%).

Table 9. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Subjects 12 Through 15 Years of Age – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | |
|--------------------------------------|--|---|
| | BNT162b2 (30 µg) (N ^a =1131) n ^b (%) | Placebo (N ^a =1129) n ^b (%) |
| Any event | 72 (6.4) | 71 (6.3) |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS | 9 (0.8) | 2 (0.2) |
| Lymphadenopathy | 9 (0.8) | 2 (0.2) |
| EAR AND LABYRINTH DISORDERS | 1 (0.1) | 2 (0.2) |
| Ear pain | 1 (0.1) | 1 (0.1) |
| Cerumen impaction | 0 | 1 (0.1) |
| EYE DISORDERS | 1 (0.1) | 1 (0.1) |
| Eyelid rash | 1 (0.1) | 0 |
| Retinal haemorrhage | 0 | 1 (0.1) |
| GASTROINTESTINAL DISORDERS | 14 (1.2) | 3 (0.3) |
| Nausea | 5 (0.4) | 1 (0.1) |
| Diarrhoea | 3 (0.3) | 1 (0.1) |
| Abdominal pain | 2 (0.2) | 0 |
| Aphthous ulcer | 1 (0.1) | 0 |
| Constipation | 1 (0.1) | 0 |
| Gastritis | 1 (0.1) | 0 |
| Lip swelling | 1 (0.1) | 0 |
| Mouth swelling | 1 (0.1) | 0 |
| Oral mucosal blistering | 1 (0.1) | 0 |
| Rectal prolapse | 1 (0.1) | 0 |

Table 9. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Subjects 12 Through 15 Years of Age – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | |
|--|--|-----------------------------------|
| | BNT162b2 (30 µg) (N ^a =1131) | Placebo (N ^a =1129) |
| | n ^b (%) | n ^b (%) |
| Toothache | 0 | 1 (0.1) |
| Vomiting | 1 (0.1) | 0 |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 16 (1.4) | 11 (1.0) |
| Injection site pain | 7 (0.6) | 7 (0.6) |
| Fatigue | 7 (0.6) | 4 (0.4) |
| Pyrexia | 5 (0.4) | 0 |
| Chills | 1 (0.1) | 1 (0.1) |
| Injection site swelling | 1 (0.1) | 0 |
| Nodule | 1 (0.1) | 0 |
| Oedema peripheral | 0 | 1 (0.1) |
| Peripheral swelling | 1 (0.1) | 0 |
| Vessel puncture site pain | 0 | 1 (0.1) |
| IMMUNE SYSTEM DISORDERS | 0 | 1 (0.1) |
| Food allergy | 0 | 1 (0.1) |
| INFECTIONS AND INFESTATIONS | 7 (0.6) | 8 (0.7) |
| Ear infection | 3 (0.3) | 0 |
| Appendicitis | 0 | 2 (0.2) |
| Conjunctivitis | 0 | 2 (0.2) |
| Body tinea | 1 (0.1) | 0 |
| Candida infection | 0 | 1 (0.1) |
| Focal peritonitis | 0 | 1 (0.1) |
| Infectious mononucleosis | 0 | 1 (0.1) |
| Otitis externa | 1 (0.1) | 0 |
| Otitis media | 1 (0.1) | 0 |
| Pilonidal cyst | 0 | 1 (0.1) |
| Subcutaneous abscess | 0 | 1 (0.1) |
| Tinea capitis | 1 (0.1) | 0 |
| Vulval abscess | 1 (0.1) | 0 |
| Vulvovaginal mycotic infection | 1 (0.1) | 0 |
| INJURY, POISONING AND PROCEDURAL COMPLICATIONS | 9 (0.8) | 13 (1.2) |
| Concussion | 3 (0.3) | 2 (0.2) |
| Ligament sprain | 1 (0.1) | 2 (0.2) |
| Accident | 1 (0.1) | 1 (0.1) |
| Clavicle fracture | 1 (0.1) | 1 (0.1) |
| Contusion | 1 (0.1) | 1 (0.1) |
| Fall | 1 (0.1) | 1 (0.1) |
| Muscle strain | 1 (0.1) | 1 (0.1) |
| Procedural pain | 0 | 2 (0.2) |

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Table 9. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Subjects 12 Through 15 Years of Age – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | |
|---|--|-----------------------------------|
| | BNT162b2 (30 µg) (N ^a =1131) | Placebo (N ^a =1129) |
| | n ^b (%) | n ^b (%) |
| Tooth fracture | 0 | 2 (0.2) |
| Foot fracture | 0 | 1 (0.1) |
| Hand fracture | 1 (0.1) | 0 |
| Humerus fracture | 0 | 1 (0.1) |
| Lip injury | 0 | 1 (0.1) |
| Patella fracture | 0 | 1 (0.1) |
| Radius fracture | 1 (0.1) | 0 |
| MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS | 9 (0.8) | 8 (0.7) |
| Arthralgia | 2 (0.2) | 3 (0.3) |
| Myalgia | 3 (0.3) | 2 (0.2) |
| Joint swelling | 0 | 1 (0.1) |
| Limb mass | 1 (0.1) | 0 |
| Mobility decreased | 1 (0.1) | 0 |
| Musculoskeletal chest pain | 0 | 1 (0.1) |
| Neck pain | 0 | 1 (0.1) |
| Osteochondrosis | 1 (0.1) | 0 |
| Pain in extremity | 1 (0.1) | 0 |
| NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS) | 0 | 2 (0.2) |
| Fibroadenoma of breast | 0 | 1 (0.1) |
| Skin papilloma | 0 | 1 (0.1) |
| NERVOUS SYSTEM DISORDERS | 13 (1.1) | 7 (0.6) |
| Headache | 5 (0.4) | 4 (0.4) |
| Dizziness | 2 (0.2) | 1 (0.1) |
| Presyncope | 1 (0.1) | 2 (0.2) |
| Migraine | 2 (0.2) | 0 |
| Neuralgia | 1 (0.1) | 0 |
| Paraesthesia | 1 (0.1) | 0 |
| Syncope | 1 (0.1) | 0 |
| PSYCHIATRIC DISORDERS | 8 (0.7) | 5 (0.4) |
| Depression | 3 (0.3) | 2 (0.2) |
| Anxiety | 1 (0.1) | 2 (0.2) |
| Attention deficit hyperactivity disorder | 0 | 1 (0.1) |
| Disorientation | 1 (0.1) | 0 |
| Generalised anxiety disorder | 1 (0.1) | 0 |
| Sleep terror | 1 (0.1) | 0 |
| Suicidal ideation | 1 (0.1) | 0 |
| Tic | 1 (0.1) | 0 |

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Table 9. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 Through Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Subjects 12 Through 15 Years of Age – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | |
|---|--|-----------------------------------|
| | BNT162b2 (30 µg) (N ^a =1131) | Placebo (N ^a =1129) |
| | n ^b (%) | n ^b (%) |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS | 2 (0.2) | 4 (0.4) |
| Rhinorrhoea | 1 (0.1) | 4 (0.4) |
| Nasal congestion | 1 (0.1) | 0 |
| SKIN AND SUBCUTANEOUS TISSUE DISORDERS | 7 (0.6) | 13 (1.2) |
| Rash | 3 (0.3) | 4 (0.4) |
| Urticaria | 2 (0.2) | 4 (0.4) |
| Acne | 1 (0.1) | 2 (0.2) |
| Dermatitis contact | 1 (0.1) | 1 (0.1) |
| Pityriasis rosea | 0 | 1 (0.1) |
| Rash maculo-papular | 0 | 1 (0.1) |

Note: MedDRA (v23.1) coding dictionary applied.

Note: Adverse events that occurred on the day of or after subjects were unblinded are excluded from this summary.

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.

b. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (04:09)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:

./nda2 unblinded/C4591001 BLA/adae s130 d1 cut soc ped saf

6.2.2.1.1.3.3. Deaths – Adolescents 12-15 Years of Age

No deaths were reported in adolescent (12-15 years of age) or young adult (16-25 years of age) groups evaluated in safety analyses up to the data cutoff date (13 March 2021).

Additional data are presented in Module 5.3.5.1:

16.2.7.7 Listing of Deaths – Subjects 12 Through 25 Years of Age

6.2.2.1.1.3.4. Serious Adverse Events – Adolescents 12-15 Years of Age

SAE analyses for adolescents and young adults are reported from Dose 1 to 1 month after Dose 2 (Section 6.2.2.1.1.3.4.1), and from Dose 1 until the data cutoff date (13 March 2021) (Section 6.2.2.1.1.3.4.2).

6.2.2.1.1.3.4.1. Dose 1 up to 1 Month After Dose 2 – Adolescents 12-15 Years of Age

From Dose 1 to 1 month after Dose 2, the proportions of adolescents and young adults (in the reactogenicity subset) who reported at least 1 SAE were similar (Table 10). Overall, ≤0.4% of participants in both age groups reported any SAE after receiving BNT162b2 or placebo.

No participants in either age group had SAEs assessed by the investigator as related to study intervention.

In the adolescent group, SAEs up to 1 month after Dose 2 were reported in the BNT162b2 group in 2 participants with depression, 1 participant with concurrent events of anxiety and depression, and 1 participant with neuralgia and 1 participant in the placebo group with concurrent events of appendicitis and focal peritonitis that were both Grade 4 (refer to Section 6.2.2.1.1.3.2.1). All SAEs in the adolescent group were reported as resolved.

The SAE of neuralgia was reported in 1 female participant 12 years of age who had 3 emergency room visits beginning 1 day after the second dose. She reported concurrent non-serious AEs of vulvar abscess, gastritis, and contact dermatitis. She subsequently had SAEs of abdominal pain and constipation. She had an extensive work-up including serial physical and laboratory examinations and was diagnosed with functional abdominal pain; she was referred to psychology and physical therapy, after which symptoms were reported as gradually improving.

In the young adult age group, SAEs up to 1 month after Dose 2 were reported by 2 participants in the BNT162b2 group (1 participant with abdominal pain and 1 participant with appendicitis) and 2 participants in the placebo group (1 participant had inguinal hernia, and 1 participant had flail chest associated with a motor vehicle accident). All SAEs in the young adult group were reported as resolved.

Additional data are presented in Module 5.3.5.1:

16.2.7.5 Listing of Serious Adverse Events – Subjects 12 Through 25 Years of Age (Reactogenicity Subset)

Table 10. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | | | | | | | |
|---|---------------------------------------|-----------------------|--------------------------------------|-----------------------|---------------------------------------|-----------------------|--------------------------------------|-----------------------|
| | BNT162b2 (30 µg) | | | | Placebo | | | |
| | 12-15 Years (N ^a =1131) | | 16-25 Years (N ^a =536) | | 12-15 Years (N ^a =1129) | | 16-25 Years (N ^a =561) | |
| | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c |
| Any event | 4 (0.4) | (0.1, 0.9) | 2 (0.4) | (0.0, 1.3) | 1 (0.1) | (0.0, 0.5) | 2 (0.4) | (0.0, 1.3) |
| GASTROINTESTINAL DISORDERS | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Abdominal pain | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Inguinal hernia | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| INFECTIONS AND INFESTATIONS | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Appendicitis | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| Focal peritonitis | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) |
| INJURY, POISONING AND PROCEDURAL COMPLICATIONS | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| Flail chest | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) |
| NERVOUS SYSTEM DISORDERS | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Neuralgia | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| PSYCHIATRIC DISORDERS | 3 (0.3) | (0.1, 0.8) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Depression | 3 (0.3) | (0.1, 0.8) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Anxiety | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |

Table 10. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | | | | | | | |
|--------------------------------------|---------------------------------------|-----------------------|--------------------------------------|-----------------------|---------------------------------------|-----------------------|--------------------------------------|-----------------------|
| | BNT162b2 (30 µg) | | | | Placebo | | | |
| | 12-15 Years (N ^a =1131) | | 16-25 Years (N ^a =536) | | 12-15 Years (N ^a =1129) | | 16-25 Years (N ^a =561) | |
| | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c |

Note: MedDRA (v23.1) coding dictionary applied.

Note: Adverse events that occurred on the day of or after subjects were unblinded are excluded from this summary.

Note: This table includes all subjects 12 through 15 years of age (all of whom are in the reactogenicity subset) and the subset of subjects 16 through 25 years of age who received an electronic diary (e-diary).

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.

b. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.

c. Exact 2-sided CI based on the Clopper and Pearson method.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (01:37)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s130_1md2_ser_ped_saf

6.2.2.1.1.3.4.2. Dose 1 to Data Cutoff Date – Adolescents 12-15 Years of Age

From Dose 1 to the data cutoff date (13 March 2021), the proportions of adolescents who reported at least 1 SAE were similar in the BNT162b2 and placebo groups (Table 11). Data for young adults are not included since they had different follow-up time up to the data cutoff date (due to enrollment starting time into the study and due to unblinding of individuals ≥ 16 years of age per protocol, for vaccination under EUA; refer to [Section 6.2.1.1](#)).

Up to the data cutoff date, 5 adolescents (0.4%) in the BNT162b2 group and 2 adolescents (0.02%) in the placebo group reported any SAE. None of the SAEs were assessed by the investigator as related to study intervention. In addition to the SAEs that were previously reported up to 1 month after Dose 2 (refer to [Section 6.2.2.1.1.3.4.1](#)), SAEs reported from after 1 month post Dose 2 up to the data cutoff date included abdominal pain and constipation reported concurrently in 1 participant (who also previously reported an SAE of neuralgia) in the BNT162b2 group. This participant was ultimately diagnosed with functional abdominal pain after an extensive work-up. An SAE of suicidal ideation was reported in 1 participant in the BNT162b2 group and an SAE of appendicitis was reported in 1 participant in the placebo group. All SAEs were reported as resolved/resolving except for the events of abdominal pain and constipation which remained unresolved as of the data cutoff date.

Additionally, 2 adolescents originally randomized to the placebo group had SAEs that occurred after they turned 16 years of age during the study and were unblinded to receive BNT162b2 (per protocol; refer to [Section 6.2.1.1](#)), therefore the data are not included in the blinded analyses. These events were also considered as life-threatening (refer to [Section 6.2.2.1.1.3.2.1](#)): an anaphylactoid reaction reported in 1 participant 3 days after receiving the first dose of BNT162b2 (Dose 3) with a duration of 1 day, considered by the investigator as related to study intervention and leading to study withdrawal; and depression reported in 1 participant 7 days after receiving the first dose of BNT162b2 (Dose 3) reported as ongoing/resolving at the time of the data cutoff date, considered by the investigator as not related to study intervention.

Table 11. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 Through Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Subjects 12 Through 15 Years of Age – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | |
|--------------------------------------|--|---|
| | BNT162b2 (30 µg) (N ^a =1131) n ^b (%) | Placebo (N ^a =1129) n ^b (%) |
| Any event | 5 (0.4) | 2 (0.2) |
| GASTROINTESTINAL DISORDERS | 1 (0.1) | 0 |
| Abdominal pain | 1 (0.1) | 0 |
| Constipation | 1 (0.1) | 0 |
| INFECTIONS AND INFESTATIONS | 0 | 2 (0.2) |

Table 11. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 Through Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Subjects 12 Through 15 Years of Age – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | |
|--------------------------------------|--|---|
| | BNT162b2 (30 µg) (N ^a =1131) n ^b (%) | Placebo (N ^a =1129) n ^b (%) |
| Appendicitis | 0 | 2 (0.2) |
| Focal peritonitis | 0 | 1 (0.1) |
| NERVOUS SYSTEM DISORDERS | 1 (0.1) | 0 |
| Neuralgia | 1 (0.1) | 0 |
| PSYCHIATRIC DISORDERS | 4 (0.4) | 0 |
| Depression | 3 (0.3) | 0 |
| Anxiety | 1 (0.1) | 0 |
| Suicidal ideation | 1 (0.1) | 0 |

Note: MedDRA (v23.1) coding dictionary applied.

Note: Adverse events that occurred on the day of or after subjects were unblinded are excluded from this summary.

