1. TITLE PAGE

Vaccine Name and Compound Number:	BNT162 RNA-Based COVID-19 Vaccines, Compound Number: PF-07302048
Report Title:	Interim Report – Adolescent 6-Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-CoV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals
Protocol Number:	Protocol C4591001
Sponsor:	BioNTech SE
Sponsor Agent:	Pfizer Inc
Phase of Development:	Phase 1/2/3
First Subject First Visit:	29 April 2020 (study start); 15 October 2020 (adolescent)
Primary Completion Date:	Not applicable
Data Cutoff Date:	02 September 2021
Serology Completion Dates:	29 October 2021
Name and Affiliation of Coordinating/Leading Investigator:	Stephen Thomas, MD SUNY Upstate Medical University 725 Irving Ave, Ste. 311 Syracuse, NY 13210 The names of the principal investigators, site addresses, and number of participants enrolled at each site are provided in the appendix titled List and Description of Investigators and Other Service Providers, Appendix 16.1.4.
Sponsor's Signatories:	John L. Perez, MD, MBA, MA Vice President, Vaccines Clinical Research and Development, Pfizer Inc

	Kenneth Koury, PhD Clinical Biostatistics Head, Vaccines Clinical Research and Development, Pfizer Inc Eleni Lagkadinou, MD, PhD Vice President, Clinical Development, BioNTech SE
Internal Reports Referenced:	C4591001 Booster Interim CSR: dated 23 August 2021 C4591001 6-Month Update Interim CSR: dated 29 April 2021 C4591001 Adolescent Interim CSR: dated 14 April 2021 C4591001 Final Analysis Interim CSR: dated 03 December 2020
Date of Current Version:	12 December 2021
Date(s) of Previous Report(s):	03 December 2021

GCP STATEMENT

This study was conducted in compliance with Good Clinical Practice (GCP) guidelines and, where applicable, local country regulations relevant to the use of new therapeutic agents in the country/countries of conduct, including the archiving of essential documents.

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4. LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Definition
AE	adverse event
ACIP	Advisory Committee on Immunization Practices
AESI	adverse event of special interest
BDR	blinded data review
BMI	body mass index
CDC	Centers for Disease Control and Prevention (United States)
CI	confidence interval
COVID-19	coronavirus disease 2019
CRF	case report form
CRO	contract research organization
CSR	clinical study report
CV	curriculum vitae
DCT	data collection tool
DMC	data monitoring committee
e-diary	electronic diary
EKG	electrocardiogram
GCP	Good Clinical Practice
GMC	geometric mean concentration
GMFR	geometric mean fold rise
GMR	geometric mean ratio
GMT	geometric mean titer
HBc Ab	hepatitis B core antibody
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HCV Ab	hepatitis C virus antibody
HIV	human immunodeficiency virus
ICD	informed consent document
ICH	International Council for Harmonisation
IEC	independent ethics committee
IgG	immunoglobulin G
IgM	immunoglobulin M
IRB	institutional review board
IRC	internal review committee
IRR	illness rate ratio
IRT	interactive response technology
IWR	interactive Web-based response
LNP	lipid nanoparticle
MedDRA	Medical Dictionary for Regulatory Activities
modRNA	nucleoside-modified messenger ribonucleic acid
NAAT	nucleic acid amplification test
N-binding	SARS-CoV-2 nucleoprotein binding
P2 S	SARS-CoV-2 full-length, P2 mutant, prefusion spike glycoprotein
PCR	polymerase chain reaction

Abbreviation	Definition
PD	protocol deviation
PT	preferred term
QA	quality assurance
QTL	quality tolerance limit
RCDC	reverse cumulative distribution curve
RDC	remote data capture
RNA	ribonucleic acid
SA	South Africa
SAE	serious adverse event
SAP	statistical analysis plan
SARS	severe acute respiratory syndrome
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SMQ	standardized MedDRA queries
SOC	system organ class
TME	targeted medical event
US	United States
VOC	variant of concern
VOI	variant of interest

5. ETHICS

5.1. Independent Ethics Committee or Institutional Review Board

The final protocol, any amendments (Appendix 16.1.1), and ICD (Appendix 16.1.3.2) were reviewed and approved by the IRBs and/or IECs for each of the investigational centers participating in the study. The IRBs and IECs are listed in Appendix 16.1.3.1.

5.2. Ethical Conduct of the Study

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all ICH GCP guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial participants.

5.3. Participant Information and Consent

In this clinical study report, the terms “participant” and “subject” are used interchangeably.

A signed and dated informed consent was required before any study-specific activity was performed. If the participant was not able to legally sign consent, the investigator, or a person designated by the investigator, obtained a signed and dated ICD from each participant’s parent(s)/guardian(s) before any study-specific activity was performed. Informed consent was collected as detailed in the protocol. Refer to Appendix 16.1.1, Protocol Section 10.1.2 for further information regarding informed consent.

6. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

This study was undertaken by Pfizer and BioNTech SE and conducted at 29 sites in the United States for adolescent participants 12 through 15 years of age as of the data cutoff date (02 September 2021) (Appendix 16.1.4.1). Due to live database and ongoing nature of the study, there is a discrepancy in the number of participants screened/randomized in Appendix 16.1.4.1 compared with the results tables.

Refer to Appendix 16.1.4 for a list of investigators and sites (including participants by country) and a list of service providers and external clinical testing laboratories involved in this study. Refer to Appendix 16.1.10 for a list of internal and external clinical testing laboratories involved in this study, with the tests that they performed.

The study was conducted by investigators contracted by and under the direction of Pfizer. The investigators were responsible for adhering to the study procedures described in the protocol, for keeping records of the study intervention, and for ensuring accurate completion of the CRFs and DCTs supplied by Pfizer.

No sites were terminated from the study to date.

7. INTRODUCTION

In December 2019, a pneumonia outbreak of unknown cause occurred in Wuhan, China. In January 2020, it became clear that a novel coronavirus was the underlying cause. On 11 March 2020, the WHO characterized the COVID-19 outbreak as a pandemic[1], which has

spread rapidly globally. A prophylactic, RNA-based SARS-CoV-2 vaccine provides one of the most flexible and fastest approaches available to immunize against COVID-19.[2,3]

This ongoing Phase 1/2/3 study is the registrational and pivotal study of the prophylactic BNT162b2 vaccine candidate against COVID-19 in healthy individuals ≥12 years of age that was initiated in April 2020.

This ongoing study has demonstrated the safety, tolerability, immunogenicity, and efficacy of BNT162b2 when administered as 2 doses of 30 µg given approximately 21 days apart, which was the basis of the current authorizations and approvals. Study C4591001 data supporting authorization or licensure for the 2-dose series in participants ≥12 years of age are summarized below:

- Phase 1 evaluated safety and immunogenicity results in healthy adult participants across dose levels of 2 vaccine candidates, BNT162b1 and BNT162b2. The Phase 1 reactogenicity and immunogenicity profiles, combined with available nonclinical animal study data, led to the selection of BNT162b2 at the 30-µg dose level to advance to Phase 2/3 evaluation.

- Phase 2/3 evaluated efficacy of BNT162b2 30 µg, and provided additional safety, efficacy, and immunogenicity data in a larger population. Prespecified efficacy (event-driven) in participants ≥12 years of age and ongoing safety data in participants ≥16 years of age with a median of at least 2 months of follow-up after Dose 2 and up to a data cutoff date of 14 November 2020 were previously reported in the C4591001 Final Analysis Interim CSR, dated 03 December 2020. On 11 December 2020, the US FDA issued an EUA for use of BNT162b2 at 30 µg in individuals ≥16 years of age.

- For adolescents (12 through 15 years of age), immunobridging and safety (median ≥2 months follow-up) were compared with young adults 16 through 25 years of age were reported in the adolescent interim CSR, dated 14 April 2021. Immunogenicity data from adolescent (and young adult) participants showed robust neutralizing GMTs after vaccination with 2 doses of BNT162b2 at 30 µg. In addition, descriptive efficacy analyses during blinded placebo-controlled follow-up period conducted on all confirmed COVID-19 cases accrued up to the data cutoff date of 13 March 2021 for adolescents (12 through 15 years of age) showed estimated VE was 100.0% for cases reported from at least 7 days after Dose 2 in individuals without and with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen. On 10 May 2021, the US FDA issued an EUA for use in individuals 12 to 15 years of age. At present, there are currently no licensed vaccines to immunize against COVID-19 for individuals 12 to 15 years of age in the US.

- Follow-up to 6 months after Dose 2 was provided in the C4591001 6-Month Update Interim CSR, dated 29 April 2021, and provided up to 6 months of additional safety, efficacy, and immunogenicity follow-up data. The report included analysis of safety during the blinded and post-unblinding (open-label) periods through 6 months post-Dose 2 for participants ≥16 years of age, and updated efficacy analysis based on all confirmed COVID-19 cases in participants ≥12 years of age that accrued in blinded follow-up to a

data cutoff date of 13 March 2021. On 23 August 2021, the US FDA granted licensure of COMIRNATY (BNT162b2) for individuals ≥16 years of age.

Based on a data cutoff date of 02 September 2021, this interim report for adolescent participants 12 to 15 years of age summarizes updated descriptive efficacy analyses from 7 days after Dose 2 during blinded placebo-controlled follow-up (Section 11.1) and the following safety data, as ordered:

- Blinded placebo-controlled follow-up period from Dose 1 to the date of unblinding for BNT162b2 and placebo participants, including new AEs that were reported after the EUA snapshot date (based on events on or after the data cutoff date of 13 March 2021) (Section 12.2.1)
- Open-label observational follow-up period of original BNT162b2 recipients from the date of unblinding to the data cutoff date (Section 12.2.2)
- Cumulative safety from Dose 1 to at least 6 months after Dose 2, inclusive of blinded data and open-label data for original BNT162b2 recipients, including new AEs that were reported after the EUA snapshot date (Section 12.2.3)
- Open-label observational follow-up period for original placebo recipients who then received BNT162b2 from the first dose of BNT162b2 to the data cutoff date (Section 12.2.4)

8. STUDY OBJECTIVES AND ENDPOINTS

8.1. Phase 1

Phase 1 results are not presented in this report. Refer to Appendix 16.1.1, Protocol Section 3.1 for the study objectives, estimands, and endpoints.

8.2. Phase 2/3

The study objectives, estimands, and endpoints presented in Table 1 are from Appendix 16.1.1, Protocol Amendment 18. This report summarizes safety and immunogenicity for adolescent participants only, as described in Section 7.

Study objectives and endpoint analyses that were either previously reported, or will be reported at a later time, are indicated with gray shading and per the ‘reference’ column in Table 1.

Table 1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
Primary Efficacy			
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 7 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 7 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants with no serological or virological evidence (up to 7 days after receipt of the second dose) of past SARS-CoV-2 infection	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020. Updated efficacy data are reported in the 6-month update interim CSR dated 29 April 2021. Efficacy data from 7 days after Dose 2 to the data cutoff date (13 March 2021) for participants 12 through 15 years of age only are reported in the adolescent interim CSR dated 14 April 2021.
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 7 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 7 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT	Interim data are reported in final analysis interim CSR dated 03 December 2020. Updated efficacy data are reported in the 6-month update interim CSR dated 29 April 2021. Efficacy data from 7 days after Dose 2 to the data cutoff date (13 March 2021) for participants 12 through 15 years of age only are reported in the adolescent interim CSR dated 14 April 2021.

Table 1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
Primary Safety			
To define the safety profile of prophylactic BNT162b2 in the first 360 participants randomized (Phase 2)	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 7 days after the second dose • SAEs from Dose 1 to 7 days after the second dose	• 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	Interim data are reported in final analysis interim CSR dated 03 December 2020.
To define the safety profile of prophylactic BNT162b2 in all participants randomized in Phase 2/3	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	• AEs • SAEs • In a subset of at least 6000 participants: o Local reactions (pain at the injection site, redness, and swelling) o Systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain)	Interim data are reported up to 1 month after Dose 2 and to the data cutoff date (14 November 2020) in final analysis interim CSR dated 03 December 2020. Cumulative interim data up to cutoff date (13 March 2021) are reported in the 6-month update interim CSR dated 29 April 2021. Interim adolescent data for local reactions and systemic events reported up to 7 days after each dose, and AEs and SAEs are reported from Dose 1 to 1 month after Dose 2 and to the data cutoff date (13 March 2021) are reported in the adolescent interim CSR dated 14 April 2021.

Table 1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
To define the safety profile of prophylactic BNT162b2 in participants 12 to 15 years of age in Phase 3	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	• 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	Interim data are reported up to 1 month after Dose 2 and to the data cutoff date (13 March 2021) in the adolescent interim CSR dated 14 April 2021. Interim data for AEs and SAEs reported up to 6 months after Dose 2 and to the data cutoff date (02 September 2021) are reported in this CSR.
To describe the safety and tolerability profile of BNT162b2$_{SA}$ given as 1 or 2 doses to BNT162b2-experienced participants, or as 2 doses to BNT162b2-naïve participants To describe the safety and tolerability profile of BNT162b2 given as a third dose to BNT162b2-experienced participants in the subset for evaluation of boostability and protection against emerging VOCs	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 last dose • SAEs from Dose 1 to 5 or 6 months after the last dose	• 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	Interim data for BNT162b2 given as a third dose to BNT162b2-experienced participants only are reported up to 1 month after Dose 3 and to the data cutoff date (17 June 2021) in the booster interim CSR dated 23 August 2021.
To describe the safety and tolerability profile of BNT162b2 given as a third dose at least 6 months after the second dose of BNT162b2 (or BNT162b2$_{SA}$) for participants who received a third dose as part of protocol amendment 18	In participants receiving at least 1 dose of study intervention, the percentage of participants reporting: • AEs from Dose 3 to 1 month after Dose 3 • SAEs from Dose 3 to 6 months after Dose 3	• AEs • SAEs	Interim data for BNT162b2 given as a third dose to BNT162b2-experienced participants only are reported up to 1 month after Dose 3 and to the data cutoff date (17 June 2021) in the booster interim CSR dated 23 August 2021.

