2.7.4 SUMMARY OF CLINICAL SAFETY

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ABBREVIATIONS

Abbreviation	Definition
ADR	adverse drug reaction
AE	adverse event
AESI	adverse events of special interest
CBER	(US Food and Drug Administration) Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CI	confidence interval
CIOMS	Council for International Organizations of Medical Sciences
CO	Clinical Overview
COVID-19	Coronavirus Disease 2019
CRF	case report form
DART	Developmental and Reproductive Toxicology
EMA	European Medicines Agency
EUA	Emergency Use Authorization
FDA	(US) Food and Drug Administration
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
ICD	informed consent document
IM	intramuscular(ly)
IND	Investigational New Drug
IR	incidence rate
IRC	(US Study C4591001) Internal Review Committee
IWR	interactive Web-based response
MAA	Marketing Authorisation Application
MedDRA	Medical Dictionary for Regulatory Activities
NAAT	nucleic acid amplification testing
PCR	polymerase chain reaction
PSP	Pediatric Study Plan
PT	Preferred Term
PY	person-years
SAE	serious adverse event

Abbreviation	Definition
SARS-CoV-2	SARS Coronavirus-2; virus causing the disease COVID-19
SCS	Summary of Clinical Safety
SOC	System Organ Class
US	United States
TME	targeted medical events
VAED	vaccine-associated enhanced disease
VAERD	vaccine-associated enhanced respiratory disease
VE	vaccine efficacy

2.7.4. SUMMARY OF CLINICAL SAFETY

This SCS presents the safety and tolerability data for BNT162b2 in healthy adolescent participants 12-15 years of age in comparison to adults in age groups of 16-25 years of age and 16-55 years of age. BNT162b2 (BioNTech code number BNT162, Pfizer code number PF-07302048) is an investigational vaccine developed by BioNTech and Pfizer intended to prevent COVID-19, which is caused by SARS-CoV-2. The data are derived from the pivotal registration study, Phase 1/2/3 Study C4591001 (BNT162-02), conducted under IND 19736.

The proposed indication and dosing administration for BNT162b2 (30 μg) are:

- **Proposed indication:** Active immunization against COVID-19 disease caused by SARS-CoV-2 virus in individuals ≥12 years of age.
- **Dosing administration:** single 0.3 mL IM dose followed by a second 0.3 mL dose 21 days later.

Nonclinical studies in this development program are summarized in the CO (Module 2.5 Section 2.5.1.2.3.1).

Safety data are collected cumulatively in Study C4591001 and are available up to the data cutoff date, 13 March 2021. Safety data in this SCS are presented up to 1 month after Dose 2 and up to the data cutoff date for blinded follow-up. Phase 3 clinical endpoints and analyses presented in this submission 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 immunogenicity and descriptive safety analysis comparisons
- Adults (16-55 years of age): protocol specified 'younger adult' age stratum, to provide reference safety data from analyses of participants with longer-term follow-up. Note, these data are for comparative purposes and do not include a full independent safety evaluation for this age stratum.

An MAA was submitted to the EMA via a rolling review procedure initiated on 5 October 2020 and completed with submission of clinical modules on 07 December 2020. Conditional marketing authorization was granted by EMA on 21 December 2020 for individuals 16 years of age and older. The conditional approval was based on the following data:

Phase 1/2 Study BNT162-01:

- Phase 1 safety and immunogenicity for both BNT162b1 and BNT162b2 vaccine candidates across age groups and dose levels up to 1 month after Dose 2.

Phase 1/2/3 Study C4591001:

- Phase 1 safety and immunogenicity for both BNT162b1 and BNT162b2 vaccine candidates across age groups and dose levels up to 1 month after Dose 2
- Phase 2 safety and immunogenicity for BNT162b2 (30 µg) up to 1 month after Dose 2
- Phase 2/3 safety for BNT162b2 (30 µg) up to a median follow-up time of at least 2 months after Dose 2 and up to the data cutoff date (14 November 2020)
- Phase 2/3 efficacy analysis including the prespecified interim analysis of 94 COVID-19 cases (data cutoff date: 04 November 2020) and the prespecified final analysis of 170 COVID-19 cases (data cutoff date: 14 November 2020).

The present submission is a Type II Variation to support the use of BNT162b2 (30 µg) in individuals 12 years of age and older, and is based on safety, immunobridging, and efficacy data from pivotal Phase 3 Study C4591001 participants 12-15 years of age with a median follow-up time of at least 2 months after Dose 2. In this SCS, additional reference safety data are provided from young adults 16-25 years of age up to 1 month after Dose 2, and from adults 16-55 years of age up to 1 month after Dose 2 and up to participant unblinding for comparative purposes.

2.7.4.1. Exposure to BNT162b2

2.7.4.1.1. Overall Safety Evaluation Plan and Narratives of Safety Studies

2.7.4.1.1.1. Safety Objective, Estimands, Endpoints (Study C4591001)

Objective

To define the safety profile of prophylactic BNT162b2 in participants 12 to 15 years of age in Phase 3.

Estimands

In participants receiving at least 1 dose of study intervention, the percentage of participants reporting:

- Local reactions for up to 7 days following each dose
- Systemic events for up to 7 days following each dose
- AEs from Dose 1 to 1 month after the second dose
- SAEs from Dose 1 to 6 months after the second dose

Endpoints

- Local reactions (pain at the injection site, redness, and swelling)

- Systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain)
- AEs
- SAEs

2.7.4.1.1.2. Overall Design (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 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. Participants in this phase were ≥12 years of age, stratified as follows: 12 to 15 years, 16 to 55 years, or >55 years).

Phase 3 participants ⩾16 years of age were enrolled at sites in the US, Brazil, Argentina, Turkey, South Africa, and Germany. Participants 12-15 years of age were 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 high efficacy with 95% vaccine efficacy (VE) observed against COVID-19. 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 or conditional marketing authorization). 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 if they had been in the placebo group). Sponsor and site personnel responsible for the ongoing conduct of the study remain blinded to individual 12-15-year-old 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.

2.7.4.1.1.3. Study Population (Study C4591001)

The full eligibility criteria for Study C4591001 can be found in the protocol (Module 5.3.5.1 C4591001 Protocol Section 5).

The following eligibility criteria were designed to select participants for whom participation in the study was considered appropriate.

Key Phase 2/3 inclusion criteria:

Participants were eligible to be included in Phase 2/3 of the study only if all of the following criteria apply:

- Male or female participants ≥12 years, at randomization
- Healthy participants as determined by medical history, physical examination (if required), and clinical judgment of the investigator to be eligible for inclusion in the study

  Note: Healthy participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, could be included. Specific criteria for Phase 3 participants with known stable infection with HIV, HCV, or HBV can be found in Module 5.3.5.1 C4591001 Protocol Section 10.8.

- Participants who, in the judgment of the investigator, were at higher risk for acquiring COVID-19 (including, but not limited to, use of mass transportation, relevant demographics, and frontline essential workers).

Key Phase 2/3 exclusion criteria:

Participants were excluded from Phase 2/3 of the study if any of the following criteria applied:

- Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study.
- History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s).
- Receipt of medications intended to prevent COVID 19.
- Previous clinical (based on COVID-19 symptoms/signs alone, if a SARS-CoV-2 NAAT result was not available) or microbiological (based on COVID-19 symptoms/signs and a positive SARS-CoV-2 NAAT result) diagnosis of COVID 19.
- Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.

- Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection.
- Women who are pregnant or breastfeeding.
- Previous vaccination with any coronavirus vaccine.
- Individuals who receive treatment with immunosuppressive therapy.
- Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study.
- Participation in other studies involving study intervention within 28 days prior to study entry through and including 6 months after the last dose of study intervention, with the exception of interventional studies for prevention of COVID-19, which are prohibited throughout study participation.
- Previous participation in other studies involving study intervention containing lipid nanoparticles.