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.

b. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (04:09)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:

.nda2 unblinded/C4591001 BLA/adae s130 d1 cut ser ped saf

6.2.2.1.1.3.5. Adverse Events Leading to Withdrawal – Adolescents 12-15 Years of Age

From Dose 1 to 1 month after Dose 2, few adolescents and young adults in the BNT162b2 group ($\leq 0.2\%$) and in the placebo group ($\leq 0.4\%$) were withdrawn due to AEs ([Table 12](#)).

In the adolescent group, 1 participant in the BNT162b2 group had an AE leading to withdrawal that was considered by the investigator as related to study intervention (pyrexia; refer to [Section 6.2.2.1.1.3.2.1](#)), and none in the placebo group.

In the young adult group, 1 participant in the BNT162b2 group had an AE leading to withdrawal that was considered by the investigator as related to study treatment (severe injection site pain that started 2 days after Dose 1 and resolved after 1 day), and none in the placebo group.

Additional data are presented in Module 5.3.5.1:

[16.2.7.6 Listing of Adverse Events Leading to Discontinuation – Subjects 12 Through 25 Years of Age \(Reactogenicity Subset\)](#)

Table 12. Number (%) of Subjects Withdrawn Because of Adverse Events From Dose 1 Through 1 Month After Dose 2, by System Organ Class and Preferred Term – Subjects 12 Through 15 and 16 Through 25 Years of Age (Reactogenicity Subset) – Safety Population

| System Organ Class Preferred Term | Vaccine Group (as Administered) | | | | | | | |
|--|---------------------------------------|-----------------------|--------------------------------------|-----------------------|---------------------------------------|-----------------------|--------------------------------------|-----------------------|
| | BNT162b2 (30 µg) | | | | Placebo | | | |
| | 12-15 Years (N ^a =1131) | | 16-25 Years (N ^a =536) | | 12-15 Years (N ^a =1129) | | 16-25 Years (N ^a =561) | |
| | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c | n ^b (%) | (95% CI) ^c |
| Any event | 2 (0.2) | (0.0, 0.6) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 2 (0.4) | (0.0, 1.3) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 1 (0.1) | (0.0, 0.5) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Injection site pain | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Pyrexia | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| INJURY, POISONING AND PROCEDURAL COMPLICATIONS | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 2 (0.4) | (0.0, 1.3) |
| Exposure during pregnancy | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 2 (0.4) | (0.0, 1.3) |
| NERVOUS SYSTEM DISORDERS | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Headache | 0 | (0.0, 0.3) | 1 (0.2) | (0.0, 1.0) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| PSYCHIATRIC DISORDERS | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Anxiety | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |
| Depression | 1 (0.1) | (0.0, 0.5) | 0 | (0.0, 0.7) | 0 | (0.0, 0.3) | 0 | (0.0, 0.7) |

Note: MedDRA (v23.1) coding dictionary applied.

Note: Adverse events that occurred on the day of or after subjects were unblinded are excluded from this summary.

Note: This table includes all subjects 12 through 15 years of age (all of whom are in the reactogenicity subset) and the subset of subjects 16 through 25 years of age who received an electronic diary (e-diary).

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.

b. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.

c. Exact 2-sided CI based on the Clopper and Pearson method.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (01:37)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s130_1md2_wd_ped_saf

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6.2.2.1.2. Safety Results – Adults 16-55 Years of Age

Safety results are presented as reference, for the protocol specified adult age stratum 16-55 years of age for whom longer-term safety data are available; data are reported from Dose 1 to 1 month after Dose 2 and from Dose 1 until the unblinding date (variable due to individuals ≥ 16 years of age being unblinded in the study as described in [Section 6.2.1.1](#)). AE data up to the unblinding date are calculated as IRs (using a denominator of 100 person-years of exposure) to adjust for variable exposure time from individual unblinding. These summary data serve a comparative/reference purpose and are not presented as a full independent safety evaluation in the context of this EUA amendment.

Open-label data for participants who were unblinded, including those originally randomized to placebo who received open-label BNT162b2 30 μ g as Dose 3/Dose 4, are not discussed further in this EUA amendment; safety results focus only on the blinded placebo-controlled data.

6.2.2.1.2.1. Study Population Characteristics – Adults 16-55 Years of Age

6.2.2.1.2.1.1. Safety Population – Adults 16-55 Years of Age

The safety population age group of adults (16-55 years of age) included 13,069 participants in the BNT162b2 group and 13,095 participants in the placebo group.

Additional study population data including medical history, concomitant vaccines, study vaccine administration, and e-diary transmission are in Module 5.3.5.1.

Additional data are presented in Module 5.3.5.1:

[Medical History – Phase 2/3 Subjects 16-55 Years of Age – Safety Population](#)

[Concomitant Vaccines Received From After Dose 1 – Phase 2/3 Subjects 16-55 Years of Age – Safety Population](#)

[Vaccine as Administered, by Vaccine Group – Phase 2/3 Subjects 16-55 Years of Age – All Randomized Subjects](#)

[Vaccine Administration Timing – Phase 2/3 Subjects 16-55 Years of Age – All Randomized Subjects](#)

[E-Diary Transmission – Phase 2/3 Subjects 16-55 Years of Age – Safety Population](#)

[16.2.2.2 Listing of Important Protocol Deviations – Phase 2/3 Subjects 16-55 Years of Age](#)

[16.2.3.2.2 Listing of Subjects Excluded From Safety Population – Phase 2/3 Subjects 16-55 Years of Age](#)

[16.2.5.2.2 Listing of Medication Errors – Phase 2/3 Subjects 16-55 Years of Age](#)

[16.1.7.1.2 Listing of Randomization Scheme and Actual Vaccine Received – Phase 2/3 Subjects 16-55 Years of Age](#)

6.2.2.1.2.1.2. Duration of Follow-Up – Adults 16-55 Years of Age

Duration of follow-up was ≥ 4 months after Dose 2 for 57.8% of adult participants (16-55 years of age) during the blinded placebo-controlled follow-up period ([Table 13](#)). As of the data cutoff date, the proportion of participants in the age group with blinded follow-up to at least 6 months after Dose 2 included 10.4% in the BNT162b2 group and 8.2% in the placebo group. When the total exposure time from Dose 2 to the data cutoff date is considered, 6666 participants 16-55 years of age (51.0%) had ≥ 6 months of follow-up time.

Table 13. Follow-up Time After Dose 2 – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

| | Vaccine Group (as Administered) | | |
|---|---|--|--|
| | BNT162b2 (30 µg) (N ^a =13069) n ^b (%) | Placebo (N ^a =13095) n ^b (%) | Total (N ^a =26164) n ^b (%) |
| Subjects (%) with length of follow-up of: | | | |
| Original blinded placebo-controlled follow-up period | | | |
| <2 Months | 917 (7.0) | 962 (7.3) | 1879 (7.2) |
| ≥2 Months to <4 months | 4448 (34.0) | 4726 (36.1) | 9174 (35.1) |
| ≥4 Months to <6 months | 6343 (48.5) | 6327 (48.3) | 12670 (48.4) |
| ≥6 Months | 1361 (10.4) | 1080 (8.2) | 2441 (9.3) |
| Total exposure from Dose 2 to cutoff date | | | |
| <2 Months | 305 (2.3) | | |
| ≥2 Months to <4 months | 552 (4.2) | | |
| ≥4 Months to <6 months | 5546 (42.4) | | |
| ≥6 Months | 6666 (51.0) | | |
| Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately. | | | |
| a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations. | | | |
| b. n = Number of subjects with the specified characteristic. | | | |
| PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 31MAR2021 (17:26) | | | |
| (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: | | | |
| ./nda2_unblinded/C4591001_EUA_1655/adsl_fu_d2_1655_saf | | | |

6.2.2.1.2.1.3. Disposition – Adults 16-55 Years of Age

The disposition of randomized adult participants (16-55 years of age) was similar in the BNT162b2 and placebo groups during the blinded follow-up period (Table 14). Most participants randomized (97.7%) received Dose 1 and Dose 2. There were 278 (2.1%) participants in the BNT162b2 group and 388 (3.0%) participants in the placebo group who discontinued from the vaccination period. Most participants (95.8%) completed the 1 month post Dose 2 visit and 25.5% of the BNT162b2 group participants completed the 6 months post Dose 2 (25.5%) visit as of the data cutoff date. There were 608 participants in the BNT162b2 and placebo groups who were withdrawn from the study (2.0% and 2.7%, respectively), mostly due to lost to follow-up (1.2%) or withdrawn by subject (0.9%).

Open-label data for participants who were unblinded, including original placebo participant who received open-label BNT162b2 30 µg as Dose 3/Dose 4, are shown in Table 14 for reference but not discussed further for safety analyses.

Table 14. Disposition of All Randomized Subjects – Phase 2/3 Subjects 16-55 Years of Age

| | Vaccine Group (as Randomized) | | |
|---|---|--|--|
| | BNT162b2 (30 µg) (N ^a =13104) n ^b (%) | Placebo (N ^a =13132) n ^b (%) | Total (N ^a =26236) n ^b (%) |
| Randomized | 13104 (100.0) | 13132 (100.0) | 26236 (100.0) |
| Not vaccinated | 31 (0.2) | 32 (0.2) | 63 (0.2) |
| Original blinded placebo-controlled follow-up period | | | |
| Vaccinated | 13073 (99.8) | 13100 (99.8) | 26173 (99.8) |
| Dose 1 | 13073 (99.8) | 13100 (99.8) | 26173 (99.8) |
| Dose 2 | 12802 (97.7) | 12825 (97.7) | 25627 (97.7) |
| Discontinued from original blinded placebo-controlled vaccination period ^c | 278 (2.1) | 388 (3.0) | 666 (2.5) |
| Reason for discontinuation | | | |
| Lost to follow-up | 132 (1.0) | 128 (1.0) | 260 (1.0) |
| Withdrawal by subject | 81 (0.6) | 117 (0.9) | 198 (0.8) |
| No longer meets eligibility criteria | 23 (0.2) | 94 (0.7) | 117 (0.4) |
| Adverse event | 15 (0.1) | 12 (0.1) | 27 (0.1) |
| Pregnancy | 6 (0.0) | 6 (0.0) | 12 (0.0) |
| Protocol deviation | 2 (0.0) | 6 (0.0) | 8 (0.0) |
| Physician decision | 3 (0.0) | 4 (0.0) | 7 (0.0) |
| Medication error without associated adverse event | 2 (0.0) | 1 (0.0) | 3 (0.0) |
| Death | 0 | 2 (0.0) | 2 (0.0) |
| Withdrawal by parent/guardian | 1 (0.0) | 0 | 1 (0.0) |
| Other | 13 (0.1) | 18 (0.1) | 31 (0.1) |
| Unblinded before 1-month post-Dose 2 visit | 175 (1.3) | 182 (1.4) | 357 (1.4) |
| Completed 1-month post-Dose 2 visit | 12586 (96.0) | 12555 (95.6) | 25141 (95.8) |
| Withdrawn from the study | 259 (2.0) | 349 (2.7) | 608 (2.3) |
| Withdrawn after Dose 1 and before Dose 2 | 138 (1.1) | 155 (1.2) | 293 (1.1) |
| Withdrawn after Dose 2 and before 1-month post-Dose 2 visit | 85 (0.6) | 104 (0.8) | 189 (0.7) |
| Withdrawn after 1-month post-Dose 2 visit | 36 (0.3) | 90 (0.7) | 126 (0.5) |
| Reason for withdrawal from the study | | | |
| Lost to follow-up | 150 (1.1) | 160 (1.2) | 310 (1.2) |
| Withdrawal by subject | 88 (0.7) | 147 (1.1) | 235 (0.9) |
| Protocol deviation | 3 (0.0) | 20 (0.2) | 23 (0.1) |
| Adverse event | 6 (0.0) | 3 (0.0) | 9 (0.0) |
| Death | 3 (0.0) | 5 (0.0) | 8 (0.0) |
| Physician decision | 2 (0.0) | 3 (0.0) | 5 (0.0) |
| No longer meets eligibility criteria | 1 (0.0) | 2 (0.0) | 3 (0.0) |
| Pregnancy | 0 | 1 (0.0) | 1 (0.0) |
| Medication error without associated adverse event | 1 (0.0) | 0 | 1 (0.0) |
| Withdrawal by parent/guardian | 1 (0.0) | 0 | 1 (0.0) |
| Other | 4 (0.0) | 8 (0.1) | 12 (0.0) |
| Open-label follow-up period | | | |
| Originally randomized to BNT162b2 | 11858 (90.5) | | |

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Table 14. Disposition of All Randomized Subjects – Phase 2/3 Subjects 16-55 Years of Age

| | Vaccine Group (as Randomized) | | |
|---|---|--|--|
| | BNT162b2 (30 µg) (N ^a =13104) n ^b (%) | Placebo (N ^a =13132) n ^b (%) | Total (N ^a =26236) n ^b (%) |
| Received Dose 2/unplanned dose | 61 (0.5) | | |
| Completed 1-month post–Dose 2 visit | 141 (1.1) | | |
| Completed 6-month post–Dose 2 visit | 3341 (25.5) | | |
| Withdrawn from the study | 58 (0.4) | | |
| Withdrawn before 6-month post–Dose 2 visit | 56 (0.4) | | |
| Withdrawn after 6-month post–Dose 2 visit | 2 (0.0) | | |
| Reason for withdrawal from the study | | | |
| Withdrawal by subject | 32 (0.2) | | |
| Protocol deviation | 17 (0.1) | | |
| Lost to follow-up | 3 (0.0) | | |
| Physician decision | 2 (0.0) | | |
| Adverse event | 1 (0.0) | | |
| No longer meets eligibility criteria | 1 (0.0) | | |
| Other | 2 (0.0) | | |
| Originally randomized to placebo | | 12299 (93.7) | |
| Withdrawn from the study after unblinding and before Dose 3 | | 284 (2.2) | |
| Received Dose 3 (first dose of BNT162b2 [30 µg]) | | 11405 (86.8) | |
| Received Dose 4 (second dose of BNT162b2 [30 µg]) | | 8586 (65.4) | |
| Discontinued from open-label vaccination period ^d | | 16 (0.1) | |
| Reason for discontinuation from open-label vaccination period | | | |
| Withdrawal by subject | | 5 (0.0) | |
| Pregnancy | | 4 (0.0) | |
| Adverse event | | 3 (0.0) | |
| Protocol deviation | | 3 (0.0) | |
| Lost to follow-up | | 1 (0.0) | |
| Completed 1-month post–Dose 4 visit | | 3424 (26.1) | |
| Withdrawn from the study | | 8 (0.1) | |
| Withdrawn after Dose 3 and before Dose 4 | | 6 (0.0) | |
| Withdrawn after Dose 4 and before 1-month post–Dose 4 visit | | 2 (0.0) | |
| Withdrawn after 1-month post–Dose 4 visit | | 0 | |
| Reason for withdrawal from the study | | | |
| Withdrawal by subject | | 7 (0.1) | |
| Protocol deviation | | 1 (0.0) | |

Table 14. Disposition of All Randomized Subjects – Phase 2/3 Subjects 16-55 Years of Age

| | Vaccine Group (as Randomized) | | |
|--|---|--|--|
| | BNT162b2 (30 µg) (N ^a =13104) n ^b (%) | Placebo (N ^a =13132) n ^b (%) | Total (N ^a =26236) n ^b (%) |
| <p>Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately.</p> <p>Note: Subjects randomized but did not sign informed consent or had a significant quality event due to lack of PI oversight are not included in any analysis population.</p> <p>Note: Because of a dosing error, Subject C4591001 1088 10881077 received an additional dose of BNT162b2 (30 µg) at an unscheduled visit after receiving 1 dose of BNT162b2 (30 µg) and 1 dose of placebo.</p> <p>a. N = number of randomized subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.</p> <p>b. n = Number of subjects with the specified characteristic.</p> <p>c. Original blinded placebo-controlled vaccination period is defined as the time period from Dose 1 to 1 month post-Dose 2.</p> <p>d. Open-label vaccination period is defined as the time period from Dose 3 (first dose of BNT162b2 [30 µg]) to 1 month post-Dose 4 (second dose of BNT162b2 [30 µg]).</p> <p>PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:20) Source Data: adds Table Generation: 31MAR2021 (18:10) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: .nda2_unblinded/C4591001_EUA_1655/adds_s002_all_1655_rand</p> | | | |

6.2.2.1.2.1.4. Demographics – Adults 16-55 Years of Age

Demographic characteristics for Phase 2/3 adults in the 16-55 years of age group were similar in the BNT162b2 and placebo groups (Table 15). Overall, most adult participants were White (78.2%), with 11.0% Black participants and 5.4% Asian participants, and other racial groups were <6.0%. There were 30.8% Hispanic/Latino participants. The median age was 40.0 years and 49.9% of participants were male. Obese adults made up 33.7% of this safety population.