Table 1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
Primary Immunogenicity			
BNT162b2-experienced participants			
To demonstrate the noninferiority of the anti–reference strain immune response after a third dose of BNT162b2 at 30 µg compared to after 2 doses of BNT162b2, in the same individuals	GMR of reference strain NT 1 month after the third dose of BNT162b2 at 30 µg to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the reference strain at 1 month after the third dose of BNT162b2 at 30 µg and 1 month after the second dose of BNT162b2	SARS-CoV-2 reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the third dose of BNT162b2 at 30 µg) of past SARS-CoV-2 infection	Interim data for BNT162b2 given as a third dose to BNT162b2-experienced participants are reported up to 1 month after Dose 3 and to the data cutoff date (17 June 2021) in the booster interim CSR dated 23 August 2021.
To demonstrate the noninferiority of the anti-SA immune response after 1 dose of BNT162b2$_{SA}$ compared to the anti-reference strain immune response after 2 doses of BNT162b2, in the same individuals	GMR of SA NT 1 month after 1 dose of BNT162b2$_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after 1 dose of BNT162b2$_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of 1 dose of BNT162b2$_{SA}$) of past SARS-CoV-2 infection	Data will be reported at a later time.
BNT162b2-naïve participants			
To demonstrate the noninferiority of the anti-SA immune response after 2 doses of BNT162b2$_{SA}$ compared to the anti-reference strain immune response after 2 doses of BNT162b2	GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$ or BNT162b2 as appropriate) of past SARS-CoV-2 infection	Data will be reported at a later time.

Table 1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
Secondary Efficacy			
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 14 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants with no serological or virological evidence (up to 14 days after receipt of the second dose) of past SARS-CoV-2 infection	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020.
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 14 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020.
To evaluate the efficacy of prophylactic BNT162b2 against confirmed severe COVID-19 occurring from 7 days and from 14 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	Confirmed severe COVID-19 incidence per 1000 person-years of follow-up in participants with no serological or virological evidence (up to 7 days and up to 14 days after receipt of the second dose) of past SARS-CoV-2 infection	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020. Updated efficacy data occurring from at least 7 days after the second dose only are reported in the 6-month update interim CSR dated 29 April 2021. Updated efficacy data occurring from at least 7 days after the second dose for participants 12 through 15 years of age only are reported in the adolescent interim CSR dated 14 April 2021.
To evaluate the efficacy of prophylactic BNT162b2 against confirmed severe COVID-19 occurring from 7 days and from 14 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	Confirmed severe COVID-19 incidence per 1000 person-years of follow-up	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020. Updated efficacy data occurring from at least 7 days after the second dose only are reported in the 6-month update interim CSR dated 29 April 2021.

Table 1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
			Updated efficacy data occurring from at least 7 days after the second dose for participants 12 through 15 years of age only are reported in the adolescent interim CSR dated 14 April 2021.
To describe the efficacy of prophylactic BNT162b2 against confirmed COVID-19 (according to the CDC-defined symptoms) occurring from 7 days and from 14 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants with no serological or virological evidence (up to 7 days and up to 14 days after receipt of the second dose) of past SARS-CoV-2 infection	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020.
To describe the efficacy of prophylactic BNT162b2 against confirmed COVID-19 (according to the CDC-defined symptoms) occurring from 7 days and from 14 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT	Prespecified complete efficacy data are reported in final analysis interim CSR dated 03 December 2020.
To evaluate the efficacy of prophylactic BNT162b2 against non-S seroconversion to SARS-CoV-2 in participants without evidence of infection or confirmed COVID-19	In participants complying with the key protocol criteria (evaluable participants): 100 × (1 – IRR) [ratio of active vaccine to placebo]	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on N-binding antibody seroconversion in participants with no serological or virological evidence of past SARS-CoV-2 infection or confirmed COVID-19	Data will be reported at a later time.
To evaluate the efficacy of prophylactic BNT162b2 against asymptomatic SARS-CoV-2 infection in participants without evidence of infection up to the start of the asymptomatic surveillance period	In participants complying with the key protocol criteria (evaluable participants): 100 × (1 – IRR) [ratio of active vaccine to placebo]	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on central laboratory–confirmed NAAT in participants with no serological or virological evidence (up to the start of	Data will be reported at a later time.

Table 1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
		the asymptomatic surveillance period) of past SARS-CoV-2 infection	
Secondary Immunogenicity			
To demonstrate the noninferiority of the immune response to prophylactic BNT162b2 in participants 12 to 15 years of age compared to participants 16 to 25 years of age	GMR, estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in the 2 age groups (12-15 years of age to 16-25 years of age) 1 month after completion of vaccination	SARS-CoV-2 neutralizing titers in participants with no serological or virological evidence (up to 1 month after receipt of the second dose) of past SARS-CoV-2 infection	Interim data are reported in the adolescent interim CSR dated 14 April 2021.
BNT162b2-experienced participants			
To demonstrate the noninferiority of the anti-SA immune response after a third dose of BNT162b2 at 30 µg compared to the anti–reference strain immune response after 2 doses of BNT162b2, in the same individuals	GMR of SA NT 1 month after the third dose of BNT162b2 at 30 µg to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the third dose of BNT162b2 at 30 µg and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the third dose of BNT162b2 at 30 µg) of past SARS-CoV-2 infection	Data will be reported at a later time.
To demonstrate the noninferiority of the anti–reference strain immune response after 1 dose of BNT162b2$_{SA}$ compared to after 2 doses of BNT162b2, in the same individuals	GMR of reference strain NT 1 month after 1 dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the reference strain at 1 month after 1 dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2	SARS-CoV-2 reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of 1 dose of BNT162b2$_{SA}$) of past SARS-CoV-2 infection	Data will be reported at a later time.

Table 1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
To descriptively compare the anti-SA immune response after 1 dose of BNT162b2$_{SA}$ and a third dose of BNT162b2 at 30 µg	GMR of SA NT 1 month after 1 dose of BNT162b2$_{SA}$ to 1 month after the third dose of BNT162b2 at 30 µg The difference in percentages of participants with seroresponse to the SA strain at 1 month after 1 dose of BNT162b2$_{SA}$ and 1 month after the third dose of BNT162b2 at 30 µg	SARS-CoV-2 SA NT in participants with no serological or virological evidence (up to 1 month after receipt of 1 dose of BNT162b2$_{SA}$ or the third dose of BNT162b2 at 30 µg) of past SARS-CoV-2 infection	Data will be reported at a later time.
To descriptively compare the anti-SA immune response after 2 doses of BNT162b2$_{SA}$ and the anti–reference strain immune response after 2 doses of BNT162b2, in the same individuals	GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$) of past SARS-CoV-2 infection	Data will be reported at a later time.
BNT162b2-naïve participants			
To demonstrate a statistically greater anti-SA immune response after 2 doses of BNT162b2$_{SA}$ compared to after 2 doses of BNT162b2	GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2	SARS-CoV-2 SA NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$ or BNT162b2 as appropriate) of past SARS-CoV-2 infection	Data will be reported at a later time.

Table 1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
To descriptively compare the anti-reference strain immune response after 2 doses of BNT162b2$_{SA}$ and after 2 doses of BNT162b2	GMR of reference strain NT 1 month after the second dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to reference strain at 1 month after the second dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2	SARS-CoV-2 reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$ or BNT162b2 as appropriate) of past SARS-CoV-2 infection	Data will be reported at a later time.
Exploratory			
To describe the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 7 days after the second dose through the blinded follow-up period in participants without, and with and without, evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of blinded follow-up based on central laboratory or locally confirmed NAAT	Interim data are reported in the 6-month update interim CSR dated 29 April 2021. Updated efficacy data from 7 days after Dose 2 through the blinded follow-up period for participants 12 through 15 years of age are provided in this CSR.
To describe the incidence of confirmed COVID-19 through the entire study follow-up period prior to receiving the third dose of BNT162b2 in participants who received BNT162b2 at initial randomization or subsequently	In participants who received BNT162b2 (at initial randomization or subsequently): Incidence per 1000 person-years of follow-up	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT	Data will be reported at a later time.
To describe the incidence of confirmed COVID-19 after receiving the third dose of BNT162b2	In participants who received the third dose of BNT162b2: Incidence per 1000 person-years of follow-up	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT	Data will be reported at a later time.

Table 1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
To evaluate the immune response over time to prophylactic BNT162b2 and persistence of immune response in participants with and without serological or virological evidence of SARS-CoV-2 infection before vaccination	GMC/GMT and GMFR at baseline and 1, 6, 12, and 24 months after completion of vaccination	• Full-length S-binding or S1-binding IgG levels • SARS-CoV-2 neutralizing titers	Interim data for Phase 2 (first 360 participants) only up to 1 month after Dose 2 are reported for S1-binding IgG levels and SARS-CoV-2 neutralizing titers in final analysis interim CSR dated 03 December 2020. GMTs and GMFRs of SARS-CoV-2 neutralizing titers up to 1 month after Dose 2 in participants 12 through 15 and 16 through 25 years of age are reported in the adolescent interim CSR dated 14 April 2021.
To describe the incidence of non-S seroconversion to SARS-CoV-2 through the entire study follow-up period in participants who received BNT162b2 at initial randomization	In participants who received BNT162b2 at initial randomization: Incidence per 1000 person-years of follow-up	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on N-binding antibody seroconversion in participants with no serological or virological evidence of past SARS-CoV-2 infection or confirmed COVID-19	Data will be reported at a later time.
To describe the efficacy of prophylactic BNT162b2 against asymptomatic SARS-CoV-2 infection in participants with evidence of infection up to the start of the asymptomatic surveillance period	In participants complying with the key protocol criteria (evaluable participants): 100 × (1 – IRR) [ratio of active vaccine to placebo]	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on central laboratory–confirmed NAAT in participants with serological or virological evidence (up to the start of the asymptomatic surveillance period) of past SARS-CoV-2 infection	Data will be reported at a later time.
To describe the serological responses to the BNT vaccine candidate and characterize the SARS-CoV-2 isolate in cases of: • Confirmed COVID-19 • Confirmed severe COVID-19 • SARS-CoV-2 infection without confirmed COVID-19		• Full S-binding or S1-binding IgG levels • SARS-CoV-2 neutralizing titers • Identification of SARS-CoV-2 variants(s)	Data will be reported at a later time.

Table 1. Phase 2/3 Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints	Reference
To describe the safety, immunogenicity, and efficacy of prophylactic BNT162b2 in individuals with confirmed stable HIV disease		• All safety, immunogenicity, and efficacy endpoints described above	Safety data only in participants with confirmed stable HIV disease are reported in the 6-month update interim CSR dated 29 April 2021.
To describe the safety and immunogenicity of prophylactic BNT162b2 in individuals 16 to 55 years of age vaccinated with study intervention produced by manufacturing "Process 1" or "Process 2"[b]		• AEs • SAEs • SARS-CoV-2 neutralizing titers	Data will be reported at a later time.
To describe the immune response to any VOCs not already specified	Geometric mean NT for any VOCs not already specified, after any dose of $BNT162b2_{SA}$ or BNT162b2	• SARS-CoV-2 NTs for any VOCs not already specified	Data will be reported at a later time.
To describe the immune response to a third dose of BNT162b2 (at 30 µg or a lower dose of 5 µg or 10 µg) or a third or fourth dose of $BNT162b2_{SA}$	• GMTs at Dose 3 and subsequent time points • GMFRs from Dose 3 to subsequent time points	• SARS-CoV-2 reference strain NTs	Interim data for BNT162b2 30 µg given as a third dose to BNT162b2-experienced participants are reported in the booster interim CSR dated 23 August 2021.
To describe the cell-mediated immune response, and additional humoral immune response parameters, to the reference strain and SA in a subset of participants: • 7 days and 1 and 6 months after $BNT162b2_{SA}$ given as 1 or 2 doses to BNT162b2-experienced participants • 7 days and 1 and 6 months after $BNT162b2_{SA}$ given as 2 doses to BNT162b2-naïve participants • 7 days and 1 and 6 months after BNT162b2 given as a third dose to BNT162b2-experienced participants			Data will be reported at a later time.

a. HIV-positive participants in Phase 3 were not included in analyses of the objectives, with the exception of the specific exploratory objective.
b. See Appendix 16.1.1, Protocol Section 6.1.1 for a description of the manufacturing process.
Source: Appendix 16.1.1, Protocol Section 3.2.

9. INVESTIGATIONAL PLAN

9.1. Overall Study Design and Plan

This is a Phase 1/2/3, randomized, multinational, placebo-controlled, observer-blind, dose finding, vaccine candidate–selection, and efficacy study in healthy individuals.

The study consists of 2 parts: Phase 1 to identify preferred vaccine candidate(s) and dose level(s); and Phase 2/3 as an expanded cohort and efficacy part. The study evaluated the safety, tolerability, and immunogenicity of 3 different SARS-CoV-2 RNA vaccine candidates against COVID-19 and the Phase 2/3 efficacy of 1 selected candidate based on Phase 1 results:

- As a 2-dose (separated by 21 days) schedule;
- At various dose levels in Phase 1;
- As a booster (Dose 3); (see Boostability and Variant Strain Evaluation)
- In various age groups:
  - Phase 1: 18 to 55 and 65 to 85 years of age;
  - Phase 2: ≥18 years of age (stratified as 18 to 55 years and >55 to 85 years);
  - Phase 3: ≥12 years of age (stratified as 12 to 15, 16 to 55, or >55 years of age).

To facilitate rapid review of data in real time, Pfizer and BioNTech staff were unblinded to vaccine allocation for the participants in Phase 1, and remain blinded for the Phase 2/3 portion of study except those who were designated for unblinded activities following the protocol and the data blinding plan.

Refer to Appendix 16.1.1, Protocol Section 4.1 for further detail on the overall study design.

Boostability and Variant Strain Evaluations

Immunogenicity and safety evaluations of boostability were conducted in a subset of Phase 3 participants at selected sites in the US who received a third dose of BNT162b2 at 30 µg at least 6 months after their second dose, and results are reported in the booster interim CSR dated 23 August 2021. Evaluations of boostability in Phase 1 participants and a further subset of Phase 3 participants receiving a third, lower, dose of BNT162b2 at 5 or 10 µg will be reported at a later time.