2.7.4.1.1.4. Analysis Sets (Study C4591001)

Populations discussed in this SCS include the following:

Population	Description
Enrolled	All participants who had a signed ICD
Randomized	All participants who were assigned a randomization number in the IWR system
Safety	All randomized participants who received at least 1 dose of the study intervention Analyses of reactogenicity endpoints will be based on a subset of the safety population that includes participants with any e-diary data reported after vaccination.

2.7.4.1.1.5. Safety Assessments (Study C4591001)

Safety assessments for Phase 3 adolescent participants 12-15 years of age were collected at planned time points as described in the protocol (Module 5.3.5.1 C4591001 Protocol). Key safety assessments included:

- A clinical assessment, including medical history, was performed on all participants at his/her first visit to establish a baseline. Significant medical history and observations from any physical examination, if performed, were documented in the CRF.
- 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): 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. Grading scales used in this study to assess local reactions and systemic events were derived from the FDA CBER guidelines on toxicity grading scales for healthy adult and adolescent volunteers enrolled in preventive vaccine clinical trials.[1]

- 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. SAEs will be recorded up to 6 months after Dose 2. Deaths are recorded to the end of study.
- Acute reactions within the first 4 hours after administration of the study intervention (for the first 5 participants vaccinated in each Phase 1 group), and within the first 30 minutes (for the remainder of participants), were assessed and documented in the AE CRF.
- Participants were surveilled for potential COVID-19 illness from Visit 1 onwards.
- Pregnancies were reported for participants in any phase of the study.

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. The TME terms are chosen 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. Taking into consideration the COVID-19 vaccine AESI lists publicly available, including from the US CDC, if events of interest were reported in the adolescent (12-15 years of age) group, they were further analyzed and characterized in this SCS (see Section 2.7.4.2.3).

2.7.4.1.1.6. Statistical Methods (Study C4591001)

Statistical methods are described in the study protocol (Module 5.3.5.1 C4591001 Protocol Section 9.4) and in the statistical analysis plan (Module 5.3.5.1 C4591001 Statistical Analysis Plan)

2.7.4.1.1.6.1. 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% CIs. Missing reactogenicity e-diary data were not imputed.

2.7.4.1.1.6.2. 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 the 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. Two-sided 95% CIs for the IRs were provided based on Poisson distribution.

2.7.4.1.1.7. Narratives

Narrative summaries were written for adolescents 12-15 years of age for:

- deaths
- SAEs
- AEs leading to study discontinuation
- AEs of clinical interest (anaphylaxis, lymphadenopathy, appendicitis, Bell's palsy)
- pregnancy exposures
- COVID-19 (participants with a case meeting severe criteria or having >1 episode of COVID-19)

The participant narratives are available in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 14.

2.7.4.1.2. Overall Extent of Exposure, Disposition, and Study Population Characteristics

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

Details and outputs regarding Phase 3 study population data for adolescents 12-15 years of age and adults 16-55 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 10.

2.7.4.1.2.1. Disposition (Phase 3, Study C4591001)

2.7.4.1.2.1.1. Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Disposition)

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 1). 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 [refer to Section 2.7.4.2.1.4.3.1], and unrelated anxiety/depression, which was an SAE [refer to Section 2.7.4.2.1.4.2.1]) 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 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 2.7.4.2.2.4.2) or other significant AEs (refer to Section 2.7.4.2.3).

Table 1. 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 (%)
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)
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.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:20) Source Data: adds Table Generation: 27MAR2021 (06:06) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adds_s002_ped_rand

2.7.4.1.2.1.2. Adults 16-55 Years of Age (Phase 3, Study C4591001, Disposition)

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 2). 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 2 for reference but not discussed further for safety analyses.

Table 2. 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)

Table 2. 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 (%)
Open-label follow-up period			
Originally randomized to BNT162b2	11858 (90.5)		
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 2. 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 (%)

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately.
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.
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.
a. N = number of randomized 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. Original blinded placebo-controlled vaccination period is defined as the time period from Dose 1 to 1 month post–Dose 2.
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]).
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2.7.4.1.2.2. Exposure (Phase 3, Study C4591001)

2.7.4.1.2.2.1. Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Exposure)

For adolescents (12-15 years of age) and young adults (16-25 years of age), almost all participants were administered study intervention as randomized. 100% received Dose 1. In participants 12-15 years of age, 99.4% and 98.9% received Dose 2 of BNT162b2 and placebo, respectively. In participants 16-25 years of age, 97.6% and 95.2% received Dose 2 of BNT162b2 and placebo, respectively.

The majority of participants received Dose 2 between 21 to 27 days after Dose 1 in the BNT162b2 (65.2% for 12-15 year-old participants and 60.3% for 16-25 year-old participants) and placebo (64.6% for 12-15 year-old participants and 58.2% for 16-25 year-old participants), followed by 14 to 20 days after Dose 1 in the BNT162b2 (31.7% for 12-15 year-old participants and 34.1% for 16-25 year-old participants) and placebo (32.2% for 12-15 year-old participants and 34.0% for 16-25 year-old participants).

2.7.4.1.2.2.2. Adults 16-55 Years of Age (Phase 3, Study C4591001, Exposure)

For adults (16-55 years of age), almost all participants were administered study intervention as randomized. 99.7% received Dose 1 and 98.1% received Dose 2 of BNT162b2 in the BNT162b2 group. In participants originally randomized to placebo, 99.7% received Dose 1 and 97.7% received Dose 2 of placebo, and 86.8% received Dose 3 and 65.4% received Dose 4 of BNT162b2 after unblinding.

For Dose 1, 2 participants randomized to the placebo group received BNT162b2, 1 participant randomized to the BNT162b2 group received placebo, and vaccination for 1 participant

randomized to the BNT162b2 group could not be determined. For Dose 2, 1 participant randomized to the placebo group received BNT162b2, and 2 participants randomized to the BNT162b2 group received placebo.

The majority of participants received Dose 2 between 21 to 27 days after Dose 1 in the BNT162b2 (62.7%) and placebo (62.7%), followed by 14 to 20 days after Dose 1 in the BNT162b2 (32.7%) and placebo (32.3%). In participants originally randomized to placebo, 86.8% received BNT162b2 after unblinding (Dose 3) and the majority of participants received Dose 4 between 21 to 27 days after Dose 3 (44.1%), followed by 14 to 20 days after Dose 3 (19.5%).

2.7.4.1.2.3. Safety Data Sets Analyzed (Phase 3, Study C4591001)

2.7.4.1.2.3.1. Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Safety Data Sets Analyzed)

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 3). Safety analysis results hereafter are presented for the 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).

Duration of Follow-Up

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 4).

Table 3. 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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Table 4. 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.
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/adsl fu d2 ped saf

2.7.4.1.2.3.2. Adults 16-55 Years of Age (Phase 3, Study C4591001, Safety Data Sets Analyzed)

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.

Duration of Follow-Up

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 5). 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 5. 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.
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2.7.4.1.2.4. Demographic and Other Characteristics of Study Population (Phase 3, Study C4591001)

2.7.4.1.2.4.1. Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Demographic and Other Characteristics of Study Population)

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 6). Overall, most adolescent participants in the BNT162b2 group 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 of adolescents in the BNT162b2 group was 14.0 years and 50.1% 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).