Table 15. Demographic Characteristics – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

| | Vaccine Group (as Administered) | | |
|--------|---|--|--|
| | BNT162b2 (30 µg) (N ^a =13069) n ^b (%) | Placebo (N ^a =13095) n ^b (%) | Total (N ^a =26164) n ^b (%) |
| Sex | | | |
| Male | 6640 (50.8) | 6412 (49.0) | 13052 (49.9) |
| Female | 6429 (49.2) | 6683 (51.0) | 13112 (50.1) |
| Race | | | |
| White | 10221 (78.2) | 10251 (78.3) | 20472 (78.2) |

Table 15. Demographic Characteristics – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

| | Vaccine Group (as Administered) | | |
|---|---|--|--|
| | BNT162b2 (30 µg) (N ^a =13069) n ^b (%) | Placebo (N ^a =13095) n ^b (%) | Total (N ^a =26164) n ^b (%) |
| Black or African American | 1429 (10.9) | 1436 (11.0) | 2865 (11.0) |
| American Indian or Alaska Native | 165 (1.3) | 153 (1.2) | 318 (1.2) |
| Asian | 703 (5.4) | 712 (5.4) | 1415 (5.4) |
| Native Hawaiian or other Pacific Islander | 43 (0.3) | 21 (0.2) | 64 (0.2) |
| Multiracial | 437 (3.3) | 438 (3.3) | 875 (3.3) |
| Not reported | 71 (0.5) | 84 (0.6) | 155 (0.6) |
| Racial designation | | | |
| Japanese | 39 (0.3) | 41 (0.3) | 80 (0.3) |
| Ethnicity | | | |
| Hispanic/Latino | 4047 (31.0) | 4023 (30.7) | 8070 (30.8) |
| Non-Hispanic/non-Latino | 8967 (68.6) | 9011 (68.8) | 17978 (68.7) |
| Not reported | 55 (0.4) | 61 (0.5) | 116 (0.4) |
| Country | | | |
| Argentina | 1975 (15.1) | 1973 (15.1) | 3948 (15.1) |
| Brazil | 1191 (9.1) | 1189 (9.1) | 2380 (9.1) |
| Germany | 134 (1.0) | 139 (1.1) | 273 (1.0) |
| South Africa | 328 (2.5) | 330 (2.5) | 658 (2.5) |
| Turkey | 190 (1.5) | 197 (1.5) | 387 (1.5) |
| USA | 9251 (70.8) | 9267 (70.8) | 18518 (70.8) |
| Age at vaccination (years) | | | |
| Mean (SD) | 39.0 (10.76) | 38.7 (10.75) | 38.9 (10.76) |
| Median | 40.0 | 40.0 | 40.0 |
| Min, max | (16, 55) | (16, 55) | (16, 55) |
| Baseline SARS-CoV-2 status | | | |
| Positive ^c | 517 (4.0) | 541 (4.1) | 1058 (4.0) |
| Negative ^d | 12466 (95.4) | 12485 (95.3) | 24951 (95.4) |
| Missing | 86 (0.7) | 69 (0.5) | 155 (0.6) |
| Body mass index (BMI) | | | |
| Underweight (<18.5 kg/m ²) | 199 (1.5) | 224 (1.7) | 423 (1.6) |
| Normal weight (≥18.5 kg/m ² - 24.9 kg/m ²) | 4208 (32.2) | 4268 (32.6) | 8476 (32.4) |
| Overweight (≥25.0 kg/m ² - 29.9 kg/m ²) | 4258 (32.6) | 4178 (31.9) | 8436 (32.2) |
| Obese (≥30.0 kg/m ²) | 4401 (33.7) | 4421 (33.8) | 8822 (33.7) |
| Missing | 3 (0.0) | 4 (0.0) | 7 (0.0) |

Table 15. Demographic Characteristics – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

| | Vaccine Group (as Administered) | | |
|--|---|--|--|
| | BNT162b2 (30 µg) (N ^a =13069) n ^b (%) | Placebo (N ^a =13095) n ^b (%) | Total (N ^a =26164) n ^b (%) |
| Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2. Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately. a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations. b. n = Number of subjects with the specified characteristic. c. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19. d. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19. PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 31MAR2021 (17:35) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001 EUA 1655/adsl s005 demo all 1655 saf | | | |

6.2.2.1.2.2. Reactogenicity – Adults 16-55 Years of Age

Reactogenicity (local reactions and systemic events) was assessed via e-diary in a subset of participants in up to 7 days after each dose.

Adult participants (16-55 years of age) in the reactogenicity subset with e-diary data included N=5807 post Dose 1 and N=5366 post Dose 2.

6.2.2.1.2.2.1. Local Reactions – Adults 16-55 Years of Age

Among adults 16-55 years of age in the BNT162b2 group, pain at the injection site was the most frequently reported local reaction, with similar frequency after Dose 1 compared with Dose 2 of BNT162b2 (Figure 3).

In the BNT162b2 group, frequencies after Dose 1 and Dose 2 were similar for redness (5.4% vs 5.6%) and swelling (6.3% vs 6.8%). In the placebo group, redness and swelling were reported infrequently ($\leq 1.0\%$) after Doses 1 and 2. Pain at injection site was reported with a higher frequency in the BNT162b2 group after Dose 1 and Dose 2 than in the placebo group (Dose 1: 83.7% vs 14.2%; Dose 2: 78.3% vs 11.6%).

Overall, pain at the injection site did not increase after Dose 2, and redness and swelling were generally similar in frequency after Dose 1 and Dose 2. After either dose, most local reactions were mild or moderate in severity. Severe local reactions were reported infrequently ($\leq 2.5\%$) in the BNT162b2 group after either dose. No Grade 4 local reactions were reported.

Local reactions for the adult age group after either dose had a median onset day on Day 1 (Day 1 was the day of vaccination) and resolved with a median duration of 1-2 days.

Additional data are presented in Module 5.3.5.1:

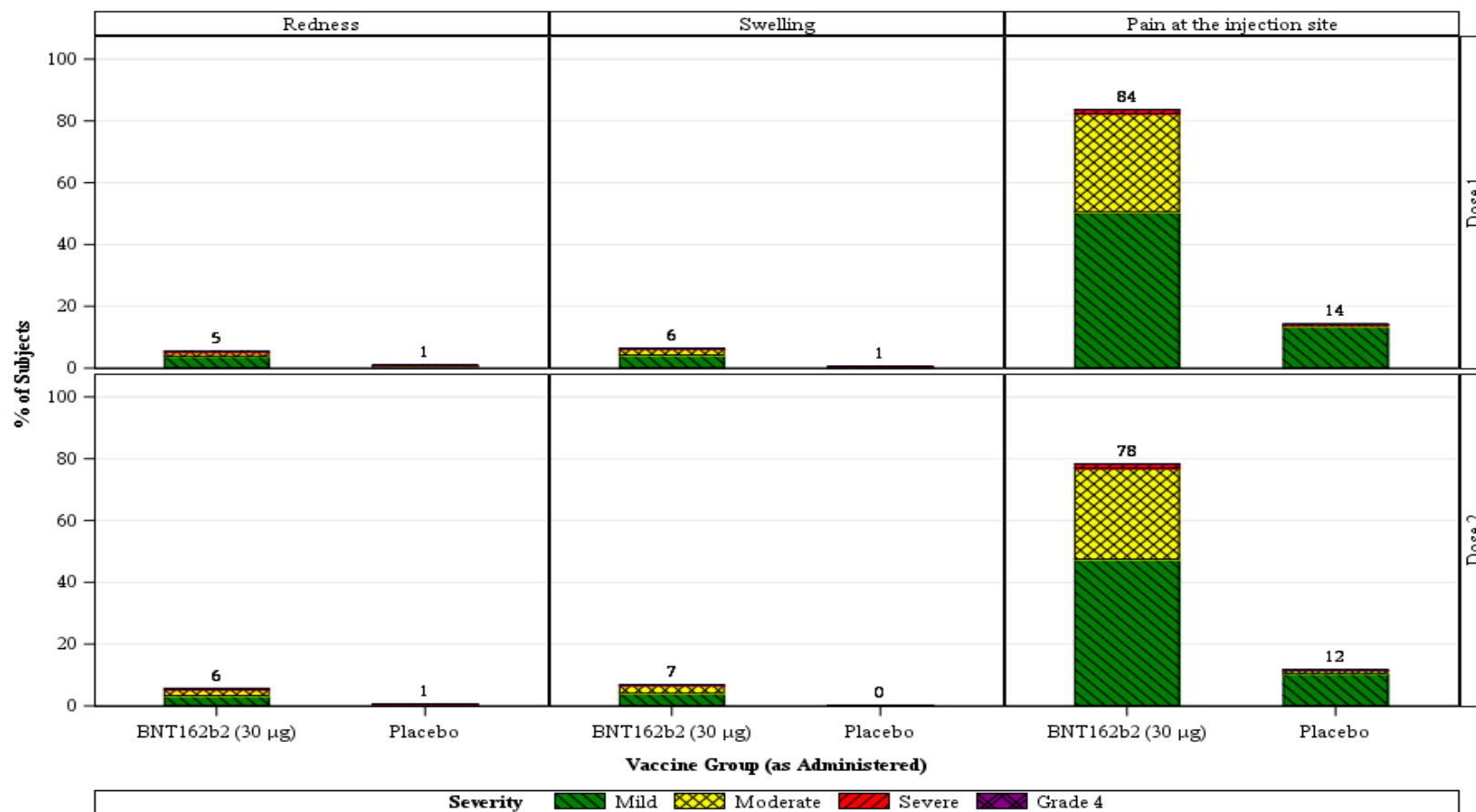
Local Reactions, by Maximum Severity, Within 7 Days After Each Dose, by Age Group (Reactogenicity Subset)
– Phase 2/3 Subjects 16-55 Years of Age – Safety Population

Onset Days for Local Reactions, by Age Group (Reactogenicity Subset) – Phase 2/3 Subjects 16-55 Years of Age
– Safety Population

Duration (Days) From First to Last Day of Local Reactions, by Age Group (Reactogenicity Subset) –
Phase 2/3 Subjects 16-55 Years of Age – Safety Population

090177e196b7d611\Approved\Approved On: 07-Apr-2021 01:46 (GMT)

Figure 3. Participants Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Reactogenicity Subset for Phase 2/3 Subjects ≥ 16 Years of Age – Safety Population by Age Group: 16-55 Years



Note: Number above each bar denotes percentage of subjects reporting the reaction with any severity.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adfacevd Table Generation: 27MAR2021 (01:55)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: /nda2_unblinded/C4591001_BLA/adce_f001_lr_max_age_p3

6.2.2.1.2.2.2. Systemic Events – Adults 16-55 Years of Age

Systemic events in the adult group (16-55 years of age) were generally increased in frequency and severity with number of doses, with the exceptions of vomiting and diarrhea which were reported infrequently and at similar incidences after each dose (Figure 4). Systemic events, in decreasing order of frequency by dose (Dose 1 vs Dose 2), were:

- fatigue: BNT162b2 (49.4% vs 61.5%) compared to placebo (33.0% vs 22.9%)
- headache: BNT162b2 (43.5% vs 54.0%) compared to placebo (33.5% vs 24.3%)
- muscle pain: BNT162b2 (22.9% vs 39.3%) compared to placebo (11.3% vs 8.8%)
- chills: BNT162b2 (16.5% vs 37.8%) compared to placebo (6.8% vs 4.2%)
- joint pain: BNT162b2 (11.8% vs 23.8%) compared to placebo (5.8% vs 5.5%)
- fever: BNT162b2 (4.1% vs 16.4%) compared to placebo (0.9% vs 0.4%)
- vomiting: reported infrequently and similar after either dose
- diarrhea: reported infrequently and similar after either dose

Systemic events were generally reported less frequently in the placebo group than in the BNT162b2 group, with some exceptions. Vomiting and diarrhea (after Dose 1 and Dose 2) were reported at similar frequencies in the placebo group and the BNT162b2 group (Figure 4).

In the BNT162b2 group, use of antipyretic/pain medication was 27.8% vs 45.2% after Dose 1 and Dose 2, respectively. Use of antipyretic/pain medication was less frequent in the placebo group after Dose 1 and Dose 2 (13.7% and 11.9%) than in the BNT162b2 group.

After the first and second dose, the majority of systemic events were mild or moderate in severity. Severe fever ($>38.9^{\circ}\text{C}$ to 40.0°C) was reported in the BNT162b2 group after Dose 1 for 0.3% and after Dose 2 for 1.5% of participants, and in the placebo group after Dose 1 for 0.1% and after Dose 2 for 0.1% of participants. Grade 4 fever ($>40^{\circ}\text{C}$) was reported for 1 participant in the BNT162b2 group and no participants in the placebo group.

Systemic events for the adult (16-55 years of age) group after either dose had a median onset day of Day 2 (Day 1 was the day of vaccination) and resolved with a median duration of 1-2 days.