Evaluations of VOC strains of SARS-CoV-2 (in participants who receive a SARS-CoV-2 variant encoding vaccine that encodes the Beta variant originally identified in South Africa

[BNT162b2$_{SA}$] as a third dose) are not included in this report and will be reported at a later time.

Refer to Appendix 16.1.1, Protocol Section 4.1.1 for further details on the booster (Dose 3) for Phase 1, and Appendix 16.1.1, Protocol Section 4.1.2 for further details on the booster (Dose 3) and new cohort for Phase 2/3 to evaluate potential homologous and heterologous protection against emerging SARS-CoV-2 VOCs.

Unblinding Considerations

The study was to be unblinded in stages once all ongoing participants either had been individually unblinded or had concluded their 6-month post–Dose 2 or post-Dose 3 study visit, in the following sequence:

- Phase 1 (after Visit 8 [6-month post-Dose 2 visit]).
- Phase 2/3, ≥16 years of age (after Visit 4 [6-month post-Dose 2 visit]).
- Phase 3, 12 through 15 years of age (after Visit 4 [6-month post-Dose 2 visit]).
- Original Phase 3 participants rerandomized to assess boostability and protection against emerging VOCs (after Visit 306) (data not included in this report).

Participants who originally received placebo and became eligible for receipt of BNT162b2 according to recommendations detailed separately, and available in the electronic study reference portal, had the opportunity to receive BNT162b2 in a phased manner as part of the study. The investigator ensured the participant met at least 1 of the recommendation criteria based upon US recommendation.

Any Phase 1 placebo recipient who had not already been offered the opportunity to receive BNT162b2 was given this opportunity no later than at the approximate time participants in Phase 2/3 reached Visit 4. Any Phase 2/3 placebo recipient who had not already been offered the opportunity to receive BNT162b2 was given this opportunity no later than 6 months after Vaccination 2 (at the time of the originally planned Visit 4).

Any participant who originally received placebo but then went on to receive BNT162b2 was moved to a new visit schedule to receive both doses of BNT162b2 at each of 2 additional vaccination visits (Visits 101 and 102) (Appendix 16.1.1, Protocol Section 1.3.3).

9.1.1. Phase 1

Phase 1 safety follow-up is ongoing, and participants are expected to participate for up to a maximum of approximately 26 months.

Refer to Appendix 16.1.1, Protocol Section 4.1.1 for further details on the Phase 1 study design.

9.1.2. Phase 2/3

The Phase 2 part of the study was comprised of the first 360 participants enrolled (1:1 randomization between BNT162b2 and placebo, stratified by age groups [18 through 55 years and >55 through 85 years] with approximately 50% in each age stratum) to assess safety data through 7 days after Dose 2 and immunogenicity data through 1 month after Dose 2 from these 360 Phase 2 participants. Enrollment continued during Phase 2 and these participants were included in the efficacy evaluation in the Phase 3 part of the study.

Participants in the ongoing Phase 3 part of the study are ≥12 years of age (stratified as 12 through 15, 16 through 55, or >55 years of age). The 12 to 15 years of age stratum comprised up to approximately 2000 participants enrolled at selected investigational sites. It was planned to enroll a minimum of 40% of participants in the >55 years of age stratum. Participants in Phase 3 were randomized 1:1 to receive either active vaccine or placebo.

Efficacy analyses for Phase 2/3 part of the study were event-driven. The prespecified interim analysis was conducted on an accrued 94 evaluable COVID-19 cases for the first primary efficacy endpoint (data cutoff date: 04 November 2020), and the final analysis was conducted on an accrued 170 evaluable COVID-19 cases for the first primary efficacy endpoint (data cutoff date: 14 November 2020). These data are reported in the final analysis interim CSR dated 03 December 2020 and included all study participants in the efficacy populations ≥12 years of age.

At the time of the final analysis of efficacy (CSR dated 03 December 2020), relatively few participants 12 to 15 years of age had enrolled in the study, and no COVID-19 cases in this age group accrued at that time. In the adolescent interim CSR dated 14 April 2021, noninferiority of immune response to prophylactic BNT162b2 in participants 12 to 15 years of age to response in participants 16 to 25 years of age was assessed based on the GMR of SARS-CoV-2 neutralizing titers using a 1.5-fold margin and reported in the adolescent interim CSR dated 14 April 2021 and in an EUA amendment, which supported issuance of the EUA for use in individuals 12 to 15 years of age. Additionally, the adolescent interim CSR also presented updated descriptive efficacy analyses for participants 12 to 15 years of age, based on confirmed cases COVID-19 reported from at least 7 days after Dose 2 through the data cutoff date (13 March 2021), with an observed VE of 100% irrespective of evidence of prior infection with SARS-CoV-2. No severe COVID-19 cases were reported in this age group, based on either protocol definition (ie, per FDA criteria) or per CDC criteria for severity.

Updated efficacy analyses during the blinded placebo-controlled follow-up period were conducted on cases accrued up to the data cutoff date of 13 March 2021 to evaluate duration of protection and reported in the 6-month update interim CSR dated 29 April 2021, which presented these analyses of all confirmed COVID-19 cases and any cases meeting protocol- and CDC-defined criteria for severe cases.

It is planned that participants would participate in the study for approximately 26 months from the time of enrollment.

This interim report for participants 12 to 15 years of age includes updated efficacy analyses from 7 days after Dose 2 and safety analyses up to 6 months after Dose 2 and to the data cutoff date (02 September 2021).

Refer to Appendix 16.1.1, Protocol Section 4.1.2 for further detail on the Phase 2/3 study design, including the planned analyses.

9.2. Discussion of Study Design, Including Choice of Control Groups

The purpose of the study is to describe the safety, tolerability, and immunogenicity of 2 BNT162 RNA-based COVID-19 vaccine candidates against COVID-19, and the efficacy of 1 (selected) candidate, in healthy individuals. Boostability is being assessed in a subset of Phase 3 participants, including with a prototype vaccine that targets a SARS-CoV-2 VOC.

The study is observer-blinded, as the physical appearance of the investigational vaccine candidates and the placebo may differ. The participant, investigator, study coordinator, and other site staff are blinded. At the study site, only the dispenser(s)/administrator(s) are unblinded.

The study consists of 3 placebo-controlled phases. Placebo is used as the control, as there is no licensed comparator vaccine available.

Phase 1 was designed to identify preferred vaccine candidate(s) and dose level(s) for further development based on safety, tolerability, and immunogenicity.

Phase 2 was designed to expand knowledge of the safety and immunogenicity of the vaccine candidate selected from Phase 1.

Phase 2/3 was designed to evaluate the efficacy of the vaccine candidate selected for development, and to provide additional safety and immunogenicity data in a larger population, including adolescents (adolescents were later permitted to enroll as part of Phase 3). Boostability was also assessed.

Refer to Appendix 16.1.1, Protocol Section 4.2 for further detail of the rationale of the study design.

9.3. Participant Selection

9.3.1. Inclusion Criteria

Participants were eligible to be included in the study only if all of the following criteria applied:

Age and Sex:

1. Male or female participants between the ages of 18 and 55 years, inclusive, and 65 and 85 years, inclusive (Phase 1), or ≥12 years (Phase 2/3), at randomization.

For the boostability and protection-against-VOCs subset:

- Existing participants enrolled to receive a third dose of BNT162b2 at 30 µg or BNT162b2$_{SA}$; male or female participants between the ages of 18 and 55 years, inclusive, at rerandomization.

- Newly enrolled participants enrolled to receive 2 doses of BNT162b2$_{SA}$; male or female participants between the ages of 18 and 55 years, inclusive, at enrollment.

- Existing participants enrolled to receive a third dose of BNT162b2 at 5 or 10 µg; male or female participants ≥18 years at rerandomization.

Note that participants <18 years of age could not be enrolled in the EU.

- Refer to Appendix 4 for reproductive criteria for male (Appendix 16.1.1, Protocol Section 10.4.1) and female (Appendix 16.1.1, Protocol Section 10.4.2) participants.

Type of Participant and Disease Characteristics:

2. Participants who were willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures.

3. Healthy participants who were 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 Appendix 16.1.1, Protocol Section 10.8.

4. **Phase 2/3 only:** 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).

5. **Boostability and protection-against-VOCs existing participant subset only:** Participants who provided a serum sample at Visit 3, with Visit 3 occurring within the protocol-specified window.

Informed Consent:

6. Capable of giving personal signed informed consent/have parent(s)/legal guardian capable of giving signed informed consent as described in Appendix 16.1.1, Protocol Appendix 1, which included compliance with the requirements and restrictions listed in the ICD and in the protocol.

9.3.2. Exclusion Criteria

Participants were excluded from the study if any of the following criteria applied:

Medical Conditions:

1. Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that increased the risk of study participation or, in the investigator's judgment, made the participant inappropriate for the study.

2. **Phases 1 and 2 only:** Known infection with HIV, HCV, or HBV.

3. History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s).

4. Receipt of medications intended to prevent COVID-19.

5. 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.

6. **Phase 1 only:** Individuals at high risk for severe COVID-19, including those with any of the following risk factors:

- Hypertension
- Diabetes mellitus
- Chronic pulmonary disease
- Asthma
- Current vaping or smoking
- History of chronic smoking within the prior year
- Chronic liver disease
- Stage 3 or worse chronic kidney disease (glomerular filtration rate <60 mL/min/1.73 m^2)
- Resident in a long-term facility
- BMI >30 kg/m^2
- Anticipating the need for immunosuppressive treatment within the next 6 months

7. **Phase 1 only:** Individuals currently working in occupations with high risk of exposure to SARS-CoV-2 (eg, healthcare worker, emergency response personnel).

8. Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.

9. **Phase 1 only:** Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention, including but not limited to: systemic or cutaneous lupus erythematosus, autoimmune arthritis/rheumatoid arthritis, Guillain-Barré syndrome, multiple sclerosis, Sjögren's syndrome, idiopathic thrombocytopenia purpura,

glomerulonephritis, autoimmune thyroiditis, giant cell arteritis (temporal arteritis), psoriasis, and insulin-dependent diabetes mellitus (type 1).

10. Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection.

11. Women who are pregnant or breastfeeding.

Prior/Concomitant Therapy:

12. Previous vaccination with any coronavirus vaccine.

13. Individuals who received treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, eg, for cancer or an autoimmune disease, or planned receipt throughout the study. If systemic corticosteroids were administered short term (<14 days) for treatment of an acute illness, participants should not have been enrolled into the study until corticosteroid therapy had been discontinued for at least 28 days before study intervention administration. Inhaled/nebulized (except for participants in Phase 1 – see exclusion criterion 14), intra-articular, intrabursal, or topical (skin or eyes) corticosteroids were permitted.

14. **Phase 1 only:** Regular receipt of inhaled/nebulized corticosteroids.

15. Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study.

Prior/Concurrent Clinical Study Experience:

16. Participation in other studies involving study intervention within 28 days prior to study entry through and including 28 days after the last dose of study intervention, with the exception of non-Pfizer interventional studies for prevention of COVID 19, which are prohibited throughout study participation.

17. Previous participation in other studies involving study intervention containing lipid nanoparticles.

Diagnostic Assessments:

18. **Phase 1 only:** Positive serological test for SARS-CoV-2 IgM and/or IgG antibodies at the screening visit.

19. **Phase 1 only:** Any screening hematology and/or blood chemistry laboratory value that meets the definition of a ≥ Grade 1 abnormality.

Note: With the exception of bilirubin, participants with any stable Grade 1 abnormalities (according to the toxicity grading scale) may be considered eligible at the discretion of the investigator. (Note: A “stable” Grade 1 laboratory abnormality is defined as a report of Grade

1 on an initial blood sample that remains ≤ Grade 1 upon repeat testing on a second sample from the same participant.)

20. **Phase 1 only:** Positive test for HIV, HBsAg, HBc Abs, or HCV Abs at the screening visit.

21. **Phase 1 only:** SARS-CoV-2 NAAT-positive nasal swab within 24 hours before receipt of study intervention.

Other Exclusions:

Investigator site staff or Pfizer/BioNTech employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members.

9.4. Investigational Product

9.4.1. Vaccines Administered

The vaccine candidate selected for Phase 2/3 evaluation was BNT162b2 at a dose of 30 µg. The study evaluated a 2-dose (separated by 21 days) schedule of the following for active immunization against COVID-19 or saline placebo in participants 12 through 15 years of age:

- BNT162b2 (BNT162 RNA-LNP vaccine containing modRNA that encodes the P2 S): 30 µg
- Normal saline (0.9% sodium chloride solution for injection)

Refer to Appendix 16.1.1, Protocol Sections 6.1 and 6.1.2 for details of other planned or ongoing study intervention(s) and study intervention administration that will be reported at a later time.

9.4.2. Identity of Investigational Product(s)

Refer to Appendix 16.1.1, Protocol Section 6.2 for details on preparation, storage, and dispensing.

A list of the study interventions administered in this study and their respective lot numbers is provided in Table 2.

Table 2. Investigational Product Lot Numbers – Interim – Adolescent 6-Month Update

Investigational Product	Manufacturer	Vendor Lot Number (Manufacturer)	Lot Number[a] (Pfizer)
BNT162b2 (30 µg)	BioNTech	BCV40720-A	PA2074172/P220395-0053L
		BCV40720-A	PA2074998/P220395-0060L
		BCV40720-B	PA2074173/P220395-0051L
		BCV40720-C	PA2074071/P220395-0052L
		ED3938	PA2074300/P220395-0021L
		ED3938	PA2074300/P220395-0022L
		ED3938	PA2074300/P220395-0023L
		EE3813	NC2075485/P220395-0068L
		EE3813	NC2075485/P220395-0074L
		EE3813	NC2075485/P220395-0077L
		EE3813	PA2074838/P220395-0020L
		EE3813	PA2074838/P220395-0024L
		ER9449Z	PA2096794/P220395-0079L
		ER9449Z	PA2096794/P220395-0082L
		EE8493Y	PA2087473/P220395-0073L
		EJ0553Z	PA2085061/P220395-0070L
Placebo (normal saline 0.9% sodium chloride solution)	Pfizer	DK2074;20-002221	PA2069407/P220395-0032L
		DK2074;20-002221	PA2069407/P220395-0033L
		DK2074;20-002221	PA2069407/P220395-0034L
		DK2074;20-002221	PA2069407/P220395-0044L
		DK2074;20-002221	PA2069407/P220395-0045L
		DK2074;20-002221	PA2069407/P220395-0046L
		DK2074;20-002221	PA2069407/P220395-0055L
		DK2074;20-002221	PA2069407/P220395-0062L
		DK2074;20-002221	PA2069407/P220395-0065L
Diluent (normal saline 0.9% sodium chloride solution)	Pfizer	DK2074	20-002221
		DK1589	20-001776
		DK1589	20-001592

Note: C4591001 End of Study Information and Quality Control (QC) Record for Study Drug Appendix (Section D) dated 08Oct2021 was used to create this table.
a. Lot number assigned to the investigational product or diluent by Pfizer Global Clinical Supply.
Protocol C4591001 Investigational Product Lot Numbers Table – Interim – Adolescent 6-Month Update, Final, Version 1.0, 15Oct2021.