Table 6. 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)

Table 6. 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/m^2.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 01APR2021 (22:23) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA1/adsl_s005_demo_ped_saf

2.7.4.1.2.4.2. Adults 16-55 Years of Age (Phase 3, Study C4591001, Demographic and Other Characteristics of Study Population)

Demographic characteristics for Phase 2/3 adults in the 16-55 years of age group were similar in the BNT162b2 and placebo groups (Table 7). 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 7. 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 7. 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 7. 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.
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2.7.4.1.2.5. E-Diary Compliance (Phase 3, Study C4591001)

The reactogenicity data were collected by participants' e-diary for reporting prompted local reactions and systemic events for 7 days after each dose.

2.7.4.1.2.5.1. Adolescents 12-15 Years of Age (Phase 3, Study C4591001, E-Diary Compliance)

Overall, transmission of e-diary data for each day during the 7 days after Dose 1 of BNT162b2 was ≥87.6% (range: 87.6% to 96.3%) and ≥87.9% (range: 87.9% to 94.8%) for participants 12-15 and 16-25 years of age, respectively. After Dose 2 of BNT162b2 for the 12-15 year-old participants, transmission of e-diary data was 75.8% on Day 1 and ranged from 81.2% to 87.5% for each day during Day 2 through Day 7. After Dose 2 of BNT162b2 for the 16-25 year-old participants, transmission of e-diary data was 71.8% on Day 1 and ranged from 78.5% to 83.2% for each day during Day 2 through Day 7. Transmission rates were similar in the BNT162b2 groups and the placebo groups.

2.7.4.1.2.5.2. Adults 16-55 Years of Age (Phase 3, Study C4591001, E-Diary Compliance)

Overall, transmission of e-diary data for adults 16-55 years of age was ≥89.1% (range: 89.1% to 94.3%) for each day during the 7 days after Dose 1 of BNT162b2. After Dose 2 of BNT162b2, transmission of e-diary data was 76.8% on Day 1 and ranged from 82.6% to 85.9% for each day during Day 2 through Day 7. Transmission rates were similar in the BNT162b2 group and the placebo group.

2.7.4.2. Safety Results for BNT162b2

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.

Safety results for the protocol specified adult age stratum 16-55 years of age for whom longer-term safety data are available are reported in Section 2.7.4.2.2. These summary data serve a comparative/reference purpose and are not presented as a full independent safety evaluation in the context of this SCS. Open-label data for participants who were unblinded, including those originally randomized to placebo who received open-label BNT162b2 30 μg as Dose 3/Dose 4, are not discussed further in this SCS; safety results focus only on the blinded placebo-controlled data.

2.7.4.2.1. Safety Results – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

2.7.4.2.1.1. Reactogenicity – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

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.

2.7.4.2.1.1.1. Local Reactions – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 local reactions for adolescents 12-15 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.1.1.

Frequency and Severity of Local Reactions

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).

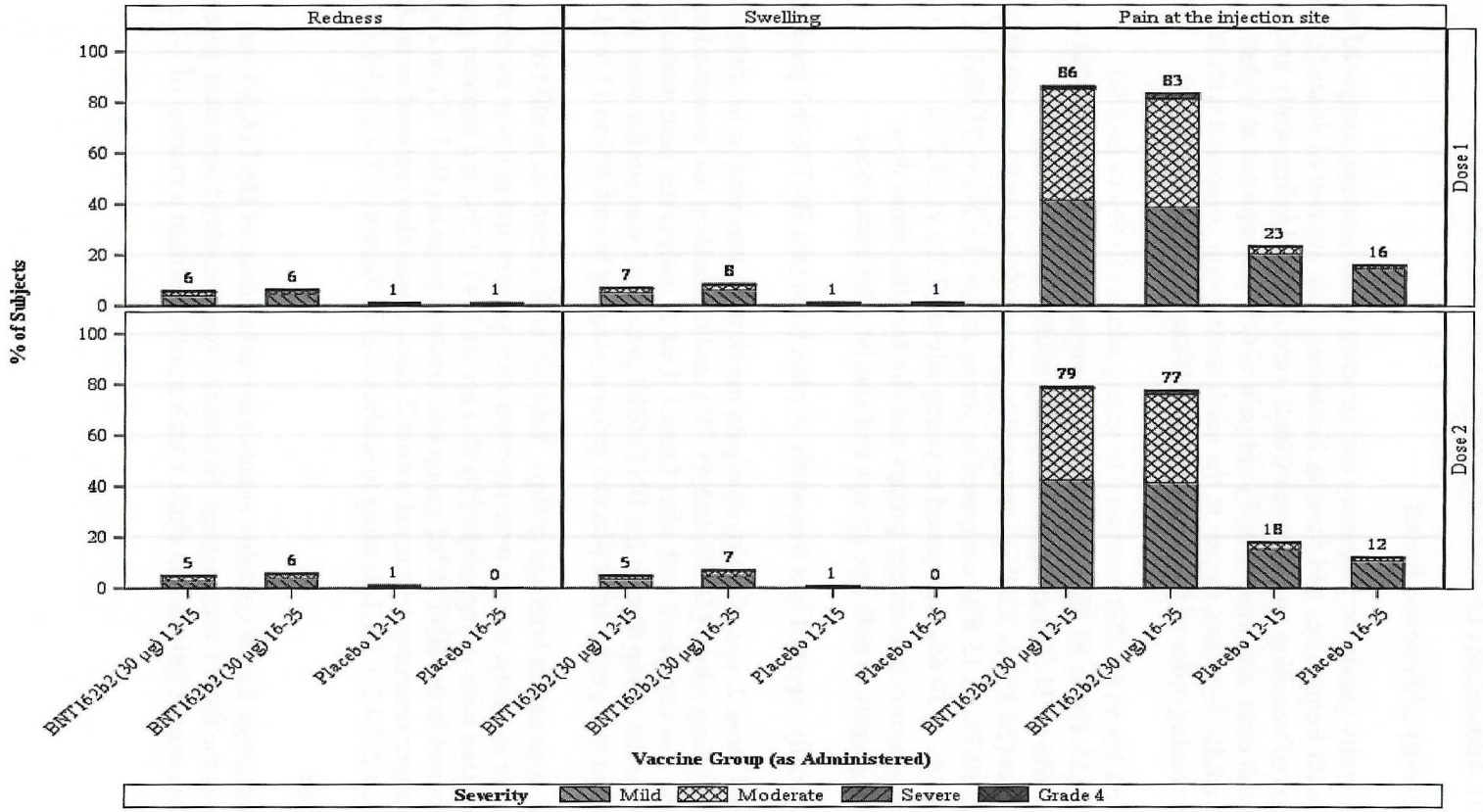
In the BNT162b2 group, frequencies of redness and swelling were similar between adolescents and young adults after Doses 1 and 2 (Figure 1). Frequencies of redness were generally low and unchanged from after Dose 1 compared with Dose 2 of BNT162b2 in adolescents (5.8% vs 5.0%) and in young adults (6.4% 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 (≤1.1%) and young adult (≤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 (≤1.5%) compared with young adults (≤3.4%) across the BNT162b2 and placebo groups after any dose. No Grade 4 local reactions were reported in either age group.

Onset and Duration

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.

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

2.7.4.2.1.1.2. Systemic Events – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 systemic events for adolescents 12-15 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.2.1.

Frequency and Severity of Systemic Events

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.