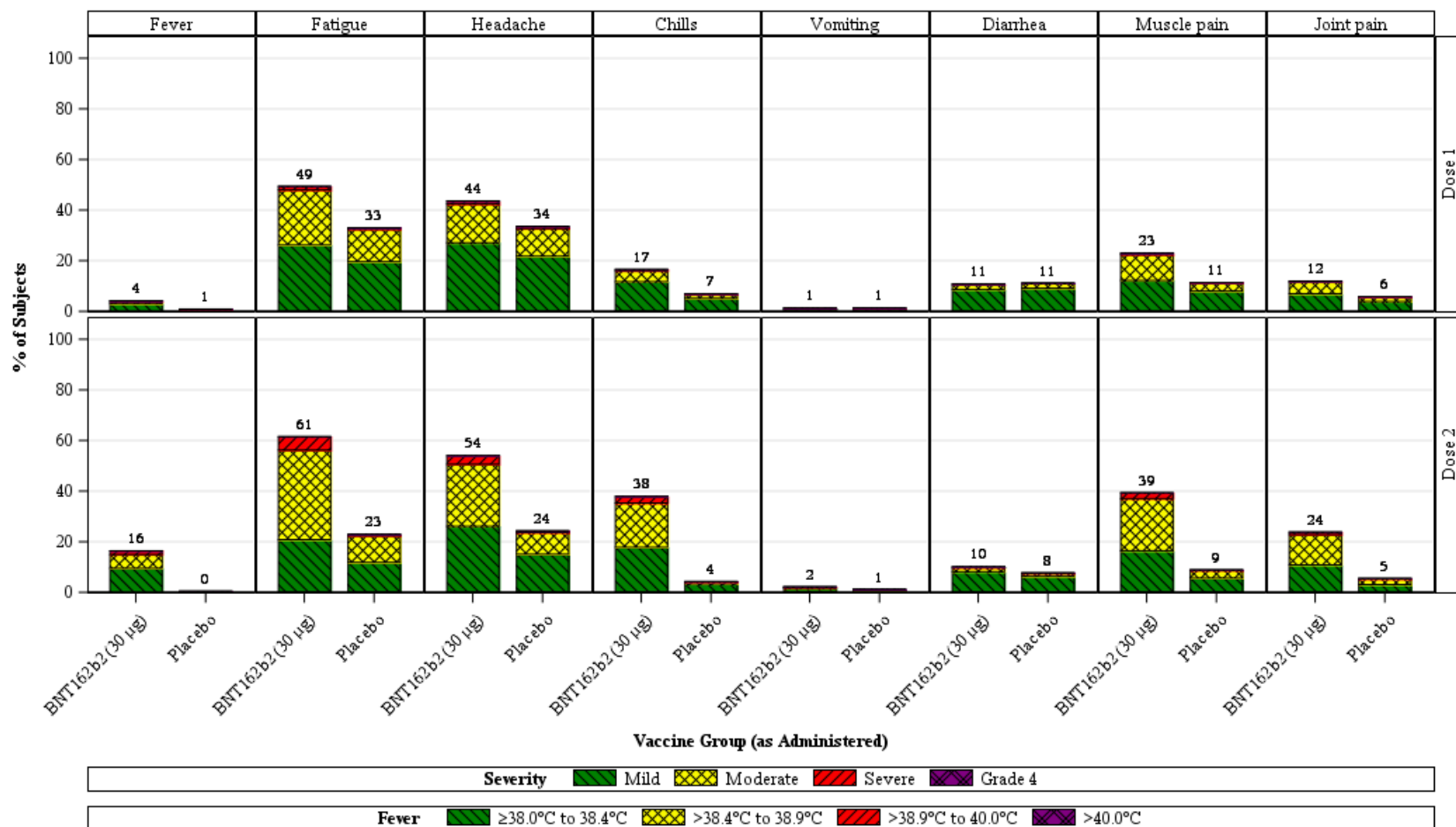
Additional data are presented in Module 5.3.5.1:

Systemic Events, by Maximum Severity, Within 7 Days After Each Dose, by Age Group (Reactogenicity Subset) – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

Onset Days for Systemic Events, by Age Group (Reactogenicity Subset) – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

Duration (Days) From First to Last Day of Systemic Events, by Age Group (Reactogenicity Subset) – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

Figure 4. Participants Reporting Systemic Events, by Maximum Severity, Within 7 Days After Each Dose – Reactogenicity Subset for Phase 2/3 Subjects ≥16 Years of Age – Safety Population by Age Group: 16-55 Years



Note: Number above each bar denotes percentage of subjects reporting the event with any severity.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adfacevd Table Generation: 27MAR2021 (01:55)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: /nda2_unblinded/C4591001_BLA/adce_f001_se_max_age_p3

6.2.2.1.2.3. Adverse Events – Adults 16-55 Years of Age

AE overviews for the adult group (16-55 years of age) are reported from Dose 1 to 1 month after Dose 2 (Section 6.2.2.1.2.3.1.1), and from Dose 1 until the unblinding date (Section 6.2.2.1.2.3.1.2). Due to unblinding of individuals ≥ 16 years of age to treatment assignment (per protocol) to receive BNT162b2 (refer to Section 6.2.1.1), AE data analyzed up to the unblinding date were calculated as IRs using 100 person-years (PYs) of exposure as the denominator to adjust for exposure time.

6.2.2.1.2.3.1. Overview of Adverse Events – Adults 16-55 Years of Age

6.2.2.1.2.3.1.1. Dose 1 to 1 Month After Dose 2 – Adults 16-55 Years of Age

An overview of AEs from Dose 1 to 1 month after Dose 2 for the adults 16-55 years of age is presented in Table 16. There was a greater frequency of participants in the BNT162b2 group compared with the placebo group who reported at least 1 AE (32.6% vs 14.4%) and at least 1 related AE (26.8% vs 6.8%). Severe AEs, SAEs, and AEs leading to withdrawal were reported by $\leq 1.2\%$, $\leq 0.4\%$, and $\leq 0.2\%$, respectively, in both groups. Discontinuations due to related AEs were reported in few participants ($\leq 0.1\%$) in the BNT162b2 and placebo groups.

Two adult participants (16-55 years of age) died between Dose 1 and 1 month after Dose 2, both in the placebo group (refer to Section 6.2.2.1.2.3.3).

Table 16. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

| Adverse Event | Vaccine Group (as Administered) | |
|---|---|------------------------------------|
| | BNT162b2 (30 µg) (N ^a =12995) | Placebo (N ^a =13026) |
| | n ^b (%) | n ^b (%) |
| Any event | 4233 (32.6) | 1871 (14.4) |
| Related ^c | 3480 (26.8) | 882 (6.8) |
| Severe | 154 (1.2) | 74 (0.6) |
| Life-threatening | 8 (0.1) | 11 (0.1) |
| Any serious adverse event | 52 (0.4) | 49 (0.4) |
| Related ^c | 2 (0.0) | 0 |
| Severe | 27 (0.2) | 31 (0.2) |
| Life-threatening | 8 (0.1) | 11 (0.1) |
| Any adverse event leading to withdrawal | 19 (0.1) | 20 (0.2) |
| Related ^c | 9 (0.1) | 7 (0.1) |
| Severe | 5 (0.0) | 4 (0.0) |
| Life-threatening | 0 | 3 (0.0) |
| Death | 0 | 2 (0.0) |

Table 16. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

| Adverse Event | Vaccine Group (as Administered) | |
|--|---|------------------------------------|
| | BNT162b2 (30 µg) (N ^a =12995) | Placebo (N ^a =13026) |
| | n ^b (%) | n ^b (%) |
| <p>a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.</p> <p>b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.</p> <p>c. Assessed by the investigator as related to investigational product.</p> <p>PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 31MAR2021 (17:46) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_EUA_1655/adae_s091_all_pd2_1655_sa</p> | | |

6.2.2.1.2.3.1.2. Dose 1 to Unblinding Date – Adults 16-55 Years of Age

An overview of AEs from Dose 1 to participants' unblinding date for adults 16-55 years of age during the blinded safety follow-up is presented in Table 17 (reported as IRs per 100 PYs adjusted for variable exposure time). The incidence of at least 1 AE reported in the BNT162b2 group as compared with the placebo group was 88.4 versus 43.5 per 100 PYs, and at least 1 related AE was 70.0 versus 18.0 per 100 PYs. Severe AEs, SAEs, and AEs leading to withdrawal were reported at incidences of ≤ 3.9 , ≤ 2.4 , and ≤ 0.6 per 100 PYs, respectively, in both groups. Incidences of discontinuations due to related AEs were low (0.2 per 100 PYs) in both the BNT162b2 and placebo groups.

A total of 7 adult (16-55 years of age) participants died prior to unblinding date, with an IR of 0.1 per 100 PYs in both groups: 3 participants in the BNT162b2 group and 4 participants in the placebo group (refer to [Section 6.2.2.1.2.3.3](#)).

Table 17. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

| Adverse Event | Vaccine Group (as Administered) | | | | | |
|----------------------|--|---------------------------|-----------------------|---|---------------------------|-----------------------|
| | BNT162b2 (30 µg) (N ^a =12995, TE ^b =49.7) | | | Placebo (N ^a =13026, TE ^b =49.1) | | |
| | n ^c | IR (/100 PY) ^d | (95% CI) ^e | n ^c | IR (/100 PY) ^d | (95% CI) ^e |
| Any event | 4396 | 88.4 | (85.8, 91.0) | 2136 | 43.5 | (41.7, 45.4) |
| Related ^f | 3484 | 70.0 | (67.7, 72.4) | 884 | 18.0 | (16.8, 19.2) |
| Severe | 193 | 3.9 | (3.4, 4.5) | 124 | 2.5 | (2.1, 3.0) |

Table 17. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

| Adverse Event | Vaccine Group (as Administered) | | | | | |
|---|--|---------------------------|-----------------------|---|---------------------------|-----------------------|
| | BNT162b2 (30 µg) (N ^a =12995, TE ^b =49.7) | | | Placebo (N ^a =13026, TE ^b =49.1) | | |
| | n ^c | IR (/100 PY) ^d | (95% CI) ^e | n ^c | IR (/100 PY) ^d | (95% CI) ^e |
| Life-threatening | 13 | 0.3 | (0.1, 0.4) | 20 | 0.4 | (0.2, 0.6) |
| Any serious adverse event | 103 | 2.1 | (1.7, 2.5) | 117 | 2.4 | (2.0, 2.9) |
| Related ^f | 3 | 0.1 | (0.0, 0.2) | 1 | 0.0 | (0.0, 0.1) |
| Severe | 56 | 1.1 | (0.9, 1.5) | 75 | 1.5 | (1.2, 1.9) |
| Life-threatening | 13 | 0.3 | (0.1, 0.4) | 20 | 0.4 | (0.2, 0.6) |
| Any adverse event leading to withdrawal | 22 | 0.4 | (0.3, 0.7) | 28 | 0.6 | (0.4, 0.8) |
| Related ^f | 9 | 0.2 | (0.1, 0.3) | 8 | 0.2 | (0.1, 0.3) |
| Severe | 5 | 0.1 | (0.0, 0.2) | 6 | 0.1 | (0.0, 0.3) |
| Life-threatening | 3 | 0.1 | (0.0, 0.2) | 5 | 0.1 | (0.0, 0.2) |
| Death | 3 | 0.1 | (0.0, 0.2) | 4 | 0.1 | (0.0, 0.2) |

a. N = number of subjects in the specified group.

b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 1 to the end of blinded follow-up. This value is the denominator for the incidence rate calculation.

c. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.

d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.

e. 2-sided CI based on Poisson distribution.

f. Assessed by the investigator as related to investigational product.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 31MAR2021 (17:27)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:

./nda2_unblinded/C4591001_EUA_1655/adae_s092_all_unb_1655_saf

6.2.2.1.2.3.2. Analysis of Adverse Events – Adults 16-55 Years of Age

6.2.2.1.2.3.2.1. Dose 1 to 1 Month After Dose 2 – Adults 16-55 Years of Age

Adverse Events by System Organ Class and Preferred Term

Most AEs reported in adults 16-55 years of age after Dose 1 up to 1 month after Dose 2 reflected reactogenicity. AE frequencies for participants in reactogenicity SOC (BNT162b2 vs placebo) were:

- general disorders and administration site conditions (24.3% vs 5.2%)
- musculoskeletal and connective tissue disorders (9.2% vs 2.3%)
- nervous system disorders (8.2% vs 3.0%)
- gastrointestinal disorders (3.4% vs 2.2%)

Beyond participants in the Phase 2/3 reactogenicity subset (refer to [Section 6.2.2.1.2.2](#)), events related to reactogenicity are no longer reported using an e-diary but are instead reported as AEs.

Based on the experience for safety reported in the current EUA, an analysis was planned *a priori* to evaluate if between-group AE imbalance from Dose 1 to 1 month after Dose 2 was attributed to reactogenicity events by examining the AEs reported within 7 days after each dose, which represents the reactogenicity reporting period. This time period was chosen because many AEs were reported in SOC of general disorders and administration site conditions, musculoskeletal and connective tissue disorders, and nervous system disorders, which include PTs consistent with and attributable to reactogenicity only if the events occurred in this time window after each dose.

PTs commonly reported from Dose 1 to 7 days after Dose 1 and from Dose 2 to 7 days after Dose 2 in the SOC of general disorders and administration site conditions (injection site pain, pyrexia, chills, and fatigue), musculoskeletal and connective tissue disorders (myalgia), and nervous system disorders (headache) represented the majority of PTs reported in those SOC. Frequencies between BNT162b2 and placebo and from after Dose 1 to after Dose 2 were similar to patterns of reactogenicity. AE frequencies for participants in these reactogenicity SOC reported at 7 days post each dose (BNT162b2 vs placebo) were as follows.

General disorders and administration site conditions:

- 7 days post Dose 1 (13.1% vs 3.1%)
- 7 days post Dose 2 (18.8% vs 2.3%)

Musculoskeletal and connective tissue disorders:

- 7 days post Dose 1 (2.7% vs 0.8%)
- 7 days post Dose 2 (6.7% vs 0.6%)

Nervous system disorders:

- 7 days post Dose 1 (2.8% vs 1.4%)
- 7 days post Dose 2 (5.9% vs 1.1%)

Overall, AEs reported from during the 7-day periods post each dose were largely attributable to reactogenicity events. This observation provides a reasonable explanation for the greater rates of AEs observed overall in the BNT162b2 group compared with the placebo group.

Additional data are presented in Module 5.3.5.1:

Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 7 Days After Dose 1, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 2 to 7 Days After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

16.2.7.4.1.2 Listing of Adverse Events – Phase 2/3 Subjects 16-55 Years of Age

16.2.7.1 Adverse Events Legend Page

Related Adverse Events – Dose 1 to 1 Month After Dose 2 – Adults 16-55 Years of Age

From Dose 1 to 1 month after Dose 2, AEs assessed as related by the investigator during the blinded follow-up period were reported by 26.8% of adult participants 16-55 years of age in the BNT162b2 group and 6.8% of participants in the placebo group (Table 16). Most related AEs were reactogenicity events and in the SOC of general disorders and administration site conditions, reported by 3118 BNT162b2 recipients (24.0%) and 608 placebo recipients (4.7%). Among the participants who had AEs of lymphadenopathy, 52 participants (0.4%) in the BNT162b2 group and 2 participants (0.0%) in the placebo group had events assessed by the investigator as related to study intervention (discussed further as events of clinical interest in Section 6.2.2.1.3).

Additional data are presented in Module 5.3.5.1:

Number (%) of Subjects Reporting at Least 1 Related Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 16 -55 Years of Age – Safety Population

Severe or Life-Threatening Adverse Events – Dose 1 to 1 Month After Dose 2 – Adults 16-55 Years of Age

From Dose 1 to 1 month after Dose 2, severe AEs reported in the adult age group (16-55 years of age) during the blinded follow-up period were low in frequency, reported in 1.2% of BNT162b2 recipients and 0.6% of placebo recipients. The frequency of severe events in the BNT162b2 group was primarily due to events in the SOC of general disorders and administration site conditions, reported by 0.6% of BNT162b2 recipients versus 0.0% of placebo recipients; the most frequently report term was pyrexia (0.3% vs 0.0%).

Life-threatening events were infrequent, reported in 8 participants (0.1%) in the BNT162b2 group and 11 participants (0.1%) in the placebo group from Dose 1 to 1 month after Dose 2.

Additional data are presented in Module 5.3.5.1:

Number (%) of Subjects Reporting at Least 1 Severe Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

Number (%) of Subjects Reporting at Least 1 Life-Threatening Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 16-55 Years of Age – Safety Population

6.2.2.1.2.3.2.2. Dose 1 to Unblinding Date – Adults 16-55 Years of Age

Adverse Events by System Organ Class and Preferred Term

Most AEs reported in adult participants 16-55 years of age after Dose 1 up to the unblinding date (reported as IRs per 100 PYs adjusted for variable exposure time) were reactogenicity events, similar to the trend observed after Dose 1 to 1 month after Dose 2. AE incidences for participants in these reactogenicity SOC's (BNT162b2 vs placebo) were:

- general disorders and administration site conditions (63.7 vs 14.1 per 100 PYs)
- musculoskeletal and connective tissue disorders (24.6 vs 7.0 per 100 PYs)
- nervous system disorders (21.8 vs 8.3 per 100 PYs)
- gastrointestinal disorders (9.5 vs 6.3 per 100 PYs)

AE analyses for adults (16-55 years of age) up through the unblinding date did not suggest any meaningful changes in the safety profile for the age group relative to that observed at 1 month after Dose 2 (refer to [Section 6.2.2.1.2.3.2.1](#)).

Additional data are presented in Module 5.3.5.1:

[Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Phase 2/3 Subjects 16-55 Years of Age – Safety Population](#)

6.2.2.1.2.3.3. Deaths – Adults 16-55 Years of Age

A total of 7 deaths were reported among Phase 2/3 adult participants (16-55 years of age) through the unblinding date (3 in the BNT162b2 group and 4 in the placebo group). No reported deaths were assessed by the investigator as related to study intervention.