9.4.3. Method of Assigning Participants to Treatment Groups

Allocation (randomization) of participants to vaccine groups proceeded through the use of an IRT system (IWR).

Refer to Appendix 16.1.1, Protocol Section 6.3.1 for details on investigational product assignment.

9.4.4. Selection of Dose Levels/Regimen

9.4.4.1. Phase 1

Section 9.4.1 provides details on the doses administered in Phase 1.

Refer to Appendix 16.1.1, Protocol Section 6 for details of the dose and regimen.

9.4.4.2. Phase 2/3

The totality of data from Phase 1 as reported in the final analysis interim C4591001 CSR dated 03 December 2020 identified BNT162b2 at 30 µg as the candidate for Phase 2/3 evaluation.

Refer to Appendix 16.1.1, Protocol Section 6 for details of the dose and regimen.

9.4.5. Blinding

The study staff receiving, storing, dispensing, preparing, and administering the study interventions were unblinded. All other study and site personnel, including the investigator, investigator staff, and participants, were blinded to study intervention assignments.

To facilitate rapid review of data in real time, Pfizer and BioNTech staff were unblinded to study intervention allocation for the participants in the Phase 1 portion of the study. Sponsor staff and all personnel directly involved in study conduct were blinded to study intervention allocation in Phase 2/3. All laboratory testing personnel performing serology assays remain blinded to study intervention assigned/received throughout all phases of the study.

The study was to be unblinded in stages once all ongoing participants either had been individually unblinded or had concluded their 6-month post–Dose 2 or post-Dose 3 study visit, as follows:

- Phase 1 (after Visit 8).
- Phase 2/3, ≥16 years (after Visit 4).
- Phase 3, 12 to 15 years (after Visit 4).
- Original Phase 3 participants rerandomized to assess boostability and protection against emerging VOCs (after Visit 306) (data will be reported at a later time).

Participants who originally received placebo and became eligible for receipt of BNT162b2 according to recommendations detailed separately, and available in the electronic study reference portal, had the opportunity to receive BNT162b2 in a phased manner as part of the study. The investigator ensured the participant met at least 1 of the recommendation criteria.

Refer to Appendix 16.1.1, Protocol Section 6.3.2 for details on blinding of the site personnel, Protocol Section 6.3.3 for details on blinding of Pfizer and BioNTech personnel, and Protocol Section 6.3.4 for circumstances when the blind could be broken.

9.4.6. Prior and Concomitant Vaccines, Medications, and Procedures

Prohibited During the Study

Participants may have been excluded from the per-protocol analysis and may not have received further required study vaccinations upon receipt of the vaccines and medications prohibited during the time periods specified in Appendix 16.1.1, Protocol Section 6.5.1; however, participants were not withdrawn from the study. Medications were not withheld if required for a participant's medical care.

Prophylactic antipyretics and other pain medication to prevent symptoms associated with study intervention administration were not permitted. However, if a participant was taking a medication for another condition, even if it had antipyretic or pain-relieving properties, it was not withheld prior to study vaccination.

Permitted During the Study

The use of antipyretics and other pain medication to treat symptoms associated with study intervention administration or ongoing conditions was permitted.

Medication other than that described as prohibited in Appendix 16.1.1, Protocol Section 6.5.1 required for treatment of preexisting stable conditions was permitted.

Inhaled, topical, or localized injections of corticosteroids (eg, intra-articular or intrabursal administration) were permitted.

Refer to Appendix 16.1.1, Protocol Section 6.5.2 for details on prior and concomitant vaccines, medications and procedures that were allowed.

9.4.7. Vaccine Compliance

Participants dosed at the site received study intervention directly from the investigator or designee, under medical supervision.

Refer to Appendix 16.1.1, Protocol Section 6.4 for details of compliance with study intervention.

9.5. Efficacy, Immunogenicity, and Safety Evaluations

9.5.1. Efficacy and Immunogenicity Evaluations

Efficacy was assessed based on all cases in participants 12 through 15 years of age accrued in blinded follow-up to a data cutoff date of 13 March 2021 in the adolescent interm CSR, dated 14 April 2021.

In this report, updated descriptive efficacy analyses for participants 12 through 15 years of age accrued during blinded placebo-controlled follow-up are summarized up to a data cutoff date of 02 September 2021.

Immunogenicity evaluations in participants 12 through 15 years of age are not included in

this interim report. The immune response to BNT162b2 30 µg in adolescents 12 through 15 years of age was previously reported to be noninferior (and in fact exceeded) the immune response in young adults 16 through 25 years of age (ie, successful immunobridging), as detailed in the adolescent interim report dated 14 April 2021.

Refer to Appendix 16.1.1, Protocol Section 8.1 for details on efficacy and immunogenicity evaluations.

9.5.2. Safety Evaluations

Safety evaluations are as described in Appendix 16.1.1, Protocol Section 8.2.

9.5.2.1. Electronic Diary

There are no new e-diary data presented in this report (previously reported in the adolescent interim CSR, dated 14 April 2021).

Refer to Appendix 16.1.1, Protocol Section 8.2.2 for additional details on use of the e-diary. Refer to Appendix 16.1.1, Protocol Section 8.2.2.2, Protocol Section 8.2.2.3, Protocol Section 8.2.2.4, Protocol Section 8.2.2.5 for details on grading of prompted local reactions, systemic events, fever, and use of antipyretic/pain medications, respectively.

9.5.2.2. Surveillance of Events That Could Represent Vaccine-Associated Enhanced COVID-19 and Phase 2/3 Stopping Rule

Participants in all phases of the study were surveilled for potential COVID-19 illness from Visit 1 onwards. If a participant experienced any potential symptoms for COVID-19 illness, a COVID-19 illness and, prior to protocol amendment 16 (28 May 2021), subsequent convalescent visit (in-person or telehealth) occurred. As part of these visits, samples (nasal [midturbinate] swab and blood) were taken for antigen and antibody assessment as well as recording of COVID-19–related clinical and laboratory information (including local diagnosis).

In Phase 2/3, the unblinded team supporting the DMC, including an unblinded medical monitor, reviewed cases of severe COVID-19 as they were received and reviewed AEs at least weekly for additional potential cases of severe COVID-19.

When the total number of severe cases was 20 or less, stopping rules and alert rules in Appendix 16.1.1, Protocol Table 10 and Table 11, respectively, applied.

Refer to Appendix 16.1.1, Protocol Section 8.13 for details on COVID-19 surveillance, and Protocol Section 8.2.4 for details on Phase 2/3 stopping rules.

9.5.2.3. Adverse Events and Serious Adverse Events

AEs were collected during the study from the signing of the ICD through and including 1 month after Dose 2 (Visit 3 for Phase 2/3 participants).

Acute reactions (immediate AEs) were collected within the first 30 minutes after administration of the study intervention.

SAEs were collected from the signing of the ICD to approximately 6 months after the last dose of study intervention (Visit 4 for Phase 2/3 participants).

For those participants who originally received placebo but went on to receive BNT162b2 at Vaccinations 3 and 4, AEs were collected from the time the participant provided informed consent (for receipt of Vaccinations 3 and 4) through and including Visit 103 (1-month follow-up after Vaccination 4). SAEs were collected from the time the participant provided informed consent (for receipt of Vaccinations 3 and 4) to approximately 6 months after the second dose of BNT162b2 (Visit 104).

Refer to Appendix 16.1.1, Protocol Section 8.3 for additional details for collecting AEs and SAEs.

9.5.2.4. Events of Special Interest

Myocarditis and pericarditis were included as AESIs in Protocol Amendment 18 (07 September 2021).

Pfizer also utilizes a safety review as part of the signal detection processes that highlights specified TMEs of clinical interest. TMEs are specific AE terms reviewed on an ongoing basis by routine safety data review procedures throughout the clinical study. Although not prespecified in the protocol, TMEs are maintained in a separate list as part of the Safety Surveillance Review Plan for the vaccine program. By definition, TMEs are considered to be AESIs specific for a product or program's protocol(s). They are based on review of known pharmacology, toxicology findings, possible class effects, published literature, and potential signals arising from safety data assessments.

The list of TMEs is customized for each development program and is dynamic. For this study, the list of TMEs includes events of interest because of their association with COVID-19 and terms of interest for vaccines in general. Terms are chosen from the MedDRA dictionary and may include PTs, high level term, high level group terms, or standardized MedDRA queries (SMQs; all evaluated as broad and narrow).

Other events of clinical interest identified by the sponsor in the reported safety dataset were also reviewed and summarized (Section 12.3.4).

9.6. Data Quality Assurance

A number of steps were taken in the planning and implementation of this study to ensure that the data collected were accurate, consistent, complete, and reliable. This study used an RDC system and handheld diary device or application. The CRFs were designed to be used with ease.

Investigators were required to review the diary data online at frequent intervals to evaluate participant compliance and as part of the ongoing safety review. Furthermore, diary data were made available to Pfizer and Pfizer's representative online to enable ongoing review.

Representatives of Pfizer conducted routine reviews, using both on-site and remote access options with the investigational sites while the study was in progress to check the accuracy

and completeness of the data being entered into the RDC system. During these visits, critical data were verified against participant source documents, and queries regarding missing or contradictory data were resolved. In addition, study procedures were reviewed, and protocol deviations were discussed with the investigator. Telephone and email contact was maintained with the investigators between site visits. In addition, the overall study conduct was subject to internal quality review by Pfizer.

The quality risk management plan used in this study documents risks and controls that are in place throughout the life of the study. In this study, QTLs were defined during the quality risk management planning.

The accuracy of the clinical database was verified through a series of processes. Potential errors were identified through the generation of automatic queries during data entry and manual queries during data review. Clinical data were reviewed on an ongoing basis, and a BDR was conducted to identify any undetected data issues or concerns requiring correction. Once all participant data had been entered and all data queries closed, a final data management review was performed, and the database was declared ready for statistical analysis.

This CSR has been subject to quality control review by Pfizer or Pfizer's designee.

Quality assurance audits were performed at selected sites by Pfizer's own independent quality assurance group or by a CRO and/or individual contract personnel under the group's direction. These audits were conducted according to Pfizer's procedures and GCP guidelines. For the time period applicable to this interim report, there were 2 audits conducted for sites that enrolled adolescent participants (Appendix 16.1.8).

Refer to the final analysis interim CSR dated 03 December 2020 for previously reported data quality issues. There were none reported in the adolescent CSR dated 14 April 2021, or in the 6-month update interim CSR dated 29 April 2021.

9.7. Statistical Methods Planned in the Protocol

9.7.1. Statistical and Analytical Plans

9.7.1.1. Analysis Sets

The analysis populations presented in this report are defined in Table 3.

Refer to Appendix 16.1.9, SAP Section 4 for details of other planned analysis sets to be reported at a later time.

Table 3. Analysis Populations

Population	Description
Enrolled	All participants who had a signed ICD.
Randomized	All participants who were assigned a randomization number in the IWR system.
Evaluable efficacy (7 days)	All eligible randomized participants who received all vaccination(s) as randomized, with Dose 2 received within the predefined window (19-42 days after Dose 1) and had no other important protocol deviations as determined by the clinician on or before 7 days after Dose 2.
Dose 1 all-available efficacy	All randomized participants who received at least 1 vaccination.
Dose 2 all-available efficacy	All randomized participants who completed 2 vaccination doses.
Safety	All randomized participants who received at least 1 dose of the study intervention.

9.7.2. Determination of Sample Size

In Phase 3, approximately 2,000 participants enrolled were anticipated to be 12 to 15 years of age based on regulatory requirements for the safety database.

Refer to Appendix 16.1.1, Protocol Section 9.2, and Appendix 16.1.9, SAP Section 5.1.3 for details of the sample size determination.

9.7.3. Efficacy Analysis

The efficacy assessment in Phase 2/3 portion of the study was event-driven. VE with respect to the first primary efficacy endpoint was assessed at the first interim analysis (at least 62 cases) at 94 cases (data cutoff date: 04 November 2020). At the final analysis (at least 164 cases) VE with respect to all efficacy endpoints was assessed on an accrued 170 evaluable COVID-19 cases (data cutoff date: 14 November 2020) for both primary and all secondary efficacy endpoints. No additional formal hypothesis testing of clinically confirmed COVID-19 cases is planned.

Assessment of VE of BNT162b2 was performed for confirmed COVID-19 cases observed at least 7 days after the receipt of Dose 2 onwards among participants either without or with or without serological or virological evidence (up to 7 days after receipt of the second dose) of past SARS-CoV-2 infection. VE was estimated by 100% × (1 – IRR), where IRR was the ratio of COVID-19 illness rate in the BNT162b2 group to the corresponding illness rate in the placebo group (Appendix 16.1.9, SAP Appendix 3 with details on the calculation of IRR and VE).

Efficacy analyses during blinded placebo-controlled follow-up were conducted for participants 12 through 15 years of age based on the data cutoff date of 13 March 2021 (adolescent interim CSR, dated 14 April 2021). The point estimate of VE in the blinded follow-up period and associated 2-sided 95% CI was derived using the Clopper Pearson method adjusted for surveillance time. In addition to the protocol definition of severe COVID-19, supportive analyses using the CDC definition of severe COVID-19 were also performed.