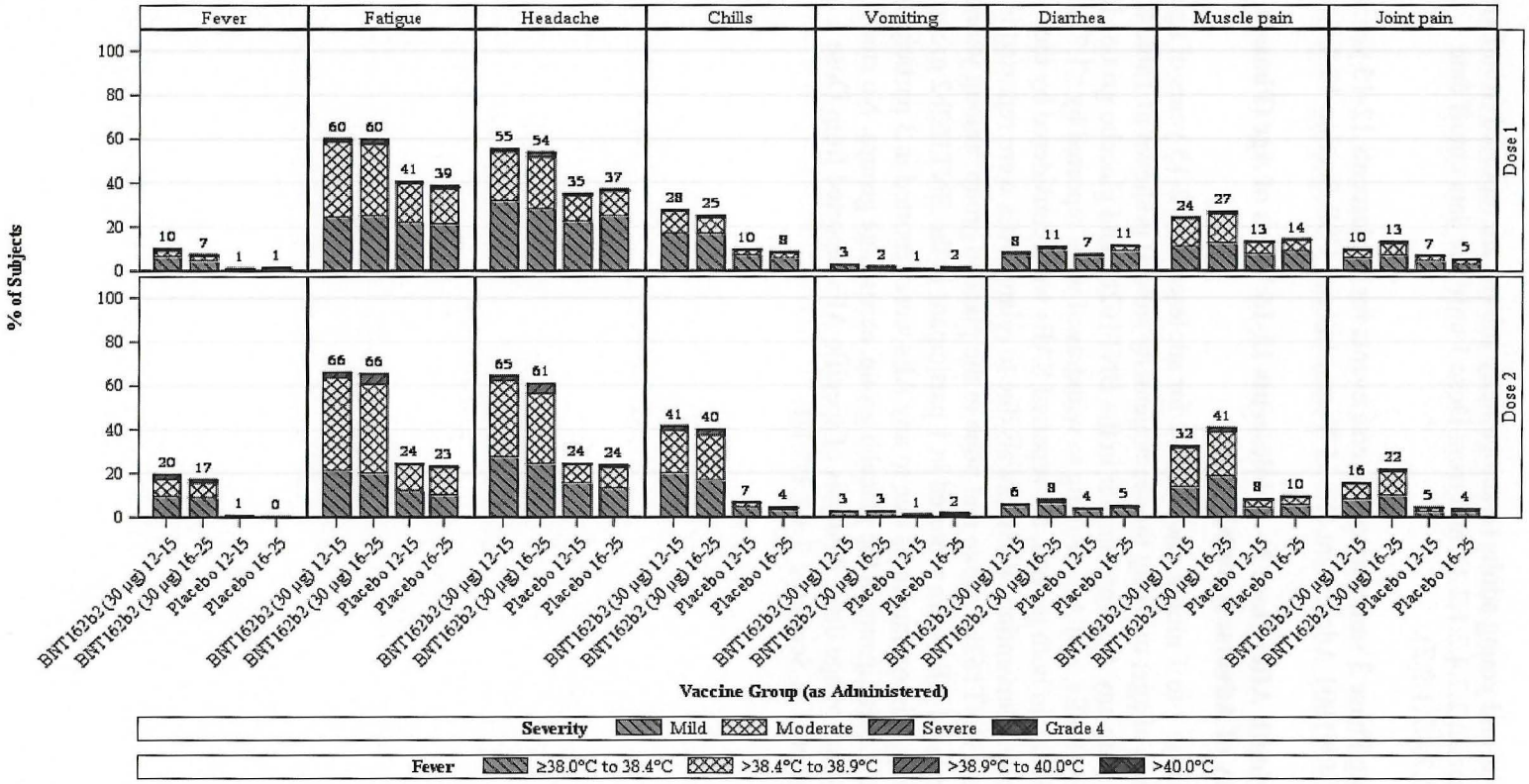
Following both Dose 1 and Dose 2, use of antipyretic/pain medication was similar in adolescents (36.6% and 50.8%) and in young adults (31.5% and 45.7%), and medication use increased in both age groups after Dose 2 as compared with after Dose 1. Use of antipyretic/pain medication was less frequent in 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 8.8% 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 (≤3.5%) compared with young adults (≤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 2.7.4.2.1.3.1.1, leading to withdrawal in Section 2.7.4.2.1.4.3.1).

Onset and Duration

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.

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

2.7.4.2.1.2. Summary of Adverse Events – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

AE overviews for adolescents and young adults (reactogenicity subset) are reported from Dose 1 to 1 month after Dose 2 (Section 2.7.4.2.1.2.1), and from Dose 1 until the data cutoff date (13 March 2021) (Section 2.7.4.2.1.2.2).

Details and outputs regarding Phase 3 summary of adverse events for adolescents 12-15 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.3.1.1.

2.7.4.2.1.2.1. Dose 1 to 1 Month After Dose 2 – Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Summary of Adverse Events)

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 8. 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 ≤1.7%, ≤0.4%, and ≤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 2 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 2.7.4.2.1.3.1.1.

Table 8. 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

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg)		Placebo	
Adverse Event	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

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

2.7.4.2.1.2.2. Dose 1 to Data Cutoff Date – Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Summary of Adverse Events)

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 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 for the age groups into the study and due to unblinding of individuals ≥16 years of age per protocol for vaccination (unlike the adolescents who remain blinded to treatment assignment; refer to Section 2.7.4.1.1.2).

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 ≤0.8%, ≤0.4%, and ≤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 2.7.4.2.1.3.1.2.

Table 9. 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

	Vaccine Group (as Administered)	
Adverse Event	BNT162b2 (30 µg) (N^a=1131) n^b (%)	Placebo (N^a=1129) 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

2.7.4.2.1.3. Analysis of Adverse Events – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

AE analyses for adolescents and young adults (reactogenicity subset) are reported from Dose 1 to 1 month after Dose 2 (Section 2.7.4.2.1.3.1.1), and from Dose 1 until the data cutoff date (13 March 2021) (Section 2.7.4.2.1.3.1.2).

Details and outputs regarding Phase 3 AEs by SOC and PT for adolescents 12-15 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.3.2.1.1.

2.7.4.2.1.3.1. Adverse Events by System Organ Class and Preferred Term – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

2.7.4.2.1.3.1.1. Dose 1 to 1 Month After Dose 2 – Adolescents 12-15 Years of Age (Phase 3, Study C4591001, 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 10. 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 SOCs (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 SOCs (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.

Table 10. 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

	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)	
System Organ Class Preferred Term	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)

Table 10. 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

	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)	
System Organ Class Preferred Term	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])
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)
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)

Table 10. 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

	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)	
System Organ Class Preferred Term	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])
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)
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)
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)

Table 10. 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

	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)	
System Organ Class Preferred Term	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])
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)
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)

Table 10. 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

	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)	
System Organ Class Preferred Term	n^b (%)	(95% CI^c)	n^b (%)	(95% CI^c)	n^b (%)	(95% CI^c)	n^b (%)	(95% CI^c)
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)
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)
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)

Table 10. 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

	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)	
System Organ Class Preferred Term	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])	n^b (%)	(95% CI[c])
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)
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

2.7.4.2.1.3.1.2. Dose 1 to Data Cutoff Date – Adolescents 12-15 Years of Age (Phase 3, Study C4591001, 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 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; refer to Section 2.7.4.1.1.2).

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 11. 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

	Vaccine Group (as Administered)	
System Organ Class Preferred Term	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
Toothache	0	1 (0.1)
Vomiting	1 (0.1)	0
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	16 (1.4)	11 (1.0)

Table 11. 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] (%)	Vaccine Group (as Administered) Placebo (N[a]=1129) n[b] (%)
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)
Tooth fracture	0	2 (0.2)
Foot fracture	0	1 (0.1)
Hand fracture	1 (0.1)	0

Table 11. 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

	Vaccine Group (as Administered)	
System Organ Class Preferred Term	BNT162b2 (30 µg) (N[a]=1131) n[b] (%)	Placebo (N[a]=1129) n[b] (%)
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
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	2 (0.2)	4 (0.4)
Rhinorrhoea	1 (0.1)	4 (0.4)
Nasal congestion	1 (0.1)	0

Table 11. 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

	Vaccine Group (as Administered)	
System Organ Class Preferred Term	BNT162b2 (30 µg) (N[a]=1131) n[b] (%)	Placebo (N[a]=1129) n[b] (%)
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

2.7.4.2.1.3.2. Related Adverse Events – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 related AEs for adolescents 12-15 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.3.2.2.1.