In the BNT162b2 group:

- 1 male participant 54 years of age died due to congestive cardiac failure 88 days after Dose 2
- 1 male participant 53 years of age died due to cardio-respiratory arrest 86 days after Dose 2
- 1 male participant 51 years of age died due to metastatic lung cancer 113 days after Dose 2

In the placebo group:

- 1 female participant 42 years of age died due to an undetermined cause 8 days after Dose 1
- 1 female participant 51 years of age died due to myocardial infarction 37 days after Dose 2
- 1 male participant 53 years of age died due to multiple drug overdose 32 days after Dose 2
- 1 male participant 47 years of age died due to cardio-respiratory arrest 82 days after Dose 2

Additionally, 1 participant (female, 56 years of age) in the HIV+ subset of Study C4591001 (per protocol, analyzed separately from the safety population) died due to COVID-19 pneumonia 76 days after Dose 2 of placebo. This participant was diagnosed based on a local COVID-19 test that was not protocol-approved and was not subsequently confirmed by a test result from the central laboratory. The death was not considered related to study intervention.

Additional data are presented in Module 5.3.5.1:

[16.2.7.7.2 Listing of Deaths – Phase 2/3 Subjects 16-55 Years of Age](#)

6.2.2.1.2.3.4. Serious Adverse Events – Adults 16-55 Years of Age

6.2.2.1.2.3.4.1. Dose 1 to 1 Month After Dose 2 – Adults 16-55 Years of Age

From Dose 1 to 1 month after Dose 2, the proportions of adult participants (16-55 years of age) who reported at least 1 SAE was similar in the BNT162b2 group (0.4%) and in the placebo group (0.4%).

The most frequently reported SAEs in the BNT162b2 group were appendicitis (6 participants) followed by acute myocardial infarction, cellulitis, urinary tract infection, intervertebral disc protrusion, subarachnoid hemorrhage, and deep vein thrombosis (in 2 participants each). None of these events were considered by the investigator as related to study intervention.

Three SAEs (2 in the BNT162b2 group and 1 in the placebo group) were assessed by the investigator as related to study intervention:

- 1 participant in the BNT162b2 group had a related event of lymphadenopathy and was withdrawn from the study, with the event reported as resolved/recovered. This event was previously identified at the time of the EUA cutoff date of 14 November 2020.
- 1 participant in the BNT162b2 group reported shoulder injury related to vaccine administration, which was reported as resolved/recovered. This event was previously identified at the time of the EUA cutoff date of 14 November 2020.
- 1 participant in the placebo group reported related event of paresthesia and was recovering at the time of data cutoff.

Additional data are presented in Module 5.3.5.1:

[Number \(%\) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 16-55 Years of Age – Safety Population](#)

[16.2.7.5.2 Listing of Serious Adverse Events – Phase 2/3 Subjects 16-55 Years of Age](#)

6.2.2.1.2.3.4.2. Dose 1 to Unblinding Date – Adults 16-55 Years of Age

From Dose 1 to the unblinding date, the incidences of adult participants (16-55 years of age) who reported at least 1 SAE were similar in the BNT162b2 (2.1) and placebo (2.4) groups; these were reported as IRs per 100 PYs adjusted for variable exposure time.

In addition to SAEs reported up to 1 month after Dose 2, reported events after 1 month post Dose 2 up to the unblinding date included 1 SAE in a placebo recipient was assessed by the

investigator as related to study intervention: 1 participant in the placebo group reported a related SAE of psoriatic arthropathy which was not resolved at the time of the data cutoff date.

Up to the unblinding date, 12 cases of appendicitis were reported in the BNT162b2 group and 7 cases in the placebo group for similar IRs of 0.2 and 0.1 per 100 PYs, respectively. None were considered related to study intervention.

Additional data are presented in Module 5.3.5.1:

[Incidence Rates of at Least 1 Serious Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Phase 2/3 Subjects 16-55 Years of Age – Safety Population](#)

6.2.2.1.2.3.5. Adverse Events Leading to Withdrawal – Adults 16-55 Years of Age

From Dose 1 to 1 month after Dose 2, few adult participants (16-55 years of age) in the BNT162b2 (0.1%) and placebo (0.2%) groups were withdrawn due to AEs.

In total, 19 participants in the BNT162b2 group and 20 participants in the placebo group had an AE leading to withdrawal during blinded follow-up, with 17 AEs considered by the investigator as related to study intervention.

- Withdrawals due to related AEs in the BNT162b2 group included: 2 participants each with injection site pain or headache and 1 participant each with lymphadenopathy, eye pain, injection site dermatitis, injection site swelling, myalgia, or urticaria.
- Withdrawals due to related AEs in the placebo group included: 2 participants with drug hypersensitivity and 1 participant each with myalgia, urticaria, vertigo, dizziness, or irregular heart rate.

The events of urticaria (1 each in the BNT162b2 and placebo groups) were Grade 1 or 2, had on onset of 4-10 days, resolved within 4-27 days, and were considered non-serious.

In addition, 1 adult participant originally randomized to placebo who was unblinded to receive BNT162b2 had events of Grade 2 urticaria (forehead, posterior neck, bilateral posterior hands and bilateral plantar areas) and Grade 1 angioedema (forehead) with an onset of 2 days post Dose 3 and resolved after 7 days; the event was non-serious and considered by the investigator as related to study intervention; the participant was withdrawn from study intervention due to AE.

Additional data are presented in Module 5.3.5.1:

[Number \(%\) of Subjects Withdrawn Because of Adverse Events From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 16 -55 Years of Age – Safety Population](#)

[16.2.7.6.2 Listing of Adverse Events Leading to Discontinuation – Phase 2/3 Subjects 16-55 Years of Age](#)

6.2.2.1.3. Other Significant Adverse Events

Adverse Events of Clinical Interest

AESIs, such as those in the CDC list of AESIs for COVID-19 that include events potentially indicative of severe COVID-19 or autoimmune and neuroinflammatory disorders, were considered in the review of reported events for the adolescent group in addition to program defined TMEs. Narratives were prepared for such events reported in adolescents (12-15 years of age) (refer to [Section 6.2.1.1.1.1](#)). If an AESI was not observed in the 12-15 years of age group, narratives were not provided for individuals 16 and above. AEs of clinical interest occurring in the adolescent group were reviewed along with corresponding reference information from adults and are summarized below.

Additional data are presented in Module 5.3.5.1:

[16.2.7.4.1.1 Listing of Adverse Events – Subjects 12 Through 25 Years of Age \(Reactogenicity Subset\)](#)

[16.2.7.4.1.2 Listing of Adverse Events – Phase 2/3 Subjects 16-55 Years of Age](#)

Anaphylaxis

No cases of anaphylaxis or anaphylactoid reactions were reported during blinded follow-up in the adolescent (12-15 years of age) or young adult (16-25 years of age) groups as of the data cutoff date (13 March 2021).

One young adult participant (reported with both the 16-25 years of age and 16-55 years of age group data) who was originally randomized to the placebo group and unblinded to receive BNT162b2 had an anaphylactoid reaction 3 days post Dose 3 (first dose of BNT162b2), with an event duration of 1 day; the event was reported as an SAE (refer to [Section 6.2.2.1.3.4.2](#)), reported as resolved, and the participant withdrew from the study. Note that this event was not counted in the summary safety tables which only included blinded follow-up data.

In adults (16-55 years of age), 1 other participant had an SAE of anaphylaxis reported as caused by a bee sting that was not considered related to study intervention that was described in the prior submission for the current EUA (cutoff date of 14 November 2020).

Lymphadenopathy

In adolescents (12-15 years of age), 7 participants (0.6%) in the BNT162b2 group and 1 participant (0.1%) in the placebo group had lymphadenopathy events assessed by the investigator as related to study intervention. The majority of these events occurred in the arm and neck region, were reported within 2-10 days after vaccination, and approximately half of events resolved within 1-10 days (others were ongoing at the time of the data cutoff date).

In young adults (16-25 years of age), 1 related event of lymphadenopathy was reported up to the data cutoff date, occurring in the axilla within 1 day of Dose 2 and resolved within 5 days.

In adults (16-55 years of age), 52 participants (0.4%) in the BNT162b2 group and 2 participants (0.0%) in the placebo group had lymphadenopathy events reported up to the unblinding date and assessed by the investigator as related to study intervention (refer to [Section 6.2.2.1.2.3.2](#)). The majority of these events occurred in the arm and neck region, were reported within 2-4 days after vaccination (usually after Dose 2), and typically resolved within approximately 1 week.

Lymphadenopathy is considered an adverse reaction to vaccine and is noted as such in the EUA Fact Sheet.

Appendicitis

In adolescents (12-15 years of age), 2 participants in the placebo group had events of appendicitis reported as SAEs (refer to [Section 6.2.2.1.1.3.4](#)) and considered as not related to study intervention.

In young adults (16-25 years of age), 1 participant in the BNT162b2 group had an event of appendicitis reported as an SAE (refer to [Section 6.2.2.1.1.3.4](#)) and considered as not related to study intervention.

In adults (16-55 years of age), 12 cases of appendicitis were reported in the BNT162b2 group and 7 cases in the placebo group during blinded follow-up through the unblinding date. All were considered as SAEs (refer to [Section 6.2.2.1.2.3.4](#)), not related to study intervention, and all participants recovered.

Bell's Palsy/Facial Paralysis/Facial Paresis

No cases of facial paralysis were reported in adolescents (12-15 years of age) as of the data cutoff date (13 March 2021).

Conclusions from Review of Adverse Events of Clinical Interest

Following review of all reported AEs and detailed review of all reported SAEs in Study C4591001 as of the data cutoff date (13 March 2021) in the adolescent (12-15 years of age) population, there were very few AEs of clinical interest corresponding to the CDC list of AESIs. Lymphadenopathy has been identified as related to BNT162b2 in individuals ≥ 16 years of age and it is clearly observed in the 12-15 years of age adolescent group. The AE of anaphylactoid reaction identified in the 16-25 years of age group is consistent with what has been observed in post-authorization safety reviews in the ≥ 16 years of age population. AEs of clinical interest will continue to be monitored in participants of all ages who remain in Study C4591001.

6.2.2.1.4. Other Safety Assessments

6.2.2.1.4.1. Severe COVID-19 Illness

Cases of COVID-19, both overall and those considered as severe, were evaluated per criteria described in [Section 6.2.1.1.1.2](#). Results and reference data (located in Module 5.3.5.1) for updated efficacy against severe disease are discussed in [Section 6.2.2.2.2.2](#).

The protocol had prespecified stopping rules that included monitoring of severe COVID-19 cases, and these stopping criteria were not met.

As of the data cutoff date (13 March 2021), no severe COVID-19 cases were reported in adolescents 12-15 years of age in Study C4591001 (refer to [Section 6.2.2.2.2](#)).

The previously completed final analyses of efficacy for all study participants ≥ 12 years of age (data cutoff date: 14 November 2020) submitted to support the current EUA showed confinement of severe cases predominantly to the placebo group, suggesting no evidence for vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD).

6.2.2.1.4.2. Pregnancy

As of the data cutoff date (13 March 2021), no pregnancies were reported in participants 12-15 years of age. Four pregnancies were reported in the young adults (16-25 years of age) that led to discontinuation from the vaccination period in Study C4591001, and 1 additional participant in the young adult group withdrew from the study due to a reported AE of exposure during pregnancy; none of these participants has given birth as of the data cutoff date.

6.2.2.1.5. Safety Conclusions

Adolescents 12-15 Years of Age

Phase 3 data from approximately 2200 adolescents 12-15 years of age with a median follow-up time of at least 2 months after Dose 2 showed BNT162b2 at 30 μ g was safe and well-tolerated.

Reactogenicity in adolescents 12-15 years of age was mostly mild to moderate and short-lived after dosing (ie, median onset between 1-3 days after dosing and resolution within 1-3 days after onset), similar to the reactogenicity data in the young adults 16-25 years of age. Local reactions presented predominantly as injection site pain with minimal effect of dose number, and systemic events generally increased in frequency and/or severity with increasing dose number; also similar to findings in the 16-25 years of age group. Adolescents tended to have less severe local reactions and systemic events after each vaccine dose compared with young adults. The rate of fever was somewhat higher in the adolescent group compared to the young adult group, especially after the second dose, but fevers were mostly mild to moderate in severity. The observed AE profile did not suggest any serious safety concerns for BNT162b2 vaccination of adolescents 12-15 years of age. Overall, AEs reported for adolescents and young adults reflect age-appropriate events consistent with the respective populations.

As of the data cutoff date (13 March 2021), there were very few AEs of clinical interest corresponding to the CDC list of AESIs reported in adolescents. Lymphadenopathy has been identified as related to BNT162b2 in study participants ≥ 16 years of age and is observed in the adolescent group. One AE of anaphylactoid reaction was identified in a young adult participant, which is consistent post-authorization safety observations in individuals ≥ 16 years of age.

The incidence of SAEs was low in the context of the number of participants enrolled and comparable between BNT162b2 and placebo. The incidence of withdrawals due to AEs was also low and similar between BNT162b2 and placebo groups. No deaths were reported in adolescents 12-15 years of age or in young adults 16-25 years of age included in the safety analyses.

Adults 16-55 Years of Age

The adult (16-25 years of age and 16-55 years of age) safety data included for reference purposes in the context of this EUA amendment for adolescents 12-15 years of age is from approximately 26,000 adults 16-55 years of age, among whom a majority in the BNT162b2 group have at least 6 months of blinded follow-up after Dose 2 in Phase 2/3 of Study C4591001. These data show BNT162b2 at 30 µg was safe and well-tolerated in this age group. Reactogenicity was mostly mild to moderate and short-lived after dosing (ie, median onset between 1-2 days after dosing and resolution within 1-2 days after onset), with local reactions presenting predominantly as injection site pain with minimal effect of dose number, and systemic events generally increasing in frequency and/or severity with increasing dose number.

The review of AEs and SAEs in the adult (16-55 years of age) population presented in this EUA amendment did not suggest new safety concerns. A full and independent safety evaluation of the adult population is being conducted to prepare a full clinical study report in support of licensing/marketing application submissions including a BLA planned in second quarter of 2021.

Comparing adolescents to young adults and adults 16-55 years of age identifies very similar reactogenicity profiles. Reactogenicity after each dose was observed in all groups with similar patterns after Dose 1 and Dose 2. Fever was highest for the adolescent group compared to the young adult group but was still within tolerable limits. Arthralgia and muscle pain were higher in the young adult group than the adolescent group for both doses of BNT162b2. Overall, the differences in reported AEs were age appropriate and not related to vaccination.

6.2.2.2. Efficacy Results

6.2.2.2.1. Efficacy Populations – Adolescents 12-15 Years of Age

The protocol prespecified final analysis of efficacy was completed with a data cutoff date of 14 November 2020. At that time, few adolescents (12-15 years of age) had enrolled in the study, precluding a meaningful efficacy evaluation. An analysis was performed with all accrued cases during blinded follow-up to a data cutoff date of 13 March 2021, for efficacy in adolescents.

In the efficacy analyses, adolescents in the efficacy populations included:

- Evaluable efficacy population without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2: N=1005 in the BNT162b2 group and N=978 in the placebo group.
- Evaluable efficacy population with or without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2: N=1119 in the BNT162b2 group and N=1110 in the placebo group.
- Dose 1 all-available efficacy population: N=1131 in the BNT162b2 group and N=1129 in the placebo group.

Since the efficacy populations include nearly the same number of participants in each group as in the safety population (refer to [Section 6.2.2.1.1.1](#)), the demographics of the efficacy populations are essentially the same as the safety population.

6.2.2.2.2. Efficacy Results – Adolescents 12-15 Years of Age

6.2.2.2.2.1. Vaccine Efficacy Against COVID-19 – Adolescents 12-15 Years of Age

Confirmed Cases of COVID-19 at Least 7 Days after Dose 2 – Evaluable Efficacy Population

Participants Without Evidence of Infection Before and During Vaccination Regimen

As of the data cutoff date for updated efficacy (13 March 2021), confirmed COVID-19 cases in the evaluable efficacy population adolescent group (12-15 years of age) without evidence of prior SARS-CoV-2 infection at least 7 days after Dose 2 included 0 cases in the BNT162b2 group and 16 cases in the placebo group. The observed VE was 100% (2-sided 95% CI: 75.3%, 100.0%) (Table 18).