In this report, updated efficacy analyses during blinded placebo-controlled follow-up were conducted for participants 12 through 15 years of age based on the data cutoff date of 02 September 2021. In addition to the protocol definition of severe COVID-19, supportive analyses using the CDC definition of severe COVID-19 were also performed.

The efficacy analysis for Phase 2/3 is also described in Appendix 16.1.1, Protocol Section 9.4.2 and Appendix 16.1.9, SAP Section 6.1.3 (primary), SAP Section 6.2.2 (secondary), and SAP Section 6.3.2 (exploratory).

9.7.4. Immunogenicity Analysis

Immunogenicity evaluations in participants 12-15 years of age are not included in this interim report.

In the adolescent interim report dated 14 April 2021, the GMR of SARS-CoV-2 50% neutralizing titers in adolescents 12-15 years of age to those in young adults 16-25 years of age and 2-sided 95% CIs were provided at 1 month after Dose 2 for noninferiority assessment. The immune response to BNT162b2 30 µg in SARS-CoV-2 50% neutralizing titers in adolescents 12-15 years of age was noninferior (and in fact exceeded) the immune response in young aduts 16-25 years of age (ie, successful immunobridging).

The immunogenicity analysis is further described in Appendix 16.1.1, Protocol Section 9.4.1, and Appendix 16.1.9, SAP Sections 6.2.1.1 through 6.2.1.3 for Phase 1, and Appendix 16.1.9, SAP Section 6.2.1.4 and SAP Section 6.3.3 for Phase 2/3.

9.7.5. Safety Analysis

The primary safety objective was evaluated by descriptive summary statistics for local reactions, systemic events, and AEs/SAEs for each vaccine group. There are no new reactogenicity data in this report (previously reported in the adolescent interim CSR, dated 14 April 2021).

Descriptive summary statistics included counts and percentages of participants with the indicated endpoint and the associated Clopper-Pearson 2-sided 95% CIs. Incidence rates accounted for differential follow-up time and the associated 2-sided 95% CI were also provided.

The safety analysis is described in Appendix 16.1.1, Protocol Section 9.4.3, and Appendix 16.1.9, SAP Section 6.1.1 (primary).

9.7.6. Other Analyses

Other analyses are described in Appendix 16.1.1, Protocol Section 9.4.4, and Appendix 16.1.9, SAP Section 6.3.4.

9.7.7. Analysis Timing

Statistical analyses for participants 12 through 15 years of age were described for the following data in the adolescent interim CSR dated 14 April 2021:

- Safety data through 1 month after Dose 2 and noninferiority comparison of SARS-CoV-2 neutralizing titers in participants 12 through 15 years of age compared to those in participants 16 through 25 years of age, 1 month after Dose 2. Safety data for participants 16 through 55 years of age were included for comparative purposes and did not include a full independent safety evaluation (these will be reported separately).

- Descriptive efficacy analysis for participants 12 through 15 years of age based on the data cutoff date of 13 March 2021.

Statistical analyses for participants 12 through 15 years of age are reported for the following data in this CSR:

- Complete safety analysis at 6 months after Dose 2 for adolescent participants in Phase 3; and analysis of available safety results up to the data cutoff date for this report.

- Updated descriptive efficacy analysis for participants 12 through 15 years of age during the blinded placebo-controlled follow-up period based on the data cutoff date of 02 September 2021.

The analysis timing is described in Appendix 16.1.1, Protocol Section 9.5, and Appendix 16.1.9, SAP Section 7.

9.8. Changes in the Conduct of Study or Planned Analyses

Changes in study conduct are described in Appendix 16.1.1, Protocol Amendment Summary of Changes Table. Changes to the original planned analysis are described in SAP v7.0 (Appendix 16.1.9, SAP Section 1).

Additional changes in study conduct or planned analysis not noted in the protocol or SAP were previously reported in Section 9.8 of the final analysis interim CSR dated 03 December 2020 and Section 9.8 of the adolescent interim CSR dated 14 April 2021. Changes in study conduct or planned analysis not noted in the protocol or SAP in this interim CSR were as follows:

- In Phase 2/3, for original adolescent placebo participants in the open-label follow-up period who then received BNT162b2 after unblinding, summary tables of AEs within 7 days after each dose were generated in order to evaluate whether AEs reported may have been attributed to reactogenicity events in participants who did not have an e diary to report reactogenicity. Although this was not specified in the SAP, this was prespecified in analysis and reporting plan before database release.

- Per regulatory request, ad hoc safety tables were generated which summarized new AEs reported after the EUA snapshot date (based on events on or after a data cutoff date of 13 March 2021) for the blinded placebo-controlled and open-label follow-up periods.

10. STUDY PARTICIPANTS

10.1. Disposition of Participants – Participants 12 Through 15 Years of Age

10.1.1. Blinded Placebo-Controlled Follow-Up Period

During the blinded placebo-controlled follow-up period, there were 3 (0.3%) participants in the BNT162b2 group and 14 (1.2%) participants in the placebo group who discontinued from the vaccination period (Dose 1 to 1 month after Dose 2) (Table 4). Most participants completed the visit at 1 month after Dose 2 (≥97.0%). Few participants in the BNT162b2 and placebo groups were withdrawn from the study (0.4% and 1.2%, respectively), and all were because of withdrawal by the participant, withdrawal by parent/guardian, or they were lost to follow-up.

10.1.2. Open-Label Follow-Up Period

Individuals have been unblinded as they became locally eligible and wished to know their vaccine assignment to confirm prior vaccination with BNT162b2 (if randomized to this group), or to receive BNT162b2 (if randomized to placebo). Participants who originally received BNT162b2 continued to be followed in an open-label manner. Participants who originally received placebo were offered BNT162b2 vaccination (Doses 3 and 4 [first and second dose of BNT162b2 30 µg, respectively]) and thereafter followed in an open-label manner.

Most participants in the BNT162b2 (98.1%) and placebo (97.0%) groups completed the 1 month post-Dose 2 visit before unblinding (Table 4).

A total of 4 (0.4%) original BNT162b2 adolescent participants received Dose 1 of BNT162b2 during the blinded placebo-controlled follow-up period and then received Dose 2 of BNT162b2 30 µg during the open-label follow-up period (when they were unblinded) (Table 4). There were 45 (4.0%) participants withdrawn from the study (Table 4), and most were because of other reasons (21 of 23 participants were enrolled into Study C4591031 to evaluate a booster dose of BNT162b2) (Appendix 16.2.1).

During the open-label follow-up period, most participants originally randomized to the placebo group received Doses 3 and 4 (89.4% and 87.8%, first and second dose of BNT162b2 30 µg, respectively). There were 47 (4.2%) participants who were withdrawn from the study after unblinding and before Dose 3. There were few participants in this group (who received at least the first dose of BNT162b2 30 µg) who were withdrawn from the study (0.5%), and most were because of withdrawals by the participant, or they were lost to follow-up (Table 4).

Table 4. Disposition of All Randomized Subjects – Phase 2/3 Subjects 12 Through 15 Years of Age

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=1134) n[b] (%)	Placebo (N[a]=1130) n[b] (%)	Total (N[a]=2264) n[b] (%)
Randomized	1134 (100.0)	1130 (100.0)	2264 (100.0)
Not vaccinated	3 (0.3)	1 (0.1)	4 (0.2)
Original blinded placebo-controlled follow-up period			
Vaccinated	1131 (99.7)	1129 (99.9)	2260 (99.8)
Dose 1	1131 (99.7)	1129 (99.9)	2260 (99.8)
Dose 2	1124 (99.1)	1117 (98.8)	2241 (99.0)
Discontinued from original blinded placebo-controlled vaccination period[c]	3 (0.3)	14 (1.2)	17 (0.8)
Reason for discontinuation			
No longer meets eligibility criteria	0	7 (0.6)	7 (0.3)
Protocol deviation	0	2 (0.2)	2 (0.1)
Adverse event	1 (0.1)	0	1 (0.0)
Physician decision	1 (0.1)	0	1 (0.0)
Withdrawal by subject	0	1 (0.1)	1 (0.0)
Withdrawal by parent/guardian	0	1 (0.1)	1 (0.0)
Other	1 (0.1)	3 (0.3)	4 (0.2)
Unblinded before 1-month post–Dose 2 visit	12 (1.1)	21 (1.9)	33 (1.5)
Completed 1-month post–Dose 2 visit	1113 (98.1)	1096 (97.0)	2209 (97.6)
Withdrawn from the study	5 (0.4)	14 (1.2)	19 (0.8)
Withdrawn after Dose 1 and before Dose 2	0	0	0
Withdrawn after Dose 2 and before 1-month post–Dose 2 visit	0	3 (0.3)	3 (0.1)
Withdrawn after 1-month post–Dose 2 visit	5 (0.4)	11 (1.0)	16 (0.7)
Reason for withdrawal from the study			
Withdrawal by subject	1 (0.1)	7 (0.6)	8 (0.4)
Withdrawal by parent/guardian	1 (0.1)	5 (0.4)	6 (0.3)
Lost to follow-up	3 (0.3)	2 (0.2)	5 (0.2)
Open-label follow-up period			
Originally randomized to BNT162b2	1107 (97.6)		
Received Dose 2/unplanned dose	4 (0.4)		
Completed 1-month post–Dose 2 visit	15 (1.3)		
Completed 6-month post–Dose 2 visit	1065 (93.9)		
Withdrawn from the study	45 (4.0)		
Withdrawn before 6-month post–Dose 2 visit	25 (2.2)		
Withdrawn after 6-month post–Dose 2 visit	20 (1.8)		
Reason for withdrawal from the study			
Withdrawal by subject	7 (0.6)		

Table 4. Disposition of All Randomized Subjects – Phase 2/3 Subjects 12 Through 15 Years of Age

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=1134) n[b] (%)	Placebo (N[a]=1130) n[b] (%)	Total (N[a]=2264) n[b] (%)
Withdrawal by parent/guardian	7 (0.6)		
Lost to follow-up	6 (0.5)		
Protocol deviation	1 (0.1)		
No longer meets eligibility criteria	1 (0.1)		
Other	23 (2.0)		
Originally randomized to placebo		1108 (98.1)	
Withdrawn from the study after unblinding and before Dose 3		47 (4.2)	
Received Dose 3 (first dose of BNT162b2 [30 µg])		1010 (89.4)	
Received Dose 4 (second dose of BNT162b2 [30 µg])		992 (87.8)	
Discontinued from open-label vaccination period[d]		5 (0.4)	
Reason for discontinuation from open-label vaccination period			
Protocol deviation		4 (0.4)	
Withdrawal by subject		1 (0.1)	
Completed 1-month post–Dose 4 visit		933 (82.6)	
Withdrawn from the study		6 (0.5)	
Withdrawn after Dose 3 and before Dose 4		5 (0.4)	
Withdrawn after Dose 4 and before 1-month post–Dose 4 visit		0	
Withdrawn after 1-month post–Dose 4 visit		1 (0.1)	
Reason for withdrawal from the study			
Withdrawal by subject		3 (0.3)	
Lost to follow-up		2 (0.2)	
Protocol deviation		1 (0.1)	

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 visit.
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]) visit.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:30) Source Data: adds Table Generation: 04NOV2021 (04:49)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adds_s002_all1_ped6

10.2. Protocol Deviations – Participants 12 Through 15 Years of Age

PDs were identified throughout the study by monitoring of informed consent documentation, source documents, and other clinical trial–related documents. In addition, PDs were identified by remote monitoring of electronic CRFs, and review of the project databases (interactive response technology, clinical and safety databases, vendor database for e-diary data, and programmatic output from the clinical database). All PDs were documented in a designated clinical trial management system.

Appendix 16.2.2 lists important PDs in all Phase 3 participants 12 through 15 years of age that may have significantly impacted the completeness, accuracy, and/or reliability of the study data or that may have significantly affected a participant's rights, safety, or well-being.

A formal acknowledgment by the study team was made that deviations were reviewed and GCP compliance was maintained.

10.3. Vaccine Administration and Timing – Participants 12 Through 15 Years of Age

All adolescent participants who received Doses 1 and 2 were administered study intervention as randomized. Three (0.3%) participants in the BNT162b2 group and 1 (0.1%) participant in the placebo group were not vaccinated with any study intervention (Table 5).

After unblinding, 89.4% of original adolescent placebo participants received Dose 3 (first dose of BNT162b2 30 µg) and 87.7% received Dose 4 (second dose of BNT162b2 30 µg) at the time of the data cutoff date.

The majority of participants received Dose 2 between 21 to 27 days after Dose 1 in the BNT162b2 (65.0%) and placebo (64.5%) groups (Table 6). After unblinding, most original placebo participants received Dose 4 (second dose of BNT162b2 30 µg) between 14 to 20 (23.4%) days and 21 to 27 (61.2%) days after Dose 3.