2.7.4.2.1.3.2.1. Dose 1 to 1 Month After Dose 2 – Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Related Adverse Events)

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 12). 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 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 2.7.4.2.3).

Table 12. 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

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg)		Placebo	
Adverse Event	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

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

2.7.4.2.1.3.3. Immediate Adverse Events – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 immediate AEs for adolescents 12-15 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.3.2.3.

2.7.4.2.1.3.3.1. Dose 1 to 1 Month After Dose 2 – Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Immediate Adverse Events)

After Dose 1, adolescents and young adults with immediate AEs were low in frequency (≤0.4%) and were reported only in the placebo groups. All immediate AEs after Dose 1 were in the SOCs 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 (≤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.

2.7.4.2.1.3.4. Severe or Life-Threatening Adverse Events – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 severe or life-threatening AEs for adolescents 12-15 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.3.2.4.1.

2.7.4.2.1.3.4.1. Dose 1 to 1 Month After Dose 2 – Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Severe or Life-Threatening Adverse Events)

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 8).

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 2.7.4.2.1.4.2.1), resolved, and the participant continued in the study
- Pyrexia (40.4 °C) reported as Grade 4 in 1 adolescent in the BNT162b2 group, occurring 2 days after Dose 1 (on Day 2) with temperature returning to normal on Day 4, 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 2.7.4.2.1.1.2)

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 2.7.4.1.1.2):

- 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 2.7.4.2.1.4.2.2), resolved, and the participant withdrew from the study; this participant has an ongoing medical history of drug hypersensitivity, food allergy, and seasonal allergy.

- 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 2.7.4.2.1.4.2.1) 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.

2.7.4.2.1.4. Deaths, Serious Adverse Events, Safety-Related Participant Withdrawals, and Other Significant Adverse Events – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

2.7.4.2.1.4.1. Deaths – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

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).

2.7.4.2.1.4.1.1. Narratives of Deaths – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

There were no deaths in adolescent participants 12-15 years of age, so there are no narratives for this group.

2.7.4.2.1.4.2. Serious Adverse Events – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

SAE analyses for adolescents and young adults are reported from Dose 1 to 1 month after Dose 2 (Section 2.7.4.2.1.4.2.1), and from Dose 1 until the data cutoff date (13 March 2021) (Section 2.7.4.2.1.4.2.2).

Details and outputs regarding Phase 3 SAEs for adolescents 12-15 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.4.2.1.

2.7.4.2.1.4.2.1. Dose 1 up to 1 Month After Dose 2 – Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Serious Adverse Events)

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 13). 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 in 1 participant in the placebo group with concurrent events of appendicitis and focal peritonitis that were both Grade 4 [refer to Section 2.7.4.2.1.3.1.1]). All SAEs in the adolescent group were reported as resolved.

The SAE of neuralgia was reported in 1 [redacted] years of age who had 3 emergency room visits beginning 1 day after the second dose. [redacted] reported concurrent non-serious AEs of vulvar abscess, gastritis, and contact dermatitis. [redacted] subsequently had SAEs of abdominal pain and constipation. [redacted] had an extensive work-up including serial physical and laboratory examinations and was diagnosed with functional abdominal pain; [redacted] 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.

Table 13. 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

	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)	
System Organ Class Preferred Term	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)

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

2.7.4.2.1.4.2.2. Dose 1 to Data Cutoff Date – Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Serious Adverse Events)

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 14). 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; refer to Section 2.7.4.1.1.2).

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 2.7.4.2.1.4.2.1), 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 2.7.4.1.1.2), therefore the data are not included in the blinded analyses. These events were also considered as life-threatening (refer to Section 2.7.4.2.1.3.4.1): 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 14. 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

	Vaccine Group (as Administered)	
System Organ Class Preferred Term	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)
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

2.7.4.2.1.4.2.3. Narratives of Serious Adverse Events – Adults 16-55 Years of Age (Phase 3, Study C4591001)

Narratives for Phase 3 adolescents 12 to 15 years of age who reported SAEs assessed as related to study intervention by the investigator who completed their visit at 1 month after Dose 2 and through the data cutoff date (13 March 2021) are provided (see Section 2.7.4.2.6).

2.7.4.2.1.4.3. Safety-Related Participant Withdrawals – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 safety-related participant withdrawals for adolescents 12-15 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.4.3.1.

2.7.4.2.1.4.3.1. Dose 1 up to 1 Month After Dose 2 – Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Safety-Related Participant Withdrawals)

From Dose 1 to 1 month after Dose 2, few adolescents and young adults in the BNT162b2 group (≤0.2%) and in the placebo group (≤0.4%) were withdrawn due to AEs (Table 15).

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 2.7.4.2.1.3.4.1), and none in the placebo group.

In the young adult group, 1 participant in the BNT162b2 group a 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.

Table 15. 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

	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)	
System Organ Class Preferred Term	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

2.7.4.2.1.4.3.2. Narratives of Safety-Related Participant Withdrawals – Adults 16-55 Years of Age (Phase 3, Study C4591001)

Narratives for Phase 3 adolescents 12 to 15 years of age who reported any AEs leading to withdrawal from the study through the data cutoff date (13 March 2021) are provided (see Section 2.7.4.2.6).

2.7.4.2.2. Safety Results – Adults 16-55 Years of Age (Phase 3, Study C4591001)

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 2.7.4.1.1.2). 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 SCS.

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

Note: Phase 3 tables and figures that include participants ≥16 years of age are titled as "Phase 2/3" to capture the fact that the 360 Phase 2 participants are included in the overall Phase 3 analyses. Individuals 12-15 years of age were not included in Phase 2.

2.7.4.2.2.1. Reactogenicity – Adults 16-55 Years of Age (Phase 3, Study C4591001)

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.

2.7.4.2.2.1.1. Local Reactions – Adults 16-55 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 local reactions for adults 16-55 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.1.2.

Frequency and Severity of Local Reactions

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).