Table 18. 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 Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|---|--|--|----------------------------------|--|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =1005) | | Placebo (N ^a =978) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 0 | 0.154 (1001) | 16 | 0.147 (972) | 100.0 | (75.3, 100.0) |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test;

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 30MAR2021 (22:23)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:

./nda2_unblinded/C4591001_BLA/adc19ef_ve_cov_7pd2_peds_wo_eval

Participants With or Without Evidence of Infection Before and During Vaccination Regimen

Confirmed COVID-19 cases in the evaluable efficacy population adolescent group (12-15 years of age) with or without evidence of prior SARS-CoV-2 infection at least 7 days after Dose 2 included 0 cases in the BNT162b2 group and 18 cases in the placebo group. The observed VE was 100.0% (2-sided 95% CI: 78.1%, 100.0%) (Table 19).

Table 19. 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

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|---|--|--|-----------------------------------|--|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =1119) | | Placebo (N ^a =1110) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 0 | 0.170 (1109) | 18 | 0.163 (1094) | 100.0 | (78.1, 100.0) |

Abbreviation: VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 30MAR2021 (22:24)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:

./nda2 unblinded/C4591001 BLA/adc19ef ve cov 7pd2 peds eval

All Confirmed Cases of COVID-19 After Dose 1 – All-Available Efficacy Population

As of the data cutoff date (13 March 2021), confirmed COVID-19 cases in the Dose 1 all-available efficacy (modified intention-to-treat) population adolescent group (12-15 years of age) included 3 cases in the BNT162b2 group and 35 cases in the placebo group, with an observed VE of 91.6% (2-sided 95% CI: 73.5%, 98.4%) (Table 20).

The time interval from after Dose 1 to prior to receiving Dose 2 included 3 cases in the BNT162b2 group and 12 cases in the placebo group; these 3 cases in the BNT162 group, which comprised all COVID-19 cases reported in the BNT162b2 group in this population at any time, all occurred within the period from after Dose 1 to <11 days after Dose 1. All 3 of these cases in the BNT162b2 group occurred in participants who had baseline SARS-CoV-2 negative status.

The observed VE for BNT162b2 in adolescents in the Dose 1 all-available population was 100.0% (ie, all cases were confined to the placebo group) for all time intervals starting from ≥ 11 days after Dose 1 to before Dose 2, through ≥ 2 months after Dose 2 and <4 months after Dose 2.

Additional data are presented in Module 5.3.5.1:

16.2.8.2 Listing of Subjects With First COVID-19 Occurrence After Dose 1 – Subjects 12 Through 15 Years of Age – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

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Table 20. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age – Dose 1 All-Available Efficacy Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|--|---|---|--------------------------------|---|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =1131) | | Placebo (N ^a =1129) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence after Dose 1 | 3 | 0.257 (1120) | 35 | 0.250 (1119) | 91.6 | (73.5, 98.4) |
| After Dose 1 to before Dose 2 | 3 | | 12 | | 75.0 | (7.4, 95.5) |
| After Dose 1 to <11 days after Dose 1 | 3 | | 4 | | 25.0 | (-343.3, 89.0) |
| ≥11 Days after Dose 1 to before Dose 2 | 0 | | 8 | | 100.0 | (41.4, 100.0) |
| Dose 2 to 7 days after Dose 2 | 0 | | 5 | | 100.0 | (-9.1, 100.0) |
| ≥7 Days after Dose 2 | 0 | | 18 | | 100.0 | (77.3, 100.0) |
| ≥7 days after Dose 2 to <2 Months after Dose 2 | 0 | | 16 | | 100.0 | (74.1, 100.0) |
| ≥2 Months after Dose 2 to <4 Months after Dose 2 | 0 | | 2 | | 100.0 | (-432.5, 100.0) |

Abbreviation: VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method (adjusted for surveillance time for overall row).

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 30MAR2021 (22:24)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:

./nda2_unblinded/C4591001_BLA/adc19ef_ve_cov_pdl_peds_aai

6.2.2.2.2. Vaccine Efficacy Against Severe COVID-19 – Adolescents 12-15 Years of Age

No severe COVID-19 cases (per protocol definition or CDC criteria) were reported in adolescents (12-15 years of age) as of the data cutoff date (13 March 2021).

Additional data are presented in Module 5.3.5.1:

[16.2.8.1.1 Listing of Subjects with First Severe COVID-19 Occurrence After Dose 1 – Subjects 12 Through 15 Years of Age – Blinded Placebo-Controlled Follow-Up Period – Dose 1 All-Available Efficacy Population – CDC+Protocol](#)

6.2.2.2.3. Efficacy Conclusions – Adolescents 12-15 Years of Age

Descriptive efficacy analyses were conducted for the adolescent group on cases accrued during blinded follow-up period through the data cutoff date of 13 March 2021.

In the adolescent group, in updated efficacy analyses in the evaluable efficacy population based on cases reported from at least 7 days after Dose 2 through the data cutoff date, the observed VE was 100% (95% CI: 75.3%, 100%) for individuals without evidence of prior SARS-CoV-2 infection before and during vaccination regimen, and 100% (2-sided 95% CI: 78.1%, 100%) for those with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen.

In the efficacy analysis for the Dose 1 all-available (modified intention-to-treat) population, included 3 cases in the BNT162b2 group and 35 cases in the placebo group, with an observed VE of 91.6% (2-sided 95% CI: 73.5%, 98.4%), with no cases reported in the BNT162b2 group starting from ≥ 11 days after Dose 1.

No severe cases were reported in the 12-15 years of age group as of the date cutoff date.

Overall, these efficacy data strongly support BNT162b2 use in adolescents 12-15 years of age.

6.2.2.3. Immunogenicity Results

6.2.2.3.1. Immunogenicity Populations – Adolescents 12-15 Years of Age

Immunogenicity population data for adolescent and young adult groups are summarized below.

Additional data are presented in Module 5.3.5.1:

[Immunogenicity Blood Samples Drawn – Subjects 12 Through 15 and 16 Through 25 Years of Age \(Immunogenicity Subset\)](#)

[16.2.3.1.1 Listing of Subjects Excluded From Immunogenicity Populations – Subjects 12 Through 25 Years of Age \(Immunogenicity Subset\)](#)

6.2.2.3.1.1. Disposition and Data Sets Analyzed – Adolescents 12-15 Years of Age

For immunogenicity analyses, it was planned to select a random sample of 280 participants in the BNT162b2 group for each of the two age groups as an immunogenicity subset for the NI assessment. To maintain blinding of the laboratory personnel, 50 participants in each placebo group were also randomly selected from each of the two age groups for serology testing.

The Dose 2 evaluable immunogenicity population for adolescents 12-15 years of age included 209 participants in the BNT162b2 group and 36 participants in the placebo group), and for young adults 16-25 years of age included 186 participants in the BNT162b2 group and 32 participants in the placebo group. Reasons for participant exclusion from the evaluable immunogenicity populations are shown in [Table 21](#). The majority of exclusions were due to participants not having at least 1 valid and determinate immunogenicity result after Dose 2, mostly as the result of testing laboratory supply limitation of the qualified viral lot (refer to [Section 6.2.1.1.1.3](#)) and were generally balanced across age and vaccine groups.

Table 21. Immunogenicity Populations – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset)

| | Vaccine Group (as Randomized) | | | |
|---|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| | BNT162b2 (30 µg) | | Placebo | |
| | 12-15 Years n ^a (%) | 16-25 Years n ^a (%) | 12-15 Years n ^a (%) | 16-25 Years n ^a (%) |
| Randomized ^b | 280 (100.0) | 280 (100.0) | 50 (100.0) | 50 (100.0) |
| Dose 2 all-available immunogenicity population | 210 (75.0) | 191 (68.2) | 36 (72.0) | 34 (68.0) |
| Subjects excluded from Dose 2 all-available immunogenicity population | 70 (25.0) | 89 (31.8) | 14 (28.0) | 16 (32.0) |
| Reason for exclusion | | | | |
| Did not receive Dose 2 | 1 (0.4) | 0 | 0 | 0 |
| Did not have at least 1 valid and determinate immunogenicity result after Dose 2 | 69 (24.6) | 89 (31.8) | 14 (28.0) | 16 (32.0) |
| Dose 2 evaluable immunogenicity population | 209 (74.6) | 186 (66.4) | 36 (72.0) | 32 (64.0) |
| Subjects excluded from Dose 2 evaluable immunogenicity population | 71 (25.4) | 94 (33.6) | 14 (28.0) | 18 (36.0) |
| Reason for exclusion ^c | | | | |
| Did not receive 2 doses of the vaccine to which they were randomly assigned | 1 (0.4) | 0 | 0 | 0 |
| Did not receive Dose 2 within 19-42 days after Dose 1 | 1 (0.4) | 2 (0.7) | 0 | 2 (4.0) |
| Did not have at least 1 valid and determinate immunogenicity result after Dose 2 | 69 (24.6) | 89 (31.8) | 14 (28.0) | 16 (32.0) |
| Did not have blood collection within 28-42 days after Dose 2 | 3 (1.1) | 16 (5.7) | 0 | 3 (6.0) |
| Had important protocol deviation(s) as determined by the clinician | 0 | 0 | 0 | 1 (2.0) |
| a. n = Number of subjects with the specified characteristic. b. These values are the denominators for the percentage calculations. c. Subjects may have been excluded for more than 1 reason. PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (00:54) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adva_s008_imm_pop_ped | | | | |

6.2.2.3.1.2. Demographics – Adolescents 12-15 Years of Age

In the Dose 2 evaluable immunogenicity population adolescent (12-15 years of age) BNT162b2 group, 50.7% of participants were male; 88.0% were White, 7.7% were Black or African American, and 2.4% were Asian; 10.5% were Hispanic/Latino; and the median age was 14 years (Table 22). Baseline SARS-CoV-2 status was positive for 4.8% of adolescent participants in the BNT162b2 group. Obese adolescents (based on age- and sex-specific body mass index) made up 8.3% (placebo group) to 11.5% (BNT162b2 group) of this age group in the evaluable immunogenicity population.

Demographics were generally similar for BNT162b2 and placebo, and between adolescents and young adults 16-25 years of age.

Demographics of the evaluable immunogenicity population were similar to those in the all-available immunogenicity population. Likewise, the immunogenicity population demographics were generally similar to those in the safety population ([Section 6.2.2.1.1.4](#)).

Additional data are presented in Module 5.3.5.1:

[Demographic Characteristics – Subjects 12 Through 15 and 16 Through 25 Years of Age \(Immunogenicity Subset\) – Dose 2 All-Available Immunogenicity Population](#)

Table 22. Demographic Characteristics – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population

| | Vaccine Group (as Randomized) | | | |
|---|--|--|---|---|
| | BNT162b2 (30 µg) | | Placebo | |
| | 12-15 Years (N ^a =209) n ^b (%) | 16-25 Years (N ^a =186) n ^b (%) | 12-15 Years (N ^a =36) n ^b (%) | 16-25 Years (N ^a =32) n ^b (%) |
| Sex | | | | |
| Male | 106 (50.7) | 92 (49.5) | 21 (58.3) | 14 (43.8) |
| Female | 103 (49.3) | 94 (50.5) | 15 (41.7) | 18 (56.3) |
| Race | | | | |
| White | 184 (88.0) | 147 (79.0) | 31 (86.1) | 28 (87.5) |
| Black or African American | 16 (7.7) | 15 (8.1) | 3 (8.3) | 2 (6.3) |
| American Indian or Alaska Native | 1 (0.5) | 3 (1.6) | 0 | 1 (3.1) |
| Asian | 5 (2.4) | 10 (5.4) | 1 (2.8) | 1 (3.1) |
| Native Hawaiian or other Pacific Islander | 0 | 3 (1.6) | 0 | 0 |
| Multiracial | 3 (1.4) | 6 (3.2) | 1 (2.8) | 0 |
| Not reported | 0 | 2 (1.1) | 0 | 0 |
| Racial designation | | | | |

Table 22. Demographic Characteristics – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population

| | Vaccine Group (as Randomized) | | | |
|--|--|--|---|---|
| | BNT162b2 (30 µg) | | Placebo | |
| | 12-15 Years (N ^a =209) n ^b (%) | 16-25 Years (N ^a =186) n ^b (%) | 12-15 Years (N ^a =36) n ^b (%) | 16-25 Years (N ^a =32) n ^b (%) |
| Japanese | 1 (0.5) | 0 | 0 | 0 |
| Ethnicity | | | | |
| Hispanic/Latino | 22 (10.5) | 31 (16.7) | 2 (5.6) | 7 (21.9) |
| Non-Hispanic/non-Latino | 187 (89.5) | 154 (82.8) | 34 (94.4) | 25 (78.1) |
| Not reported | 0 | 1 (0.5) | 0 | 0 |
| Country | | | | |
| USA | 209 (100.0) | 186 (100.0) | 36 (100.0) | 32 (100.0) |
| Age at vaccination (years) | | | | |
| Mean (SD) | 13.5 (1.12) | 20.6 (3.09) | 13.4 (1.17) | 20.3 (3.05) |
| Median | 14.0 | 21.0 | 13.0 | 19.5 |
| Min, max | (12, 15) | (16, 25) | (12, 15) | (16, 25) |
| Baseline SARS-CoV-2 status | | | | |
| Positive ^c | 10 (4.8) | 8 (4.3) | 2 (5.6) | 1 (3.1) |
| Negative ^d | 194 (92.8) | 178 (95.7) | 33 (91.7) | 31 (96.9) |
| Missing | 5 (2.4) | 0 | 1 (2.8) | 0 |
| Body mass index (BMI) Obese ^e | | | | |
| Yes | 24 (11.5) | 43 (23.1) | 3 (8.3) | 4 (12.5) |
| No | 185 (88.5) | 143 (76.9) | 33 (91.7) | 28 (87.5) |

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately.

a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.

b. n = Number of subjects with the specified characteristic.

c. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.

d. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.

e. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm. For 16 through 25 years age group, obesity is defined as BMI ≥ 30.0 kg/m².

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 02APR2021 (00:07) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:

./nda2_unblinded/C4591001_BLA1/adsl_s005_demo_ped_d2_ci

6.2.2.3.2. Noninferiority Between 12-15 Years of Age and 16-25 Years of Age Groups

Geometric Mean Ratio (GMR) in Neutralization Titers

The immune response to BNT162b2 in adolescents 12-15 years of age was noninferior to that observed in young adults 16-25 years of age, based on SARS-CoV-2 50% neutralizing titers at 1 month after Dose 2, in participants without prior evidence of SARS-CoV-2 infection, and in fact greatly exceeded the response observed in young adults. The GMT ratio of adolescents to young adults was 1.76 (2-sided 95% CI: 1.47, 2.10), meeting the 1.5-fold NI criterion (ie, lower bound of the 2-sided 95% CI for GMR >0.67) ([Table 23](#)). Of note, the lower bound of the 2-sided 95% CI for the GMR is >1 which indicates a statistically greater response in the adolescents than that of young adults.

Seroresponse

Among participants without prior evidence of SARS-CoV-2 infection up to 1 month after Dose 2 of BNT162b2, high proportions (97.9% of adolescents and 100.0% of young adults) had a ≥ 4 -fold rise (seroresponse) in SARS-CoV-2 50% neutralizing titers from before vaccination to 1 month after Dose 2. The difference in proportions of participants who had a ≥ 4 -fold rise between the two age groups (adolescents – young adults) was -2.1% (2-sided 95% CI: -6.0%, 0.9%) ([Table 24](#)).