Table 5. Vaccine as Administered – Phase 2/3 Subjects 12 Through 15 Years of Age – All Randomized Subjects

Vaccine (as Administered)	Vaccine Group (as Randomized)	
	BNT162b2 (30 µg) (N[a]=1134) n[b] (%)	Placebo (N[a]=1130) n[b] (%)
Vaccinated	1131 (99.7)	1129 (99.9)
Not vaccinated	3 (0.3)	1 (0.1)
Dose 1		
BNT162b2 (30 µg)	1131 (99.7)	0
Placebo	0	1129 (99.9)
Dose 2		

Table 5. Vaccine as Administered – Phase 2/3 Subjects 12 Through 15 Years of Age – All Randomized Subjects

Vaccine (as Administered)	Vaccine Group (as Randomized)	
	BNT162b2 (30 µg) (N[a]=1134) n[b] (%)	Placebo (N[a]=1130) n[b] (%)
BNT162b2 (30 µg)	1128 (99.5)	0
Placebo	0	1119 (99.0)
Dose 3		
First dose BNT162b2 (30 µg)		1010 (89.4)
Dose 4		
Second dose BNT162b2 (30 µg)		992 (87.8)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic.
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(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/advx_s002_adm1_ped6

Table 6. Vaccine Administration Timing – Phase 2/3 Subjects 12 Through 15 Years of Age – All Randomized Subjects

	Vaccine Group (as Randomized)	
	BNT162b2 (30 µg) (N[a]=1134) n[b] (%)	Placebo (N[a]=1130) n[b] (%)
Randomized	1134 (100.0)	1130 (100.0)
Not vaccinated	3 (0.3)	1 (0.1)
Dose 1	1131 (99.7)	1129 (99.9)
Dose 2[c]	1128 (99.5)	1119 (99.0)
Protocol defined window		
<19 Days	2 (0.2)	1 (0.1)
19-23 Days[d]	1073 (94.6)	1065 (94.2)
>23 Days	53 (4.7)	53 (4.7)
Weekly Intervals		
<14 Days	0	0
14-20 Days	358 (31.6)	364 (32.2)
21-27 Days	737 (65.0)	729 (64.5)
28-34 Days	23 (2.0)	15 (1.3)

Table 6. Vaccine Administration Timing – Phase 2/3 Subjects 12 Through 15 Years of Age – All Randomized Subjects

	Vaccine Group (as Randomized)	
	BNT162b2 (30 µg) (N[a]=1134) n[b] (%)	Placebo (N[a]=1130) n[b] (%)
35-41 Days	4 (0.4)	4 (0.4)
42-48 Days	1 (0.1)	1 (0.1)
49-55 Days	1 (0.1)	3 (0.3)
>55 Days	4 (0.4)	3 (0.3)
Dose 3 (first dose of BNT162b2 [30 µg])		1010 (89.4)
Dose 4 (second dose of BNT162b2 [30 µg])[e]		992 (87.8)
Protocol defined window		
<19 Days		6 (0.5)
19-23 Days[d]		905 (80.1)
>23 Days		81 (7.2)
Weekly Intervals		
<14 Days		0
14-20 Days		264 (23.4)
21-27 Days		691 (61.2)
28-34 Days		26 (2.3)
35-41 Days		5 (0.4)
42-48 Days		3 (0.3)
49-55 Days		2 (0.2)
>55 Days		1 (0.1)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic.
c. Days calculated since Dose 1.
d. Protocol-specified time frame.
e. Days calculated since Dose 3.
PFIZER CONFIDENTIAL SDTM Creation: 30SEP2021 (11:35) Source Data: adsl Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/advx_s002_time1_ped6

10.4. Data Sets Analyzed – Participants 12 Through 15 Years of Age

10.4.1. Safety Population – Participants 12 Through 15 Years of Age

The safety population of adolescent participants included 1131 participants in the BNT162b2 group and 1129 participants in the placebo group (Table 7). Four participants were excluded from the safety population because they did not receive any study intervention.

Table 7. Safety Population – Phase 2/3 Subjects 12 Through 15 Years of Age

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) n[a]	Placebo n[a]	Total n[a] (%)
Randomized[b]			2264
Vaccinated	1131	1129	2260 (99.8)
Safety population	1131	1129	2260 (99.8)
Excluded from safety population			4 (0.2)
Reason for exclusion			
Subject did not receive study vaccine			4 (0.2)

a. n = Number of subjects with the specified characteristic, or the total sample.
b. This value is the denominator for the percentage calculations.
PFIZER CONFIDENTIAL SDTM Creation: 30SEP2021 (11:35) Source Data: adsl Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adsl_s003_saf1_ped6

During the blinded placebo-controlled follow-up period, median follow-up time for adolescent participants was 4.4 months. There were 634 (56.1%) and 629 (55.7%) of participants in the BNT162b2 and placebo groups, respectively, who had follow-up time between ≥4 months to <6 months after Dose 2 (Table 8). From Dose 2 to the cutoff date, 740 (65.4%) of participants in the BNT162b2 group had a total follow-up time between ≥8 to <10 months, which was composed of blinded and unblinded exposure. There were few participants (18 total) with follow-up time of <6 months, as most adolescent participants 12-15 years of age should have had ≥6 months of follow-up by the data cutoff date (02 September 2021), and also corresponding with the number of participants who withdrew from the study (Table 4).

For original adolescent placebo recipients who received at least the first dose of BNT162b2, median follow-up time was 3.8 months, and 65.0% of these participants had follow-up time between ≥2 months to <4 months after Dose 1 of BNT162b2 (Table 9).

Table 8. Follow-up Time After Dose 2 – Phase 2/3 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] (%)

Table 8. Follow-up Time After Dose 2 – Phase 2/3 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] (%)
Original blinded placebo-controlled follow-up period			
<2 Months	45 (4.0)	62 (5.5)	107 (4.7)
≥2-<4 Months	300 (26.5)	294 (26.0)	594 (26.3)
≥4-<6 Months	634 (56.1)	629 (55.7)	1263 (55.9)
≥6 Months	152 (13.4)	144 (12.8)	296 (13.1)
Mean (SD)	4.5 (1.24)	4.4 (1.27)	4.4 (1.26)
Median	4.4	4.4	4.4
Min, max	(0.0, 10.8)	(0.0, 9.1)	(0.0, 10.8)
Total follow-up period from Dose 2 to cutoff date			
<2 Months	8 (0.7)		
≥2-<4 Months	0		
≥4-<6 Months	10 (0.9)		
≥6-<8 Months	326 (28.8)		
≥8-<10 Months	740 (65.4)		
≥10 Months	47 (4.2)		
Mean (SD)	8.3 (1.03)		
Median	8.4		
Min, max	(0.0, 10.9)		

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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Table 9. Follow-up Time After Dose 1 of BNT162b2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received Placebo) – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=1010) n[b] (%)
Open-label follow-up period	
<2 Months	66 (6.5)
≥2-<4 Months	656 (65.0)
≥4-<6 Months	228 (22.6)
≥6 Months	60 (5.9)
Mean (SD)	3.8 (1.09)
Median	3.8
Min, max	(0.1, 8.6)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic.
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(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adsl_fu_d11_ped6

10.4.2. Efficacy Populations – Updated Analysis – Participants 12 Through 15 Years of Age

The proportions of participants included in the updated efficacy populations were similar in the BNT162b2 and placebo groups (Table 10). Most participants excluded from the evaluable efficacy population were because they did not receive all vaccinations as randomized or did not receive Dose 2 within the predefined window (19-42 days after Dose 1).

Table 10. Efficacy Populations – Subjects 12 Through 15 Years of Age – Blinded Placebo-Controlled Follow-up Period

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) n[a] (%)	Placebo n[a] (%)	Total n[a] (%)
Randomized[b]	1134 (100.0)	1130 (100.0)	2264 (100.0)
Dose 1 all-available efficacy population	1131 (99.7)	1129 (99.9)	2260 (99.8)

Table 10. Efficacy Populations – Subjects 12 Through 15 Years of Age – Blinded Placebo-Controlled Follow-up Period

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) n[a] (%)	Placebo n[a] (%)	Total n[a] (%)
Subjects without evidence of infection before Dose 1	1083 (95.5)	1078 (95.4)	2161 (95.5)
Subjects excluded from Dose 1 all-available efficacy population	3 (0.3)	1 (0.1)	4 (0.2)
Reason for exclusion[c]			
Did not receive at least 1 vaccination	3 (0.3)	1 (0.1)	4 (0.2)
Dose 2 all-available efficacy population	1123 (99.0)	1117 (98.8)	2240 (98.9)
Subjects without evidence of infection prior to 7 days after Dose 2	1061 (93.6)	1037 (91.8)	2098 (92.7)
Subjects excluded from Dose 2 all-available efficacy population	11 (1.0)	13 (1.2)	24 (1.1)
Reason for exclusion[c]			
Did not receive 2 vaccinations	10 (0.9)	13 (1.2)	23 (1.0)
Unblinded prior to 7 days after Dose 2	1 (0.1)	0	1 (0.0)
Evaluable efficacy (7 days) population	1119 (98.7)	1109 (98.1)	2228 (98.4)
Subjects without evidence of infection prior to 7 days after Dose 2	1057 (93.2)	1030 (91.2)	2087 (92.2)
Subjects excluded from evaluable efficacy (7 days) population	15 (1.3)	21 (1.9)	36 (1.6)
Reason for exclusion[c]			
Randomized but did not meet all eligibility criteria	1 (0.1)	1 (0.1)	2 (0.1)
Did not receive all vaccinations as randomized or did not receive Dose 2 within the predefined window (19-42 days after Dose 1)	14 (1.2)	19 (1.7)	33 (1.5)
Unblinded prior to 7 days after Dose 2	1 (0.1)	0	1 (0.0)
Had other important protocol deviations on or prior to 7 days after Dose 2	0	3 (0.3)	3 (0.1)

a. n = Number of subjects with the specified characteristic.
b. These values are the denominators for the percentage calculations.
c. Subjects may have been excluded for more than 1 reason.
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(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adsl_eff_pop_peds

10.5. Demographic and Other Baseline Characteristics – Participants 12 Through 15 Years of Age

10.5.1. Safety Population – Participants 12 Through 15 Years of Age

10.5.1.1. Overall

Demographic characteristics for adolescents (12-15 years of age) were similar in the BNT162b2 and placebo groups in the safety population, and all adolescents were enrolled at

sites in the United States (Table 11). Most adolescent participants in the BNT162b2 group were White (85.8%), with 4.6% Black or African American participants and 6.4% Asian participants, and other racial groups were ≤2.1%. 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 of this age group (based on age- and sex-specific BMI) made up 11.3% (placebo group) to 12.6% (BNT162b2 group).

Table 11. Demographic Characteristics – Phase 2/3 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] (%)
Sex			
Male	567 (50.1)	585 (51.8)	1152 (51.0)
Female	564 (49.9)	544 (48.2)	1108 (49.0)
Race			
White	970 (85.8)	962 (85.2)	1932 (85.5)
Black or African American	52 (4.6)	57 (5.0)	109 (4.8)
All others	109 (9.6)	110 (9.7)	219 (9.7)
American Indian or Alaska Native	4 (0.4)	3 (0.3)	7 (0.3)
Asian	72 (6.4)	71 (6.3)	143 (6.3)
Native Hawaiian or other Pacific Islander	3 (0.3)	0	3 (0.1)
Multiracial	24 (2.1)	29 (2.6)	53 (2.3)
Not reported	6 (0.5)	7 (0.6)	13 (0.6)
Racial designation			
Japanese	5 (0.4)	2 (0.2)	7 (0.3)
Ethnicity			
Hispanic/Latino	132 (11.7)	130 (11.5)	262 (11.6)
Non-Hispanic/non-Latino	997 (88.2)	996 (88.2)	1993 (88.2)
Not reported	2 (0.2)	3 (0.3)	5 (0.2)
Country			
USA	1131 (100.0)	1129 (100.0)	2260 (100.0)
Baseline SARS-CoV-2 status			
Positive[c]	46 (4.1)	50 (4.4)	96 (4.2)
Negative[d]	1083 (95.8)	1078 (95.5)	2161 (95.6)
Missing	2 (0.2)	1 (0.1)	3 (0.1)
Comorbidities[e]			
Yes	249 (22.0)	242 (21.4)	491 (21.7)

Table 11. Demographic Characteristics – Phase 2/3 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] (%)
No	882 (78.0)	887 (78.6)	1769 (78.3)
Obese[f]			
Yes	143 (12.6)	128 (11.3)	271 (12.0)
No	988 (87.4)	1001 (88.7)	1989 (88.0)
Age at vaccination (years)			
Mean (SD)	13.6 (1.11)	13.6 (1.11)	13.6 (1.11)
Median	14.0	14.0	14.0
Min, max	(12, 15)	(12, 15)	(12, 15)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
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. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥95th percentile.
f. Obese is defined as BMI ≥95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.
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Overall, there were 96 (4.2%) and 2161 (95.6%) participants who were baseline SARs-CoV-2 positive and negative, respectively (Table 11, and Supplemental Tables 14.1 and 14.2). Considering the baseline positive subgroup had fewer participants than the negative subgroup overall, there were no clinically meaningful differences in demographics in the 2 vaccine groups by SARS-CoV-2 status.

Adolescent participants had a diverse medical history profile consistent with that of individuals in the general population in the same age group (Supplemental Table 14.3). For adolescents in the BNT162b2 group, conditions in the immune system disorders (399 [35.3%]; of which 241 [21.3%] were seasonal allergy); psychiatric disorders (293 [25.9%], with frequently reported PTs of attention deficit hyperactivity disorder (182 [16.1%]), anxiety (107 [9.5%]), and depression (51 [4.5%]); respiratory, thoracic, and mediastinal disorders (179 [15.8%]); and skin and subcutaneous tissue disorders (170 [15.0%]) SOCs were most frequently reported.

There were 123 (10.9%) and 136 (12.0%) participants in the BNT162b2 and placebo groups, respectively, who had any comorbidity (per the Charlson comorbidity index) (Supplemental Table 14.4), which was mostly chronic pulmonary disease (119 [10.5%] and 127 [11.2%] participants, respectively).

10.5.1.2. Participants With At Least 6 Months Follow-Up Time – Original BNT162b2 Recipients 12 Through 15 Years of Age

Demographic characteristics for all original BNT162b2 adolescent recipients who had at least 6 months of follow-up time after Dose 2 are presented in Supplemental Table 14.5 and were similar to demographic characteristics in the BNT162b2 group overall (Table 11).

10.5.1.3. Original Placebo Recipients 12 Through 15 Years of Age Who Then Received BNT162b2

Demographic characteristics for all original placebo adolescent recipients who then received BNT162b2 later during the open-label follow-up period are presented in Supplemental Table 14.6 and were similar to demographic characteristics in the placebo group overall (Table 11).

10.5.2. Evaluable Efficacy (7 Days) Population – Blinded Placebo-Controlled Follow-up Period – Participants 12 Through 15 Years of Age

Demographics of participants in the evaluable efficacy (7 days) population for adolescent participants without evidence of infection prior to 7 days after Dose 2 were similar in the BNT162b2 and placebo groups (Supplemental Table 14.7). This analysis population had generally similar demographics compared with the safety population (refer to Section 10.5.1.1).