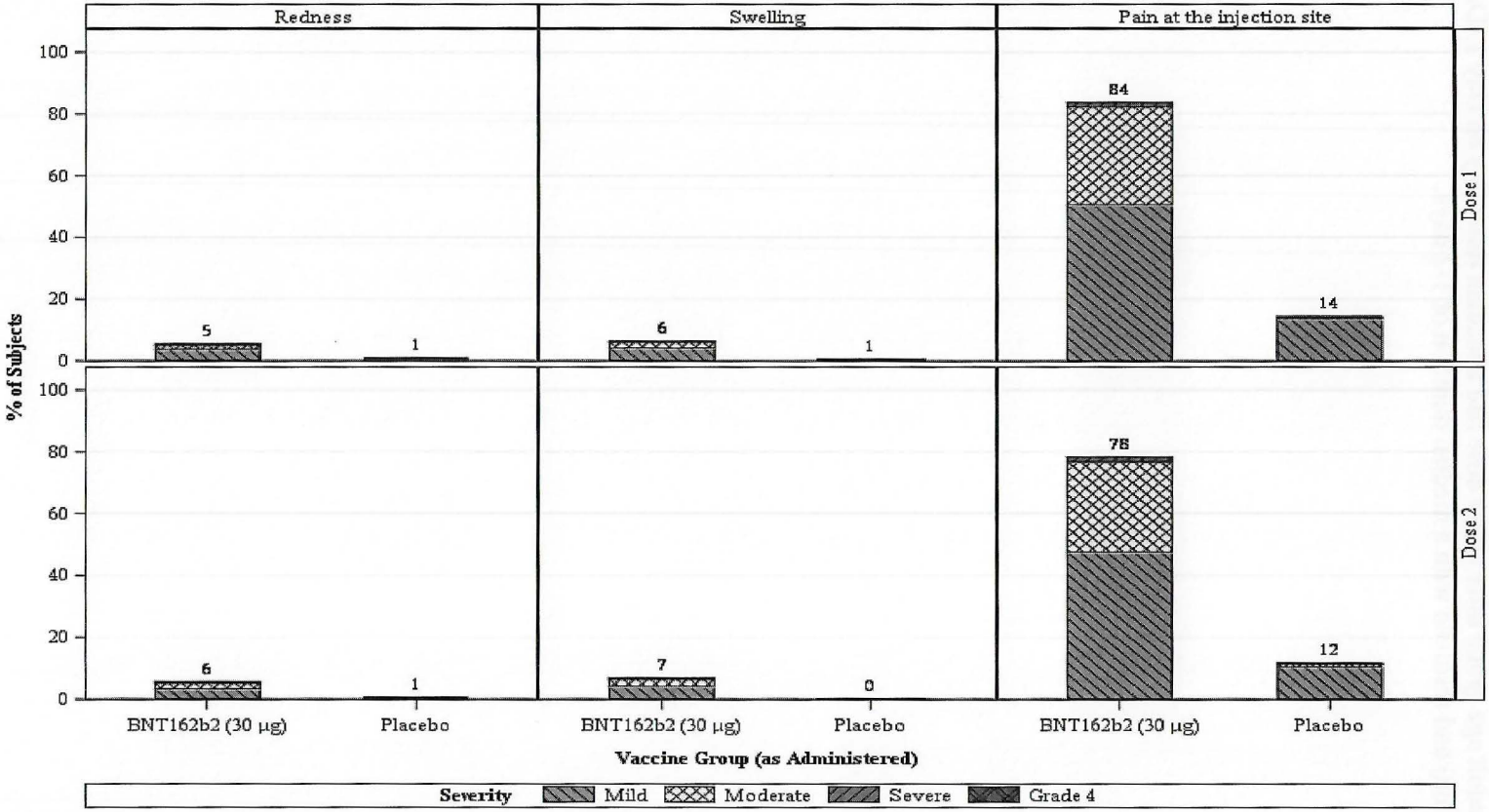
In the BNT162b2 group, frequencies after Dose 1 and Dose 2 were similar for redness (5.4% vs 5.6%) and swelling (6.3% vs 6.8%). In the placebo group, redness and swelling were reported infrequently (≤1.0%) after Doses 1 and 2. Pain at injection site was reported with a higher frequency in the BNT162b2 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 (≤2.5%) in the BNT162b2 group after either dose. No Grade 4 local reactions were reported.

Onset and Duration

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.

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

2.7.4.2.2.1.2. Systemic Events – Adults 16-55 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 systemic events for adults 16-55 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.2.2.

Frequency and Severity of Local Reactions

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).

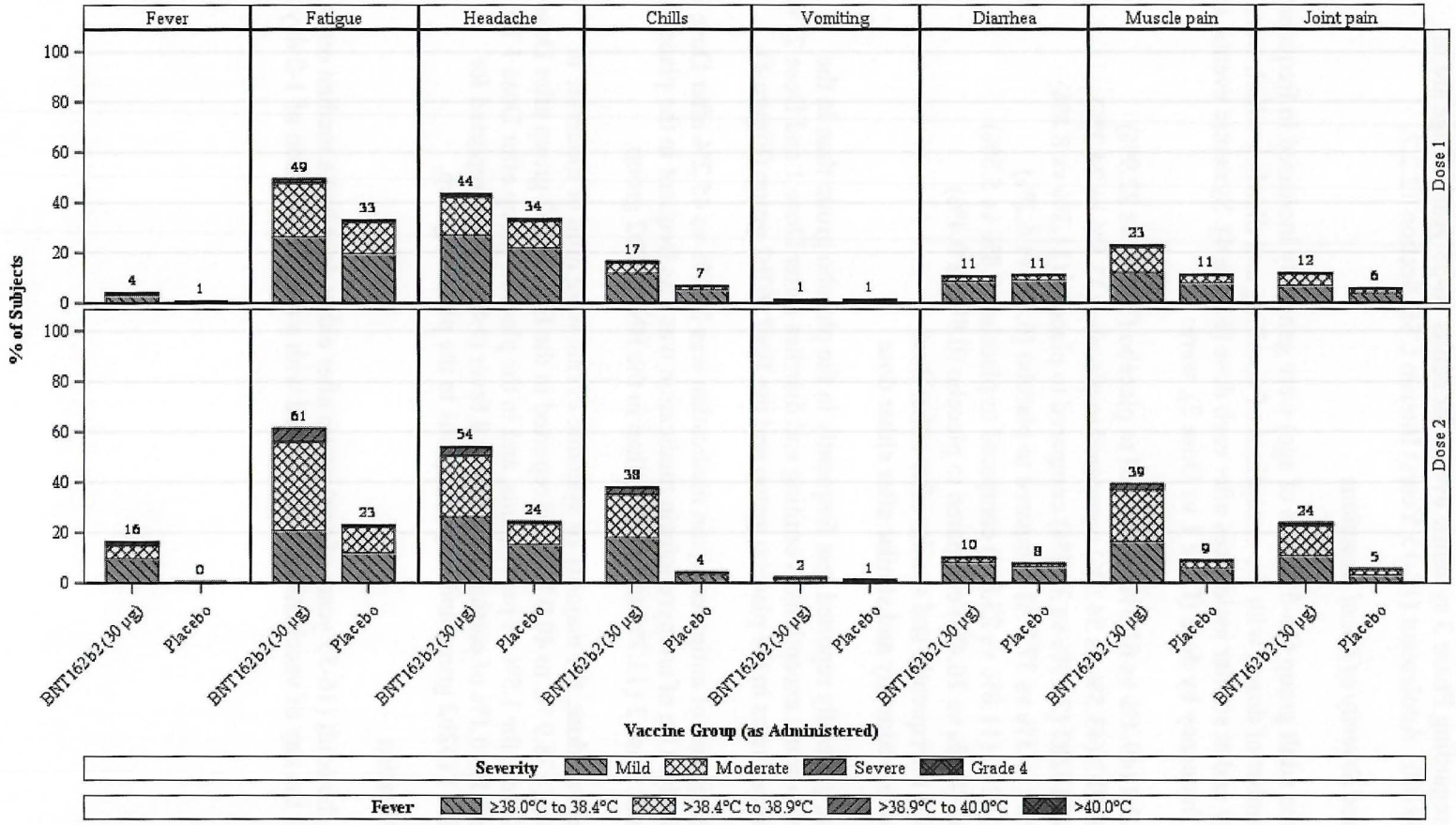
In the BNT162b2 group, use of antipyretic/pain medication was 27.8% vs 45.2% after Dose 1 and Dose 2, respectively. Use of antipyretic/pain medication was less frequent in the placebo group after Dose 1 and Dose 2 (13.7% and 11.9%) than in the BNT162b2 group.

After the first and second dose, the majority of systemic events were mild or moderate in severity. Severe fever (>38.9 °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 °C) was reported for 1 participant in the BNT162b2 group and no participants in the placebo group.

Onset and Duration

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.