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Table 23. Summary of Geometric Mean Ratio – NT50 – Comparison of Subjects 12 Through 15 Years of Age to Subjects 16 Through 25 Years of Age (Immunogenicity Subset) – Subjects Without Evidence of Infection up to 1 Month After Dose 2 – Dose 2 Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Vaccine Group (as Randomized) | | | | | |
|--|--|-------------------------------|--|----------------|--|--|--|
| | | BNT162b2 (30 µg) | | | | | |
| | | 12-15 Years | | 16-25 Years | | 12-15 Years/16-25 Years | |
| | | n ^b | GMT ^c (95% CI ^c) | n ^b | GMT ^c (95% CI ^c) | GMR ^d (95% CI ^d) | Met Noninferiority Objective ^e (Y/N) |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 2/1 Month | 190 | 1239.5 (1095.5, 1402.5) | 170 | 705.1 (621.4, 800.2) | 1.76 (1.47, 2.10) | Y |

Abbreviations: GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Subjects who had no serological or virological evidence (up to 1 month after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 were included in the analysis.

a. Protocol-specified timing for blood sample collection.

b. n = Number of subjects with valid and determinate assay results for the specified assay at the given dose/sampling time point.

c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to $0.5 \times \text{LLOQ}$.

d. GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers (Group 1 [12-15 years] – Group 2 [16-25 years]) and the corresponding CI (based on the Student t distribution).

e. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:25) Source Data: adva Table Generation: 27MAR2021 (04:54)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adva_s001_gmr_ped_ev_eval

Table 24. Number (%) of Subjects Achieving a ≥ 4 -Fold Rise From Before Vaccination to Each Subsequent Time Point 1 Month After Dose 2 – NT50 – Comparison of Subjects 12 Through 15 Years of Age to Subjects 16 Through 25 Years of Age (Immunogenicity Subset) – Subjects Without Evidence of Infection up to 1 Month After Dose 2 – Dose 2 Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Vaccine Group (as Randomized) | | | | | |
|--|--|-------------------------------|--|----------------|--|--------------------------------------|-------------|
| | | BNT162b2 (30 µg) | | | | Difference (95% CI ^f) | |
| | | 12-15 Years | | 16-25 Years | | | |
| | | N ^b | n ^c (%) (95% CI ^d) | N ^b | n ^c (%) (95% CI ^d) | % ^e | |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 2/1 Month | 143 | 140 (97.9) (94.0, 99.6) | 124 | 124 (100.0) (97.1, 100.0) | -2.1 | (-6.0, 0.9) |

Abbreviations: LLOQ = lower limit of quantitation; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Subjects who had no serological or virological evidence (up to 1 month after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 were included in the analysis.

Note: Baseline assay results below the LLOQ were set to LLOQ in the analysis.

a. Protocol-specified timing for blood sample collection.

b. N = number of subjects with valid and determinate assay results for the specified assay both before vaccination and at the given dose/sampling time point. These values are the denominators for the percentage calculations.

c. n = Number of subjects with ≥ 4 -fold rise from before vaccination for the given assay at the given dose/sampling time point.

d. Exact 2-sided CI based on the Clopper and Pearson method.

e. Difference in proportions, expressed as a percentage (12-15 years – 16-25 years).

f. 2-Sided CI, based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:25) Source Data: adva Table Generation: 27MAR2021 (05:56)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adva_s003_4fold_ped_eval

6.2.2.3.3. SARS-CoV-2 Neutralizing Titers and Fold Rises – Adolescents 12-15 Years of Age

SARS-CoV-2 neutralizing titer data for adolescents and young adults are summarized below for the Dose 2 evaluable immunogenicity population. Results for the Dose 2 all-available immunogenicity population were similar to those observed for the Dose 2 evaluable immunogenicity population.

Additional data are presented in Module 5.3.5.1:

16.2.6.1 Listing of Assay Data – Subjects 12 Through 25 Years of Age

Summary of Geometric Mean Titers, by Baseline SARS-CoV-2 Status – NT50 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 All-Available Immunogenicity Population

Summary of Geometric Mean Fold Rise From Before Vaccination to Each Subsequent Time Point, by Baseline SARS-CoV-2 Status – NT50 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 All-Available Immunogenicity Population

Immunogenicity results were summarized by baseline SARS-CoV-2 status (ie, participants with or without serological or virological evidence of SARS-CoV-2 infection before vaccination). Positive baseline SARS-CoV-2 status was defined as positive by N-binding antibody at Visit 1, or positive NAAT at Visit 1, or a medical history of COVID-19; negative baseline SARS-CoV-2 status was defined as negative by N-binding antibody and negative NAAT at Visit 1. Results are summarized for all participants and by baseline SARS-CoV-2 status.

Geometric Mean Titers (GMTs)

At 1 month after Dose 2 (Day 52) of BNT162b2, substantial increases in SARS-CoV-2 50% neutralizing GMTs were observed in both age groups, with a greater magnitude of increase in the adolescent group compared with the young adult group (Figure 5, Figure 6, Table 25).

The neutralizing GMT in adolescents at 1 month after Dose 2 was approximately 1.76-fold that of the young adult group. As expected, the neutralizing GMTs were low in both placebo groups.

Geometric Mean Titers (GMTs) by Baseline SARS-CoV-2 Status

Vaccination with BNT162b2 induced an increased immune response at 1 month after Dose 2 for all participants, regardless of baseline SARS-CoV-2 positive or negative status. Adolescents who were baseline SARS-CoV-2 positive had SARS-CoV-2 50% neutralizing GMTs approximately 1.89-fold that of adolescents who were baseline negative (Table 25). A similar pattern was observed for baseline SARS-CoV-2 positive versus negative young adults.

Geometric Mean Fold-Rise (GMFR) in Titers

The GMFRs of SARS-CoV-2 50% serum neutralizing titers from before vaccination to 1 month after Dose 2 of BNT162b2 were robust, with a greater magnitude of rise in the adolescent group (118.3) compared with the young adult group (71.2) (Table 26).

Geometric Mean Fold-Rise (GMFR) in Titers by Baseline SARS-CoV-2 Status

The GMFRs were higher in the adolescent compared to young adult group 1 month after the second dose. Given the limited sample size for those positive at baseline, the GMFRs were numerically higher in those who were negative at baseline ([Table 26](#)).

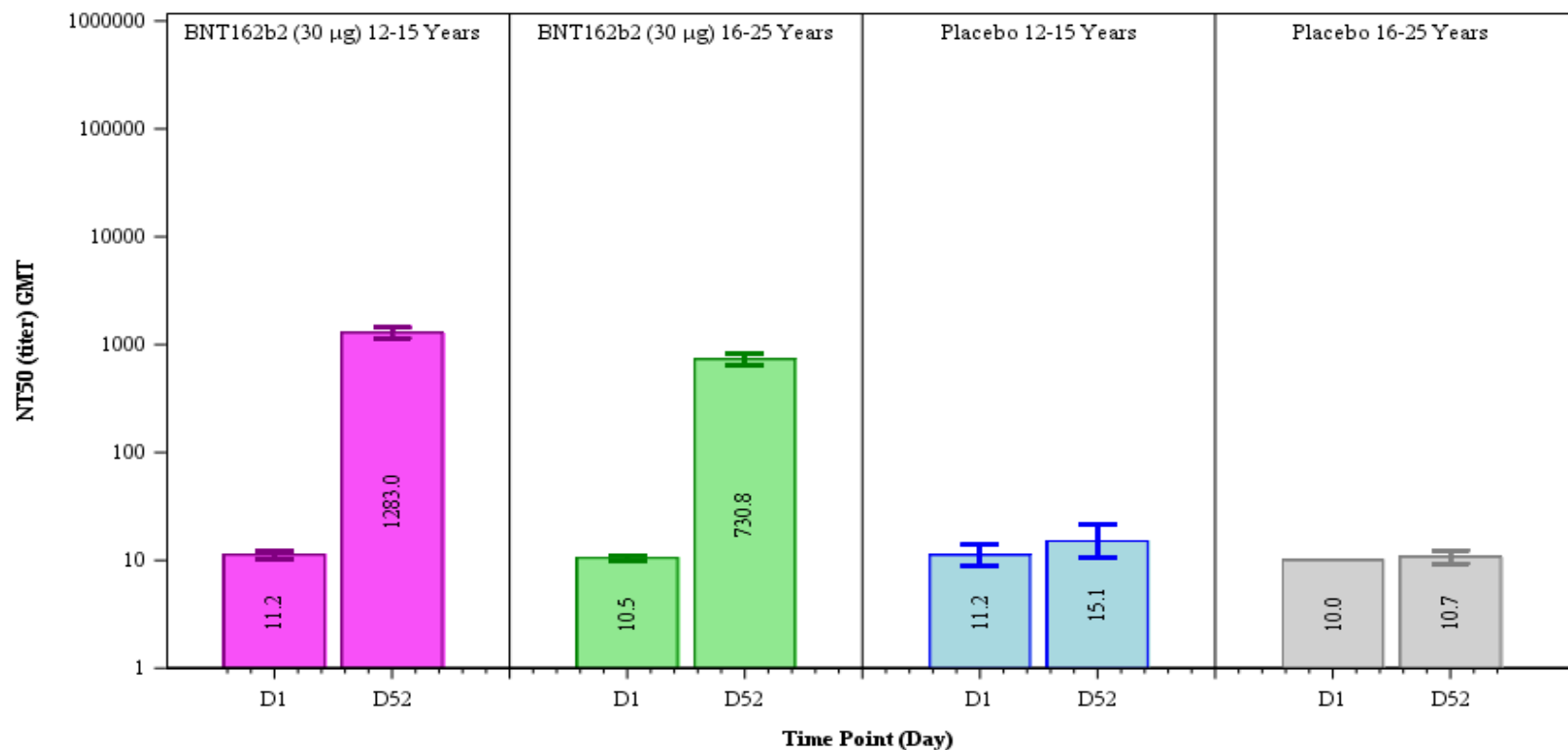
Seroresponse Rate

Proportions of participants with a ≥ 4 -fold rise in SARS-CoV-2 50% neutralizing titers from before vaccination to 1 month after Dose 2 of BNT162b2 (seroresponse rate) were 98.1% in adolescents and 99.3% in young adults ([Table 27](#)). As expected, very few placebo participants reached a ≥ 4 -fold rise in SARS-CoV-2 neutralizing titers from before to 1 month after Dose 2.

Seroresponse Rate by Baseline SARS-CoV-2 Status

Adolescents who were baseline SARS-CoV-2 positive or negative had similar seroresponse rates (100.0% vs 97.9%) ([Table 27](#)).

Figure 5. Geometric Mean Titers: SARS-CoV-2 Neutralization Assay – NT50 – Subjects 12-15 and 16-25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population



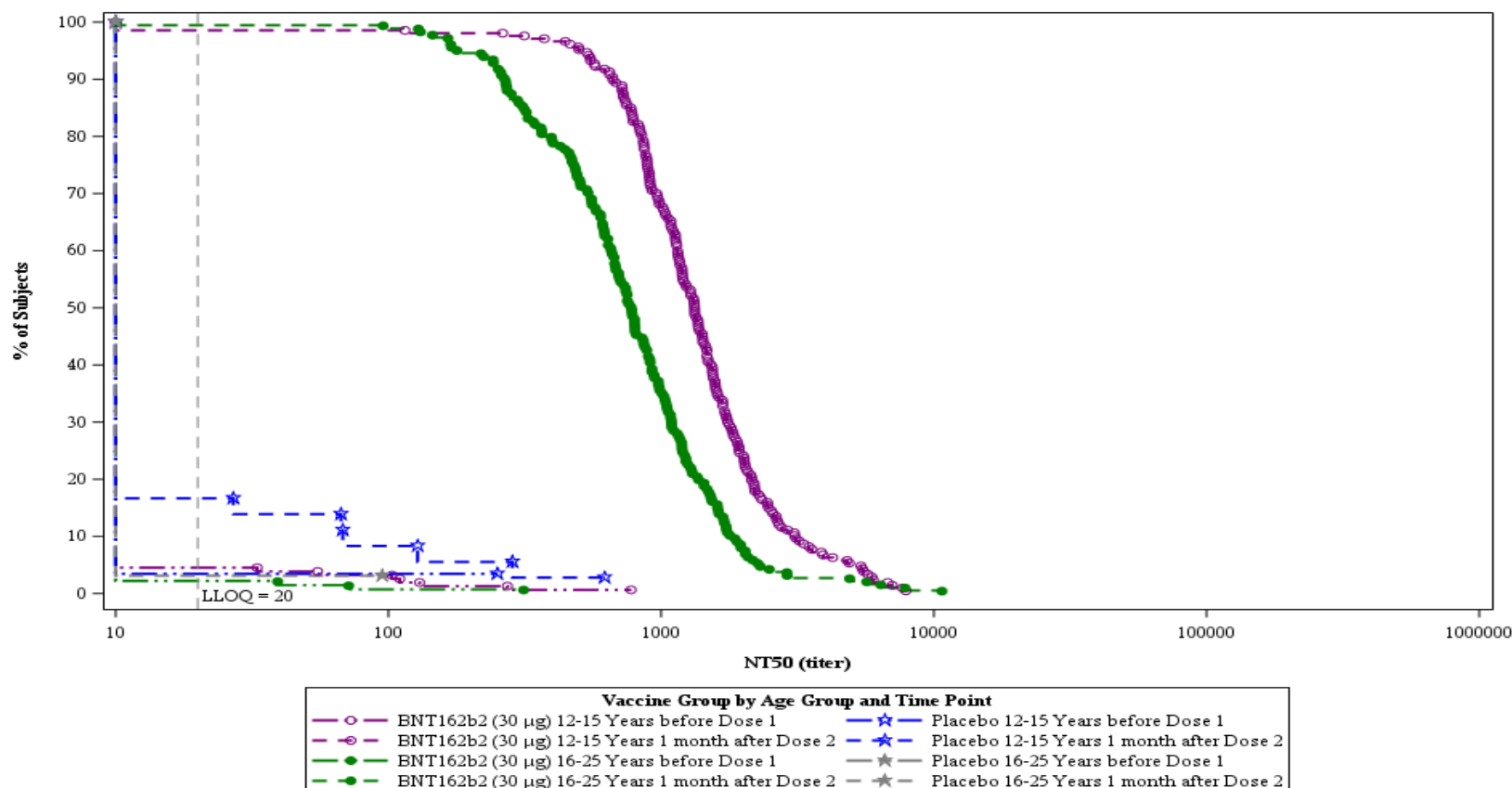
Abbreviations: D = day; GMT = geometric mean titer; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Number within each bar denotes geometric mean titer.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:25) Source Data: adva Table Generation: 27MAR2021 (04:54)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: /nda2_unblinded/C4591001_BLA/adva_f002_sars_50_ped

Figure 6. Reverse Cumulative Distribution Curves, SARS-CoV-2 Neutralization Assay – NT50 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population



Abbreviations: LLOQ = lower limit of quantitation; NT50 = 50% neutralizing titer; RCDC = reverse cumulative distribution curve;

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: LLOQ value is represented using a vertical line. Assay results below the LLOQ were set to $0.5 \times \text{LLOQ}$ in the analysis.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:25) Source Data: adva Table Generation: 27MAR2021 (04:54)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: /nda2_unblinded/C4591001_BLA/adva_f003_sars_50_ped