Demographic characteristics for the Dose 1 all-available efficacy population and for participants with or without evidence of infection prior to 7 days after Dose 2 (evaluable efficacy [7 days] population) were similar to those in the evaluable efficacy (7 days) population (Supplemental Tables 14.8 and 14.9, respectively).

10.6. Participant Compliance – Participants 12 Through 15 Years of Age

10.6.1. Immunogenicity Blood Samples

Refer to the adolescent interim C4591001 CSR dated 14 April 2021, Section 10.6.1 for details about immunogenicity blood samples taken in adolescent participants.

10.6.2. E-Diary

Refer to the adolescent interim C4591001 CSR dated 14 April 2021, Section 10.6.2 for details of transmission about e-diary data in adolescent participants.

10.7. Prior and Concomitant Vaccines, Medications, and Procedures – Participants 12 Through 15 Years of Age

A small percentage of adolescent participants in either group (≤2.8%) received a concomitant vaccine after Dose 1, and the most concomitant vaccine received was the influenza vaccine (Supplemental Table 14.10).

11. EFFICACY EVALUATION

11.1. Updated Efficacy Results – Participants 12 Through 15 Years of Age

In this CSR, updated descriptive efficacy analyses in adolescent participants 12 through 15 years of age were performed with all cases accrued during blinded placebo-controlled follow-up (through the cut-off date of 02 September 2021), including subgroup analyses, and for protocol-defined severe cases and CDC-defined severe cases.

11.1.1. Updated Analysis of Efficacy – Blinded Placebo-Controlled Follow-Up Period

11.1.1.1. Vaccine Efficacy From 7 Days After Dose 2 – Updated Analysis

Among adolescent participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 100.0% (2-sided 95% CI: 86.8%, 100.0%), with 0 and 28 cases in the BNT162b2 and placebo groups, respectively (Table 12).

The VE of BNT162b2 for the same efficacy endpoint based on the Dose 2 all-available efficacy population was 100.0% (2-sided 95% CI: 87.2%, 100.0%), with 0 and 29 cases in the BNT162b2 and placebo group, respectively (Supplemental Table 14.11).

Table 12. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=1057)		Placebo (N[a]=1030)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence from 7 days after Dose 2	0	0.343 (1043)	28	0.322 (1019)	100.0	(86.8, 100.0)
≥7 days after Dose 2 to <2 Months after Dose 2	0	0.138 (1043)	15	0.133 (1019)	100.0	(73.2, 100.0)
≥2 Months after Dose 2 to <4 Months after Dose 2	0	0.148 (1008)	10	0.139 (957)	100.0	(58.0, 100.0)
≥4 Months after Dose 2	0	0.057 (723)	3	0.050 (682)	100.0	(-112.1, 100.0)

Table 12. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=1057)		Placebo (N[a]=1030)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2, and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2) were included in the analysis.
a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period for the overall row and from start to the end of the range stated for each time interval.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
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Among participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen, estimated VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 100.0% (2-sided 95% CI: 87.5%, 100.0%), with 0 and 30 cases in the BNT162b2 and placebo groups, respectively (Table 13). For the 2 additional cases in adolescent participants with evidence of SARS-CoV-2 infection (as compared with those without evidence of infection from Table 12), both participants were SARS-CoV-2 negative at baseline.

Table 13. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=1119)		Placebo (N[a]=1109)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence from 7 days after Dose 2	0	0.362 (1098)	30	0.345 (1088)	100.0	(87.5, 100.0)
≥7 days after Dose 2 to <2 Months after Dose 2	0	0.146 (1098)	17	0.142 (1088)	100.0	(76.4, 100.0)
≥2 Months after Dose 2 to <4 Months after Dose 2	0	0.155 (1061)	10	0.148 (1022)	100.0	(57.4, 100.0)
≥4 Months after Dose 2	0	0.061 (767)	3	0.055 (726)	100.0	(-117.8, 100.0)

Abbreviation: VE = vaccine efficacy.
a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period for the overall row and from start to the end of the range stated for each time interval.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adc19ef Table Generation: 05NOV2021 (10:58)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adc19ef_ve_cov_7pd2_peds_eval

11.1.1.1.1. Subgroup Analyses

In the evaluable efficacy (7 days) population, among participants without and with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE was 100.0% for all subgroups (Table 14 and Supplemental Table 14.12, respectively).

Table 14. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=1057)		Placebo (N[a]=1030)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence from 7 days after Dose 2						
Overall	0	0.343 (1043)	28	0.322 (1019)	100.0	(86.8, 100.0)
Sex						
Male	0	0.175 (524)	16	0.165 (526)	100.0	(75.5, 100.0)
Female	0	0.169 (519)	12	0.157 (493)	100.0	(66.5, 100.0)
Race						
White	0	0.293 (898)	26	0.272 (867)	100.0	(85.8, 100.0)
Black or African American	0	0.017 (41)	2	0.018 (49)	100.0	(-470.9, 100.0)
Ethnicity						
Hispanic/Latino	0	0.042 (119)	7	0.036 (113)	100.0	(41.2, 100.0)
Non-Hispanic/non-Latino	0	0.300 (922)	21	0.285 (903)	100.0	(81.7, 100.0)
Country						
USA	0	0.343 (1043)	28	0.322 (1019)	100.0	(86.8, 100.0)
Comorbidities[f]						
Yes	0	0.078 (230)	9	0.068 (213)	100.0	(55.5, 100.0)
No	0	0.266 (813)	19	0.254 (806)	100.0	(79.5, 100.0)
Obese[g]						
Yes	0	0.046 (134)	6	0.036 (110)	100.0	(33.9, 100.0)
No	0	0.298 (909)	22	0.287 (909)	100.0	(82.4, 100.0)

Table 14. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=1057)		Placebo (N[a]=1030)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2, and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2) were included in the analysis.
a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. Comorbidities are defined as having at least one of the Charlson comorbidity index category or obesity (BMI ≥95th percentile).
g. Obese is defined as BMI ≥95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.
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11.1.1.2. All Confirmed Cases of COVID-19 After Dose 1 – All-Available Efficacy Population

All reports of COVID-19 with onset at any time after Dose 1 are accounted for in Table 15, which provides a summary of VE for all adolescent participants in the Dose 1 all-available efficacy (modified intention-to-treat) population adjusted for exposure, regardless of evidence of infection before or during the vaccination regimen. Among these participants, the estimated VE against confirmed COVID-19 occurring after Dose 1 was 94.0% (2-sided 95% CI: 81.3%, 98.8%), with 3 and 48 cases of COVID-19 in the BNT162b2 and placebo groups, respectively. All 3 cases in the BNT162b2 group occurred <11 days after Dose 1 and in participants who had baseline SARS-CoV-2 negative status, and represented all cases reported in this group at any time.

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

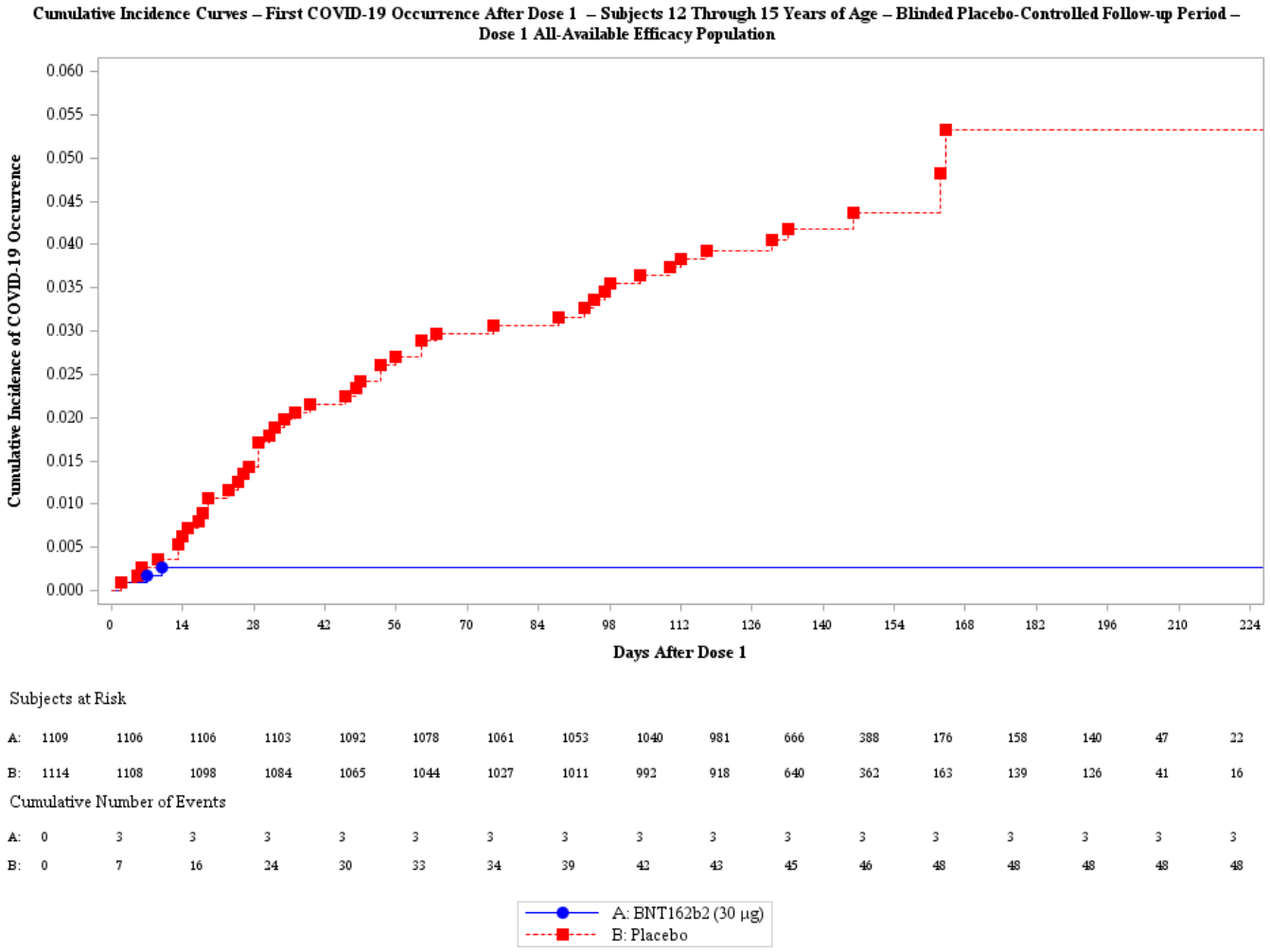
Table 15. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=1131)		Placebo (N[a]=1129)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence after Dose 1	3	0.450 (1109)	48	0.434 (1114)	94.0	(81.3, 98.8)
After Dose 1 to before Dose 2	3	0.065 (1109)	12	0.065 (1114)	75.1	(7.6, 95.5)
After Dose 1 to <11 days after Dose 1	3	0.033 (1109)	4	0.033 (1114)	24.7	(-345.0, 89.0)
≥11 Days after Dose 1 to before Dose 2	0	0.032 (1106)	8	0.031 (1110)	100.0	(42.0, 100.0)
Dose 2 to 7 days after Dose 2	0	0.021 (1103)	5	0.021 (1100)	100.0	(-8.7, 100.0)
≥7 Days after Dose 2	0	0.364 (1102)	31	0.348 (1095)	100.0	(87.9, 100.0)
≥7 days after Dose 2 to <2 Months after Dose 2	0	0.146 (1102)	17	0.143 (1095)	100.0	(76.3, 100.0)
≥2 Months after Dose 2 to <4 Months after Dose 2	0	0.156 (1065)	10	0.149 (1029)	100.0	(57.3, 100.0)
≥4 Months after Dose 2	0	0.062 (770)	4	0.056 (732)	100.0	(-37.7, 100.0)

Abbreviation: VE = vaccine efficacy.
a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period for the overall row and from start to the end of the range stated for each time interval.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adc19ef Table Generation: 03NOV2021 (11:38)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adc19ef_ve_cov_pd1_st_peds_aai

The early onset of protection is readily apparent in Figure 1, which displays cumulative incidence for the first COVID-19 occurrence after Dose 1 among all vaccinated participants based on Dose 1 all-available efficacy (modified intention-to-treat) population. Disease onset appears to track together for BNT162b2 and placebo until approximately 11 days after Dose 1 (consistent with the data shown in Table 15), at which point the curves diverge, with cases steadily accumulating in the placebo group, while remaining flat with no more cases in the BNT162b2 group.

Figure 1. Cumulative Incidence Curves for the First COVID-19 Occurrence After Dose 1 – Subjects 12 Through 15 Years of Age – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population



11.1.1.2.1. Subgroup Analyses

Additionally, in subgroup analyses for VE based on the Dose 1 all-available efficacy (modified intention-to-treat) population (Supplemental Table 14.13), the observed subgroup VEs based on the Dose 1 all-available population were generally similar to those based on the evaluable efficacy population except for a few subgroups that the number of participants and cases were too small to provide robust estimates. The observed VEs for all subgroups were ≥88.7% except for one subgroup (race, all others) with 1 case in each group: American Indian or Alaska native in placebo and Asian in BNT162b2. Due to the small number of participants, the data must be interpreted with caution.

11.1.2. Updated Analysis of Severe COVID-19 Cases

No severe COVID-19 cases (per protocol definition or CDC criteria) were reported in participants 12-15 years of age as of the data cutoff date (02 September 2021) (Appendix 16.2.8.1.1).

11.1.2.1. COVID-19 Narratives – Updated Analysis

One participant in the placebo group had multiple positive COVID-19 NAAT results (Appendix 16.2.8.4.1). The narrative for this participant is provided in Section 14 COVID-19 Case (Severe and/or Multiple).

11.1.3. Variants of Concern

Among the 30 placebo participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen and had COVID-19 cases, most variants sequenced were neither VOI nor VOC except for the B.1.1.7 (Alpha) (Table 17), which was found in 23.3% of placebo participants (Table 16). There were no cases belonging to the Beta, Gamma, Delta, Lambda, or Mu variants (Table 17). Importantly, all of the cases in the efficacy analyses occurred between 02 November 2020 to 19 May 2021, which is before the Delta surge in the US. (Appendix 16.2.8.1.2).