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

2.7.4.2.2.2. Summary of Adverse Events – Adults 16-55 Years of Age (Phase 3, Study C4591001)

AE overviews for the adult group (16-55 years of age) are reported from Dose 1 to 1 month after Dose 2 (Section 2.7.4.2.2.2.1), and from Dose 1 until the unblinding date (Section 2.7.4.2.2.2.2). Due to unblinding of individuals ≥16 years of age to treatment assignment (per protocol) to receive BNT162b2 (refer to Section 2.7.4.1.1.2), 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.

Details and outputs regarding Phase 3 summary of adverse events for adults 16-55 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.3.1.2.

2.7.4.2.2.2.1. Dose 1 to 1 Month After Dose 2 – Adults 16-55 Years of Age (Phase 3, Study C4591001, Summary of Adverse Events)

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 ≤1.2%, ≤0.4%, and ≤0.2%, respectively, in both groups. Discontinuations due to related AEs were reported in few participants (≤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 2.7.4.2.2.4.1).

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

	Vaccine Group (as Administered)	
Adverse Event	BNT162b2 (30 µg) (N^a=12995) n^b (%)	Placebo (N^a=13026) 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)

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: 31MAR2021 (17:46)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 EUA 1655/adae s091 all pd2 1655 sa

2.7.4.2.2.2. Dose 1 to Unblinding Date – Adults 16-55 Years of Age (Phase 3, Study C4591001, Summary of Adverse Events)

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 2.7.4.2.2.4.1).

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

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=12995, TE[b]=49.7)			Placebo (N[a]=13026, TE[b]=49.1)		
Adverse Event	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)
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

2.7.4.2.2.3. Analysis of Adverse Events – Adults 16-55 Years of Age (Phase 3, Study C4591001)

2.7.4.2.2.3.1. Adverse Events by System Organ Class and Preferred Term – Adults 16-55 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 AEs by SOC and PT for adults 16-55 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.3.2.1.2.

2.7.4.2.2.3.1.1. Dose 1 to 1 Month After Dose 2 – Adults 16-55 Years of Age (Phase 3, Study C4591001, 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 SOCs (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 2.7.4.2.2.1), 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 and MAA, 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 SOCs 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 SOCs 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 SOCs. 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 SOCs 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.

2.7.4.2.2.3.1.2. Dose 1 to Unblinding Date – Adults 16-55 Years of Age (Phase 3, Study C4591001, 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 SOCs (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 2.7.4.2.2.3.1.1).

2.7.4.2.2.3.2. Related Adverse Events – Adults 16-55 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 related AEs for adults 16-55 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.3.2.2.2.

2.7.4.2.2.3.2.1. Dose 1 to 1 Month After Dose 2 – Adults 16-55 Years of Age (Phase 3, Study C4591001, Related Adverse Events)

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 2.7.4.2.3).

2.7.4.2.2.3.3. Severe or Life-Threatening Adverse Events – Adults 16-55 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 severe or life-threatening AEs for adults 16-55 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.3.2.4.2.

2.7.4.2.2.3.3.1. Dose 1 to 1 Month After Dose 2 – Adults 16-55 Years of Age (Phase 3, Study C4591001, Severe or Life-Threatening Adverse Events)

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.

2.7.4.2.2.4. Deaths, Serious Adverse Events, Safety-Related Participant Withdrawals, and Other Significant Adverse Events – Adults 16-55 Years of Age (Phase 3, Study C4591001)

2.7.4.2.2.4.1. Deaths – Adults 16-55 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 deaths for adults 16-55 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.4.1.

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 [redacted] years of age died due to congestive cardiac failure 88 days after Dose 2
- 1 [redacted] years of age died due to cardio-respiratory arrest 86 days after Dose 2
- 1 [redacted] years of age died due to [redacted] 113 days after Dose 2

In the placebo group:

- 1 [redacted] years of age died due to an undetermined cause 8 days after Dose 1
- 1 [redacted] years of age died due to myocardial infarction 37 days after Dose 2
- 1 [redacted] years of age died due to [redacted] 32 days after Dose 2
- 1 [redacted] years of age died due to cardio-respiratory arrest 82 days after Dose 2

Additionally, 1 participant ([redacted] 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.

2.7.4.2.2.4.2. Serious Adverse Events – Adults 16-55 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 SAEs for adults 16-55 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.4.2.2.

2.7.4.2.2.4.2.1. Dose 1 up to 1 Month After Dose 2 – Adults 16-55 Years of Age (Phase 3, Study C4591001, Serious Adverse Events)

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 and MAA 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 and MAA 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.

2.7.4.2.2.4.2.2. Dose 1 to Unblinding Date – Adults 16-55 Years of Age (Phase 3, Study C4591001, Serious Adverse Events)

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.

2.7.4.2.2.4.3. Safety-Related Participant Withdrawals – Adults 16-55 Years of Age (Phase 3, Study C4591001)

Details and outputs regarding Phase 3 safety-related participant withdrawals for adults 16-55 years of age are in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 12.4.3.2.

2.7.4.2.2.4.3.1. Dose 1 up to 1 Month After Dose 2 – Adults 16-55 Years of Age (Phase 3, Study C4591001, Safety-Related Participant Withdrawals)

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 discontinued study intervention due to AE.

2.7.4.2.3. Other Significant Adverse Events – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

AEs of clinical interest were reviewed for the adolescent (12-15 years of age) group, which also considered programmed defined TMEs and terms in the CDC list of AESIs for COVID 19 that are potentially indicative of severe COVID-19 or autoimmune and neuroinflammatory disorders. Narratives were prepared for such events reported in adolescents (12-15 years of age) (refer to Section 2.7.4.1.1.5). Note, if an AE of clinical interest term was not observed in the 12 15 years of age group, further characterization was not elaborated for participants 16 55 years of age; a full independent safety evaluation of the

16-55 years of age group will be provided in a separate submission planned in second quarter 2021. AEs of clinical interest identified in the adolescent group, along with corresponding reference information from adults, are summarized below.

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 (symptoms not specified) assessed as related, 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 2.7.4.2.1.4.2.2), reported as resolved, and the participant withdrew from the study (this participant has an ongoing medical history of drug hypersensitivity, food allergy, and seasonal allergy). 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 caused by a bee sting that was not considered related to study intervention that was described in the prior submission for the current EUA and MAA (cutoff date of 14 November 2020).

Lymphadenopathy

Lymphadenopathy is an adverse reaction (see Section 2.7.4.2.4) to BNT162b2 and is noted as such in the current product labeling.

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 2.7.4.2.2.3). 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.

Appendicitis

In adolescents (12-15 years of age), 2 participants in the placebo group had events of appendicitis reported as SAEs (refer to Section 2.7.4.2.1.4.2) 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 2.7.4.2.1.4.2) 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 2.7.4.2.2.4.2), 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.

2.7.4.2.3.1. Narratives of Other Significant Adverse Events (Phase 3, Study C4591001)

Narratives of other signicant AEs, including AEs of clinical interest (anaphylaxis, lymphadenopathy, appendicitis, Bell's palsy), as of the data cutoff date (13 March 2021), are provided (see Section 2.7.4.2.6).

2.7.4.2.4. Analysis of Adverse Events by Organ System or Syndrome – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

Safety data from Phase 3 of Study C4591001 were reviewed to determine if any Adverse Drug Reactions (ADRs) – adverse events for which there is reason to conclude that the vaccine caused the event – should be identified for the 12-15-year-old age group. The review included AE data, as well as local reactions and systemic events collected systematically by e-diaries. It was determined that the adverse reactions identified for individuals ≥16 years of age were also applicable to the 12-15-year-old age group. No further ADRs, specific to the 12-15-year-old age group, were identified from review of the safety data from Phase 3 of Study C4591001.