Table 25. Summary of Geometric Mean Titers, by Baseline SARS-CoV-2 Status – NT50 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Baseline SARS-CoV-2 Status ^b | Vaccine Group (as Randomized) | | | | | | | |
|---|--|---|-------------------------------|---|----------------|---|----------------|---|----------------|---|
| | | | BNT162b2 (30 µg) | | | | Placebo | | | |
| | | | n ^c | 12-15 Years GMT ^d (95% CI ^d) | n ^c | 16-25 Years GMT ^d (95% CI ^d) | n ^c | 12-15 Years GMT ^d (95% CI ^d) | n ^c | 16-25 Years GMT ^d (95% CI ^d) |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 1/Prevax | ALL | 155 | 11.2 (10.3, 12.3) | 136 | 10.5 (9.9, 11.2) | 29 | 11.2 (8.9, 14.0) | 24 | 10.0 (10.0, 10.0) |
| | | POS | 8 | 54.1 (19.7, 148.7) | 5 | 38.6 (6.4, 232.9) | 1 | 251.0 (NE, NE) | 0 | NE (NE, NE) |
| | | NEG | 146 | 10.3 (9.7, 10.9) | 131 | 10.0 (10.0, 10.0) | 27 | 10.0 (10.0, 10.0) | 24 | 10.0 (10.0, 10.0) |
| | 2/1 Month | ALL | 207 | 1283.0 (1139.6, 1444.5) | 185 | 730.8 (646.7, 825.8) | 36 | 15.1 (10.7, 21.4) | 32 | 10.7 (9.3, 12.4) |
| | | POS | 10 | 2342.2 (1308.7, 4191.8) | 8 | 1439.2 (727.1, 2848.7) | 2 | 191.0 (1.2, 30873.6) | 1 | 10.0 (NE, NE) |
| | | NEG | 192 | 1239.2 (1096.6, 1400.5) | 177 | 708.7 (626.4, 802.0) | 33 | 13.1 (9.7, 17.7) | 31 | 10.8 (9.3, 12.5) |

Abbreviations: COVID-19 = coronavirus disease 2019; GMT = geometric mean titer; LLOQ = lower limit of quantitation;

NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein-binding; NE = not estimable; NEG = negative;

NT50 = 50% neutralizing titer; POS = positive; Prevax = before vaccination; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

a. Protocol-specified timing for blood sample collection.

b. POS = positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19. NEG = negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19. ALL = irrespective of baseline SARS-CoV-2 status, including missing baseline status.

c. n = Number of subjects with valid and determinate assay results for the specified assay at the given dose/sampling time point.

d. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to $0.5 \times \text{LLOQ}$.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:25) Source Data: adva Table Generation: 27MAR2021 (04:54)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adva_s001_gm_ped_eval

Table 26. Summary of Geometric Mean Fold Rise From Before Vaccination to Each Subsequent Time Point, by Baseline SARS-CoV-2 Status – NT50 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Baseline SARS-CoV-2 Status ^b | Vaccine Group (as Randomized) | | | | | | | |
|--|--|---|-------------------------------|--|----------------|--|----------------|--|----------------|--|
| | | | BNT162b2 (30 µg) | | | | Placebo | | | |
| | | | n ^c | 12-15 Years GMFR ^d (95% CI ^d) | n ^c | 16-25 Years GMFR ^d (95% CI ^d) | n ^c | 12-15 Years GMFR ^d (95% CI ^d) | n ^c | 16-25 Years GMFR ^d (95% CI ^d) |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 2/1 Month | ALL | 154 | 118.3 (101.4, 137.9) | 135 | 71.2 (61.3, 82.7) | 29 | 1.4 (1.0, 1.9) | 24 | 1.1 (0.9, 1.3) |
| | | POS | 8 | 47.6 (26.4, 86.0) | 5 | 47.1 (3.1, 721.4) | 1 | 1.1 (NE, NE) | 0 | NE (NE, NE) |
| | | NEG | 145 | 125.0 (106.9, 146.2) | 130 | 72.3 (62.9, 83.2) | 27 | 1.4 (1.0, 2.0) | 24 | 1.1 (0.9, 1.3) |

Abbreviations: COVID-19 = coronavirus disease 2019; GMFR = geometric mean fold rise; LLOQ = lower limit of quantitation; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein-binding; NE = not estimable; NEG = negative; NT50 = 50% neutralizing titer; POS = positive; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

a. Protocol-specified timing for blood sample collection.

b. POS = positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19. NEG = negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19. ALL = irrespective of baseline SARS-CoV-2 status, including missing baseline status.

c. n = Number of subjects with valid and determinate assay results for the specified assay both prevaccination time points and at the given dose/sampling time point.

d. GMFRs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to $0.5 \times \text{LLOQ}$ in the analysis.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:25) Source Data: adva Table Generation: 27MAR2021 (04:54)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adva_s002_gmfr_ped_eval

Table 27. Number (%) of Subjects Achieving a ≥ 4 -Fold Rise From Before Vaccination to Each Subsequent Time Point, by Baseline SARS-CoV-2 Status – NT50 – Subjects 12 Through 15 and 16 Through 25 Years of Age (Immunogenicity Subset) – Dose 2 Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Baseline SARS-CoV-2 Status ^b | Vaccine Group (as Randomized) | | | | | | | |
|---|--|---|-------------------------------|--|----------------|--|----------------|--|----------------|--|
| | | | BNT162b2 (30 µg) | | | | Placebo | | | |
| | | | 12-15 Years | | 16-25 Years | | 12-15 Years | | 16-25 Years | |
| | | | N ^c | n ^d (%) (95% CI ^e) | N ^c | n ^d (%) (95% CI ^e) | N ^c | n ^d (%) (95% CI ^e) | N ^c | n ^d (%) (95% CI ^e) |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 2/1 Month | ALL | 154 | 151 (98.1) (94.4, 99.6) | 135 | 134 (99.3) (95.9, 100.0) | 29 | 1 (3.4) (0.1, 17.8) | 24 | 1 (4.2) (0.1, 21.1) |
| | | POS | 8 | 8 (100.0) (63.1, 100.0) | 5 | 4 (80.0) (28.4, 99.5) | 1 | 0 (0.0) (0.0, 97.5) | 0 | 0 (NE) (NE, NE) |
| | | NEG | 145 | 142 (97.9) (94.1, 99.6) | 130 | 130 (100.0) (97.2, 100.0) | 27 | 1 (3.7) (0.1, 19.0) | 24 | 1 (4.2) (0.1, 21.1) |

Abbreviations: LLOQ = lower limit of quantitation; NE = not estimable; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Baseline assay results below the LLOQ were set to LLOQ in the analysis.

a. Protocol-specified timing for blood sample collection.

b. POS = positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19. NEG = negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19. ALL = irrespective of baseline SARS-CoV-2 status, including missing baseline status

c. N = number of subjects with valid and determinate assay results for the specified assay both before vaccination and at the given dose/sampling time point. These values are the denominators for the percentage calculations.

d. n = Number of subjects with ≥ 4 -fold rise from before vaccination for the given assay at the given dose/sampling time point.

e. Exact 2-sided CI based on the Clopper and Pearson method.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:25) Source Data: adva Table Generation: 27MAR2021 (06:29)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adva_s001_4fold_ped_eval

6.2.2.3.4. Immunogenicity Conclusions – Adolescents 12-15 Years of Age

Immune response to Pfizer-BioNTech COVID-19 Vaccine in SARS-CoV-2 50% neutralizing titers in adolescents 12-15 years of age was noninferior to (and in fact exceeded) the immune response in young adults 16-25 years of age, which provides immunobridging for adolescents in pivotal Study C4591001. Substantial increases over baseline in neutralizing GMTs and high seroresponse rates were observed at 1 month after Dose 2 in both age groups, which were observed for participants with baseline SARS-CoV-2 positive and negative status. The vast majority of BNT162b2 recipients in both age groups achieved a ≥ 4 -fold rises from before vaccination to 1 month after Dose 2.

7. POTENTIAL RISKS AND BENEFITS

7.1. Risk-Benefit Assessment

7.1.1. Risks

This EUA amendment includes an evaluation of safety data from Phase 3 of Study C4591001 from approximately 2200 participants 12-15 years of age among whom a majority had follow-up to at least 2 months after Dose 2. Corresponding data from young adults 16-25 years of age is presented for reference as is safety data up to approximately 6 months after Dose 2 from the protocol specified younger adult group (16-55 years of age).

The reactogenicity profile of adolescents was typically mild to moderate, arose within the first 1-3 days after dosing, with reactions or events that were short-lived. The most common prompted local reaction in adolescents was injection site pain. The most common prompted systemic events reported in adolescents included fatigue, headache, muscle and joint pain, and chills. The frequency of any severe systemic event after dosing was low.

Comparing adolescents to young adults and adults 16-55 years of age identifies similar reactogenicity profiles. Reactogenicity after each dose was observed in all groups with similar patterns after Dose 1 and Dose 2. Fever incidence was somewhat higher for the adolescent group compared to the young adult group but was still within tolerable limits. Arthralgia and muscle pain were higher in the young adult group than the adolescent group for both doses of BNT162b2. Overall, the differences in reported AEs were age appropriate and not related to vaccination.

The AE profile among adolescents mostly reflects reactogenicity events, with low incidences of severe and/or related events. The incidence of SAEs in adolescents was low and similar between the vaccine and placebo groups. Few adolescents withdrew from the study due to AEs. No deaths occurred in the adolescent group. Review of AEs, SAEs, and events of clinical interest suggested no clear patterns or additional safety concerns among adolescents. Safety follow-up in the larger study population of adults 16-55 years of age has suggested no new safety signals and continues to support a safe and tolerable profile for BNT162b2.

As of the safety data cutoff date (13 March 2021), no severe COVID-19 cases were reported in adolescent group.

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Study participants continue to be followed for 2 years or end of study. AE monitoring and surveillance plans for Pfizer-BioNTech COVID-19 Vaccine recipients under an EUA are referenced in [Section 13](#).

7.1.2. Benefits

COVID-19 is a serious and potentially fatal or life-threatening human infection. Based on the available clinical data in adolescents, including immunobridging between adolescents and young adults, it is expected that Pfizer-BioNTech COVID-19 Vaccine will elicit an immune response that is likely to confer protection against COVID-19 in individuals 12-15 years of age. The duration of protection is currently unknown.

Immunobridging based on NI of SARS-CoV-2 neutralizing GMTs for adolescents compared to young adults provides evidence of vaccine effectiveness in the adolescent group. Immunogenicity data from adolescent and young adult participants showed robust neutralizing GMTs after vaccination with 2 doses of BNT162b2 at 30 µg in both adolescents and young adults. This response was evident in the 50% neutralizing GMTs of participants with SARS-CoV-2 negative status, and further boosted in baseline SARS-CoV-2 positive participants with prior evidence of SARS-CoV-2 infection. Declaration of NI for neutralizing GMTs was based on a 1.5-fold margin for the adolescent versus young adult groups; adolescent immune responses actually exceeded that of young adults. These data provide reassurance that the vaccine will provide a robust immune response to SARS-CoV-2 in the adolescent population.

Updated descriptive efficacy analyses for adolescents, based on confirmed cases COVID-19 reported from at least 7 days after Dose 2 through the data cutoff date (13 March 2021), included observed VE of 100.0% (2-sided 95% CI: 75.3%, 100.0%) for individuals without evidence of prior SARS-CoV-2 infection before and during vaccination regimen, and 100.0% (2-sided 95% CI: 78.1%, 100.0%) for individuals with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen. In the Dose 1 all-available (modified intention-to-treat) population, 3 participants in the BNT162b2 group and 35 participants in the placebo group had COVID-19 cases occurring after Dose 1, for an observed VE of 91.6% (2-sided 95% CI: 73.5%, 98.4%). All 3 cases in the BNT162b2 group occurred within the period from after Dose 1 up to <11 days after Dose 1 (prior to Dose 2), after which time the VE was 100.0% for BNT162b2 (assessed up to ≥2 months after Dose 2 and <4 months after Dose 2). No severe COVID-19 cases were reported in individuals in the 12-15 years of age group, based on either protocol definition (ie, per FDA criteria) or per CDC criteria for severity.

Taken together, efficacy and immunogenicity data strongly support a positive benefit for the Pfizer-BioNTech COVID-19 Vaccine 2-dose regimen in adolescents 12-15 years of age. The vaccine provides protection against COVID-19 and induces a robust immune response for individuals 12-15 years of age that has greater magnitude than that observed in young adults, including immune responses for individuals with and without prior exposure to SARS-CoV-2.

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7.1.3. Risk-Benefit Assessment

The available clinical evidence for Pfizer-BioNTech COVID-19 Vaccine effectiveness includes induction of strong immune responses and overwhelmingly high vaccine efficacy with a satisfactory profile, suggesting that the vaccine confers safe and effective protection against COVID-19 in individuals ≥ 12 years of age.

The potential risks are based on the observed clinical study safety profile to date, which shows mostly mild reactogenicity, low incidence of severe or serious events, and no new clinically concerning safety observations or safety concerns. The vaccine has been shown to be safe and well-tolerated across age groups and irrespective of prior infection with SARS-CoV-2. Confinement of severe COVID-19 cases mostly to placebo recipients versus BNT162b2 recipients (all reported in adult age groups to date) suggests no evidence of VAED.

Post-authorization safety reviews including spontaneous safety reporting from all countries/regions in which BNT162b2 is authorized or conditionally approved, of which a summary report is submitted to regulatory authorities on a monthly basis, have suggested no new important risks except for anaphylaxis which is now an identified risk added to the Pharmacovigilance Plan (refer to [Section 13](#)).

Efficacy data suggest highly effective protection against COVID-19 in a broad population of individuals across demographic characteristics including age and prior SARS-CoV-2 infection, with 100% VE observed in adolescents 12-15 years of age. Immunobridging for adolescents 12-15 years of age, who had noninferior neutralizing GMTs compared to young adults 16-25 years of age, supports evidence of vaccine effectiveness in the adolescent age group.

Overall, the potential risks and benefits, as assessed by the safety profile and the efficacy and immunogenicity of the Pfizer-BioNTech COVID-19 Vaccine, are balanced in favor of the potential benefits to prevent COVID-19 in immunized individuals 12-15 years of age. Important risks of the Pfizer-BioNTech COVID-19 Vaccine are described in the Pharmacovigilance Plan and will continue to be assessed and minimized as described in the updated Pharmacovigilance Plan (refer to Section 13). The public health impacts that include individual and community health, education, and socio-economic outcomes also weigh in favor of amending the current EUA to include individuals 12 years of age and older for Pfizer-BioNTech COVID-19 Vaccine.

7.2. Contraindications

Refer to the [Full EUA Prescribing Information](#) (Full EUA PI) provided in Module 1.14.1.

7.3. Special Populations

The Full EUA PI (Module 1.14.1) includes information on administration to special populations.

The safety and effectiveness of Pfizer-BioNTech COVID-19 Vaccine in individuals < 12 years of age have not been established at this time. Other special populations (ie, geriatric, pregnant and nursing, or immunocompromised individuals) are described in the Full EUA PI (Module 1.14.1).

8. CHEMISTRY, MANUFACTURING, AND CONTROLS

There are no updates to CMC related to this amendment.

9. FACT SHEET FOR VACCINATION PROVIDERS

Refer to the [Fact Sheet for Healthcare Providers Administering Vaccine](#) (Vaccination Providers) located in Module 1.14.1.

10. FACT SHEET FOR RECIPIENTS AND CAREGIVERS

Refer to the [Fact Sheet for Recipients and Caregivers](#) located in Module 1.14.1.

11. PROGRAM SCHEMA

There are no updates to program schema related to this amendment.

12. INSTRUCTIONS FOR USE

Refer to the [Full EUA PI](#) located in Module 1.14.1.

13. ADVERSE EVENT AND MEDICATION ERROR MONITORING

Refer to the [Pharmacovigilance Plan](#) located in Module 1.16.1.

In addition to pharmacovigilance activities and post-authorization studies to which Pfizer/BioNTech have already committed, we will continue to comply with all safety reporting requirements in consultation with the relevant regulatory authorities.

14. LABELING

Refer to the Full EUA PI located in Module 1.14.1.

Refer to the Fact Sheets located in Module 1.14.1 for additional information that will be provided to Pfizer-BioNTech COVID-19 Vaccination Providers and Recipients and Caregivers.

15. RECORD KEEPING, REPORTING, AND RECORD ACCESS BY FDA

There are no updates to record keeping, reporting, or record access related to this amendment.

16. REFERENCES

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 - ⁶ Centers for Disease Control and Prevention (CDC). Coronavirus Disease (COVID-19). Available at: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>. Accessed 09 December 2020.