The CIOMS frequency categories for adverse reactions are as follows:

- Very common: ≥10%
- Common: ≥1% and <10%
- Uncommon: ≥0.1% and <1%
- Rare: ≥0.01% and <0.1%
- Very rare: <0.01%

Reactogenicity ADRs in adolescents 12-15 years of age that occurred with a very common frequency, based on any dose in the BNT162b2 group, from the reactogenicity subset of data as of 13 March 2021, are:

- Injection site pain: 1023/1131 (90.5%)
- Fatigue: 876/1131 (77.5%)
- Headache: 854/1131 (75.5%)
- Chills: 557/1131 (49.2%)
- Muscle pain: 477/1131 (42.2%)
- Joint pain: 229/1131 (20.2%)
- Fever: 275/1131 (24.3%)

An ADR considered as uncommon in adolescents in the BNT162b2 group was identified from AE data in the safety population as of 13 March 2021, compared to placebo for reference:

- Lymphadenopathy: 9/1131 (0.8%) in the BNT162b2 group vs 2/1129 (0.2%) in the placebo group

The following additional ADRs were identified in the post-authorization setting for individuals ≥16 years of age. Frequencies for these ADRs in individuals 12-15 years of age were obtained from adolescent clinical trial data (Study C4591001) when possible, as per labeling guidance.

- Diarrhea (very common)
- Vomiting (common)
- Rash (uncommon)

- Pain in Extremity (uncommon)
- Urticaria (uncommon)
- Anaphylaxis (unknown)

Any ADR updates identified upon full independent review of safety data for individuals ⩾16 years of age will be provided in a future submission.

2.7.4.2.5. Other Safety Assessments – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

2.7.4.2.5.1. Severe COVID-19 Illness – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

Cases of COVID-19, both overall and those considered as severe, were evaluated per criteria described in Module 2.7.3 Summary of Clinical Efficacy. Results and reference data (located in Module 5.3.5.1) for updated efficacy against severe disease are discussed in Module 2.7.3 Summary of Clinical Efficacy.

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.

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 and MAA 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).

2.7.4.2.5.2. Pregnancies– Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

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.

2.7.4.2.5.3. Narratives for Other Safety Assessments– Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

Narratives of other safety assessments, including severe COVID-19 illness and pregnancies, as of the data cutoff date (13 March 2021), are provided (see Section 2.7.4.2.6).

2.7.4.2.6. Narratives – Adolescents 12-15 Years of Age (Phase 3, Study C4591001)

Narratives for Phase 3 adolescents 12 to 15 years of age (including for deaths, SAEs, AEs leading to withdrawal, COVID-19 cases, pregnancies, and AEs of clinical interest) are provided in Module 5.3.5.1 C4591001 Adolescent (12-15 Years) Interim CSR Section 14. Since participants 16 through 55 years of age are presented in this report for comparative purposes only, narratives for SAEs in these participants will be reported separately along with the full independent safety evaluation of these participants.

2.7.4.2.7. Conclusions (Phase 3, Study C4591001)

2.7.4.2.7.1. Adolescents 12-15 Years of Age (Phase 3, Study C4591001, Conclusions)

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 μg 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 mostly 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 in the study reflect age-appropriate events consistent with the respective general 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 (who has an ongoing medical history of drug hypersensitivity and non-drug allergies), 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.

2.7.4.2.7.2. Adults 16-55 Years of Age (Phase 3, Study C4591001, Conclusions)

The adult (16-25 years of age and 16-55 years of age) safety data included for reference purposes in the context of this SCS 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 SCS 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.

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.

2.7.4.3. Safety in Special Groups and Situations

2.7.4.3.1. Intrinsic Factors

2.7.4.3.1.1. Geriatric Use

Clinical studies of BNT162b2 (30 µg) include participants 65 years of age and older whose data contribute to overall assessment of safety and efficacy.

The clinical data previously provided (on 07 December 2020) have demonstrated a predominantly mild reactogenicity profile in older adults, overall and compared with younger adults. This is coupled with evidence of robust immune response following the two-dose vaccine regimen, and overwhelming efficacy comparable to younger adults (>90%).

However, there is no basis to definitively determine whether the geriatric population will respond differently overall to the vaccine compared to younger adults.

2.7.4.3.1.2. Pediatric Use

The safety and effectiveness of BNT162b2 in participants <12 years of age have not been established at the time of this submission.

Further study of pediatric use of the vaccine and/or immunobridging study will be undertaken to characterize the vaccine response in children.

2.7.4.3.1.3. Use in Immunocompromised Individuals

Individuals who are immunocompromised or taking immunosuppressive therapy at the time of vaccine administration may have diminished response to immunization. Study C4591001

included enrollment of individuals with medical history of immunocompromised condition or immunosuppressive therapy (Section 2.7.4.1.1.3). There are limited data on the safety of the vaccine in this patient population at the time of this application.

2.7.4.3.2. Extrinsic Factors

Not applicable.

2.7.4.3.3. Drug Interactions

Refer to Module 5.3.5.1 C4591001 Protocol Section 6.5 for details regarding prior and concomitant vaccines, medications and procedures that were allowed or prohibited.

2.7.4.3.4. Use in Pregnancy and Lactation

Women who were pregnant or breastfeeding were not eligible to participate in Study C4591001 (Section 2.7.4.1.1.3). Any participants who become pregnant while in the study (refer to Section 2.7.4.2.5.2) continue to be followed for pregnancy outcomes. No pregnancies were reported in the 12-15 years of age group as of the data cutoff date (13 March 2021).

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. Available data on BNT162b2 administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy. In a DART study, no vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for vaccination with BNT162b2 and any potential adverse effects on the breastfed child from BNT162b2 or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

2.7.4.3.5. Overdose

For this study, any dose of study intervention greater than 30µg within a 24-hour time period was considered an overdose (refer to Module 5.3.5.1 C4591001 Protocol Section 8.4 for more information). An error in dilution during the study resulted in 52 participants (≥16 years of age) receiving a higher than intended dose of BNT162b2; instead of receiving 30 µg of BNT162b2, 58 µg of BNT162b2 was administered. The participants did not report an increase in reactogenicity or adverse events.

2.7.4.3.6. Drug Abuse

Not applicable.

2.7.4.3.7. Withdrawal and Rebound

Not applicable.

2.7.4.3.8. Effects on Ability to Drive or Operate Machinery or Impairment of Mental Ability

BNT162b2 has no or negligible influence on the ability to drive and use machines.

2.7.4.4. Post-marketing Data

A review of the Pfizer safety database for spontaneously reported AEs in individuals 12-15 years of age (inclusive), received up to the date 28 February 2021, returned 11 cases. The cases were from 4 countries (8 cases from US and the remaining 3 cases were from Germany, Israel, and Italy, respectively). Subjects were aged 15 years (4 cases), 14 and 12 years (3 cases each) and 13 years (1 case). There were no adverse events co-reported for these cases of off-label use.

The limited amount of safety information conveyed in these reports does not substantially contribute to the base of knowledge of the product safety profile in this age group.

2.7.4.5. Overall Conclusions

Phase 3 data from Study C4591001 show that BNT162b2 at 30 µg, administered as 2-dose schedule (21 days apart) for the prevention of COVID-19 in adolescents 12-15 years of age, has an acceptable tolerability and safety profile that is consistent with that of older age groups.

2.7.4.6. REFERENCES

1 US Food and Drug Administration, Guidance for Industry Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trial. Rockville, MD: Center for Biologics Evaluation and Research; September 2007. Available: https://www.fda.gov/media/73679/download. Accessed: 14 April 2021.