Table 16. Summary of SARS-CoV-2 Variants for the First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=0)	Placebo (N[a]=30)	Total (N[a]=30)
SARS-CoV-2 Lineage[b] (WHO Classification)	n[c](%)	n[c](%)	n[c](%)
B.1	0	1 (3.3)	1 (3.3)

Table 16. Summary of SARS-CoV-2 Variants for the First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=0)	Placebo (N[a]=30)	Total (N[a]=30)
SARS-CoV-2 Lineage[b] (WHO Classification)	n[c](%)	n[c](%)	n[c](%)
B.1.1.222	0	1 (3.3)	1 (3.3)
B.1.1.29	0	1 (3.3)	1 (3.3)
B.1.1.519	0	1 (3.3)	1 (3.3)
B.1.1.7 (Alpha)	0	7 (23.3)	7 (23.3)
B.1.142	0	1 (3.3)	1 (3.3)
B.1.2	0	10 (33.3)	10 (33.3)
B.1.243	0	1 (3.3)	1 (3.3)
B.1.361	0	1 (3.3)	1 (3.3)
B.1.369	0	1 (3.3)	1 (3.3)
B.1.400	0	1 (3.3)	1 (3.3)
B.1.427	0	2 (6.7)	2 (6.7)
B.1.526	0	1 (3.3)	1 (3.3)
Unknown[d]	0	1 (3.3)	1 (3.3)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
a. N = number of subjects with first COVID-19 occurrence. This value is the denominator for the percentage calculations.
b. Based on PANGO lineages (cov-lineages.org).
c. n = Number of subjects with the specified characteristic.
d. Include indeterminate result and not quantifiable (QNS) samples.
PFIZER CONFIDENTIAL SDTM Creation: 02NOV2021 (15:56) Source Data: adxb Table Generation: 04NOV2021 (14:59)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adxb_seq_var_cov_7pd2_peds_eval

Table 17. Summary of SARS-CoV-2 Variants of Concern or Variants of Interest for the First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)		
SARS-CoV-2 Lineage[b] (WHO Classification)	BNT162b2 (30 µg) (N[a]=0) n[c](%)	Placebo (N[a]=30) n[c](%)	Total (N[a]=30) n[c](%)
B.1.1.7 (Alpha)	0	7 (23.3)	7 (23.3)
B.1.351 (Beta)	0	0	0
P.1 (Gamma)	0	0	0
B.1.617.2 (Delta)	0	0	0
C.37 (Lambda)	0	0	0
B.1.621 (Mu)	0	0	0
Other	0	22 (73.3)	22 (73.3)
Unknown[d]	0	1 (3.3)	1 (3.3)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
a. N = number of subjects with first COVID-19 occurrence. This value is the denominator for the percentage calculations.
b. Based on PANGO lineages (cov-lineages.org).
c. n = Number of subjects with the specified characteristic.
d. Include indeterminate result and not quantifiable (QNS) samples.
PFIZER CONFIDENTIAL SDTM Creation: 02NOV2021 (15:56) Source Data: adxb Table Generation: 04NOV2021 (14:59)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adxb_seq_cov_7pd2_peds_eval

11.2. Efficacy Conclusions – Updated Analysis – Participants 12 Through 15 Years of Age

- In the updated descriptive efficacy analysis (data cutoff date 02 September 2021), among participants in the evaluable efficacy population without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 100% (2-sided 95% CI: 86.8%, 100%), with 0 cases in the BNT162b2 group and 28 cases in the placebo group. Among participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 100% (2-sided 95% CI: 87.5%, 100%), with 0 and 30 cases in the BNT162b2 and placebo groups, respectively. For the 2 additional cases in adolescent participants with evidence of SARS-CoV-2 infection as compared with those without evidence of infection, both participants were SARS-CoV-2 negative at baseline.

- Among participants without and with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen (evaluable efficacy population), VE against COVID-19 occurring at least 7 days after Dose 2 was evaluated for demographic and risk subgroups, and the estimated VE was 100.0% for all subgroups.

- From the analysis of all cases of confirmed COVID-19 based on the all-available (modified intention-to-treat) population (regardless of evidence of infection before or during the vaccination regimen), the estimated VE against all cases occurring at any time after Dose 1 was 94.0% (2-sided 95% CI: 81.3%, 98.8%), with 3 cases in the BNT162b2 group (all occurring within <11 days after Dose 1 and in participants who had baseline SARS-CoV-2 negative status) and 48 cases in the placebo group.

- No severe COVID-19 cases (per protocol definition or CDC criteria) were reported in participants 12-15 years of age as of the data cutoff date (02 September 2021).

- Most variants sequenced were neither VOI nor VOC except for the B.1.1.7 (Alpha) found in 23.3% of placebo participants. All of the cases in the efficacy analyses occurred between 02 November 2020 to 19 May 2021, which is before the Delta surge in the US.

12. SAFETY EVALUATION

Refer to the C4591001 6-Month Update Interim CSR, dated 29 April 2021, Sections 12.1 and 12.2, for details of safety evaluations previously conducted in Phase 1and Phase 2/3 of the study (as previously submitted).

12.1. Local Reactions and Systemic Events – Participants 12 Through 15 Years of Age

There are no new reactogenicity data presented in this report since the adolescent interim CSR, dated 14 April 2021.

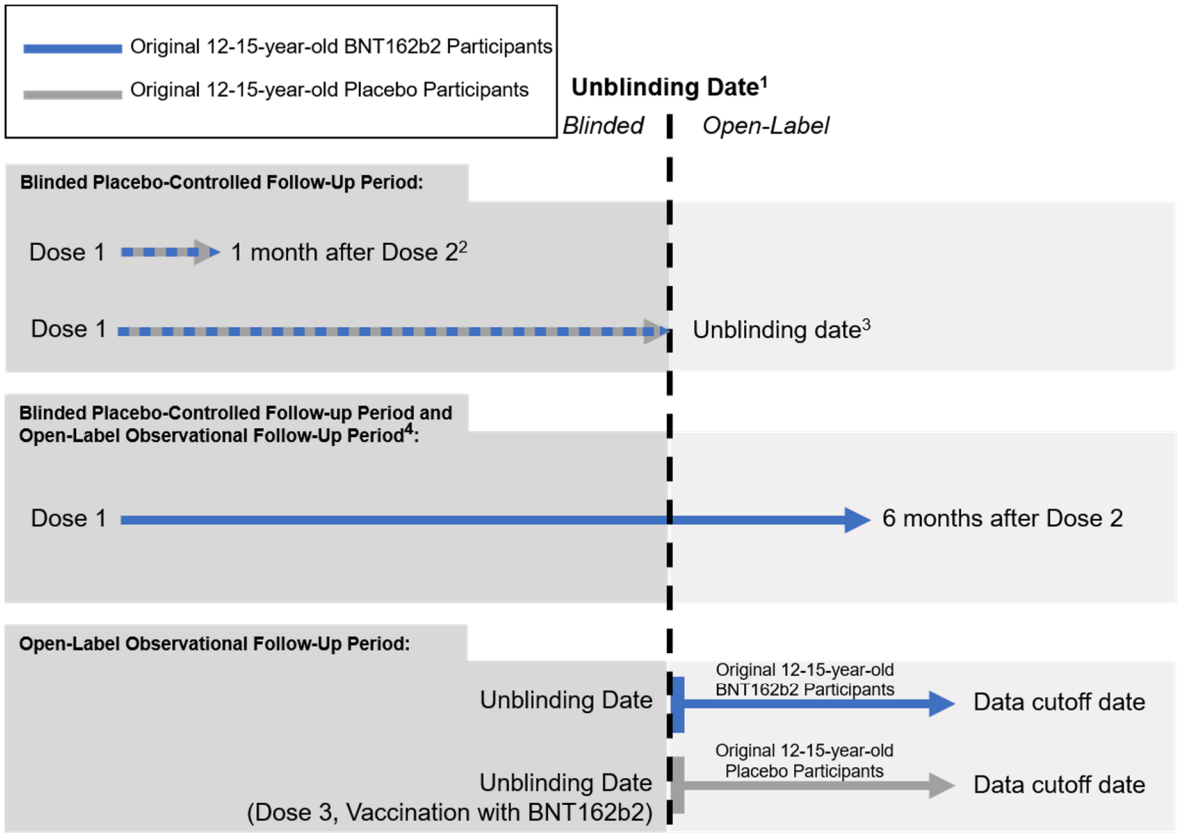
The majority of reactogenicity events previously reported in adolescent participants were mild or moderate in severity and short-lived after dosing (ie, median onset mostly between 1-3 days after dosing and resolution within 1-3 days after onset) (full details in Sections 12.1.1 and 12.1.2 of the adolescent interim C4591001 CSR dated 14 April 2021).

12.2. Adverse Events – Participants 12 Through 15 Years of Age

AE safety data are from either the blinded placebo-controlled follow-up period, the open-label observational follow-up period, or both. The time periods and safety analysis groups are presented below and in Figure 2. AEs reported from Dose 1 to 1 month after Dose 2 during the blinded placebo-controlled follow-up period were previously reported in the adolescent interim CSR, dated 14 April 2021. For each time period, overall safety will be presented in addition to new AEs that were reported since the EUA snapshot occurred (based on a data cutoff date of 13 March 2021), in the following order:

- Blinded placebo-controlled follow-up period from Dose 1 to the unblinding date, including separate summaries for new AEs that were reported after the EUA snapshot date (Section 12.2.1)
- Open-label follow-up period – original BNT162b2 recipients (Section 12.2.2)
- Blinded placebo-controlled and open-label follow-up periods from Dose 1 to 6 months after Dose 2 – original BNT162b2 participants, including separate summaries for new AEs that were reported after the EUA snapshot date (Section 12.2.3)
- Open-label follow-up period – original placebo recipients who then received at least 1 dose of BNT162b2 after unblinding (Section 12.2.4)

Figure 2 Phase 2/3 Safety Analyses of Adolescent Participants: Time Periods and Analysis Groups



[1] Will vary by participant. Adverse event data analyzed from Dose 1 to unblinding date or from unblinding date to data cutoff date are reported as incidence rates adjusted for exposure time.
[2] Data previously reported in the adolescent interim CSR dated 14 April 2021.
[3] Up to ~6 months after Dose 2.
[4] Cumulative BNT162b2 follow-up to at least 6 months after Dose 2.

12.2.1. Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

12.2.1.1. Summary of Adverse Events – Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

An overview of AE IRs adjusted for exposure time from Dose 1 to the unblinding date for adolescent participants during the blinded placebo-controlled follow-up period is presented in Table 18, and total exposure time in 100 PY was similar in the BNT162b2 and placebo groups (4.6 vs 4.5 per 100 PY, respectively). Hence, frequencies are summarized in the safety results.

The percentage of adolescent participants with any AE was similar in the BNT162b2 and placebo groups (8.4% and 10.0%, respectively). Severe AEs, SAEs, and AEs leading to withdrawal were reported by ≤1.1%, ≤0.9%, and ≤0.1%, respectively, in both groups. All reported SAEs were assessed by the investigator as not related to study intervention. Withdrawals due to related AEs were reported in 1 adolescent participant in the BNT162b2 group (pyrexia occurring 1 day after Dose 1; previously reported in adolescent interim CSR dated 14 April 2021, Section 12.3.2.4.1), and none in the placebo group. There were no deaths.

Table 18. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	95 (8.4)	20.8	(16.8, 25.4)	113 (10.0)	25.1	(20.7, 30.1)
Related[f]	36 (3.2)	7.9	(5.5, 10.9)	24 (2.1)	5.3	(3.4, 7.9)
Severe	13 (1.1)	2.8	(1.5, 4.9)	5 (0.4)	1.1	(0.4, 2.6)
Life-threatening	2 (0.2)	0.4	(0.1, 1.6)	1 (0.1)	0.2	(0.0, 1.2)
Any serious adverse event	10 (0.9)	2.2	(1.0, 4.0)	2 (0.2)	0.4	(0.1, 1.6)
Related[f]	0	0.0	(0.0, 0.8)	0	0.0	(0.0, 0.8)
Severe	7 (0.6)	1.5	(0.6, 3.2)	1 (0.1)	0.2	(0.0, 1.2)
Life-threatening	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
Any nonserious adverse event	89 (7.9)	19.5	(15.6, 24.0)	111 (9.8)	24.6	(20.3, 29.6)
Related[f]	36 (3.2)	7.9	(5.5, 10.9)	24 (2.1)	5.3	(3.4, 7.9)
Severe	6 (0.5)	1.3	(0.5, 2.9)	4 (0.4)	0.9	(0.2, 2.3)
Life-threatening	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Any adverse event leading to withdrawal	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)

Table 18. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Related[f]	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Severe	0	0.0	(0.0, 0.8)	0	0.0	(0.0, 0.8)
Life-threatening	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Death	0	0.0	(0.0, 0.8)	0	0.0	(0.0, 0.8)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. 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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:22)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s092_all_unb1_ped6

12.2.1.1.1. Subgroup Analyses

Total exposure time in 100 PY was similar in the BNT162b2 and placebo groups for each subgroup analysis. An overview of AEs from Dose 1 to the unblinding date by subgroup are presented in the following tables:

Baseline SARS-CoV-2 Status: Positive	Supplemental Table 14.14
Baseline SARS-CoV-2 Status: Negative	Supplemental Table 14.15
Ethnicity: Hispanic/Latino	Supplemental Table 14.16
Ethnicity: Non-Hispanic/Non-Latino	Supplemental Table 14.17
Race: White	Supplemental Table 14.18
Race: Black or African American	Supplemental Table 14.19
Race: All Others	Supplemental Table 14.20
Sex: Male	Supplemental Table 14.21
Sex: Female	Supplemental Table 14.22

There were 4 (8.7%) and 91 (8.4%) participants who were baseline SARS-CoV-2 positive and negative in the BNT162b2 group who reported at least 1 AE, respectively, and 4 (8.0%) and 109 (10.1%) participants who were baseline SARS-CoV-2 positive and negative in the placebo group who reported at least 1 AE, respectively (Supplemental Tables 14.14 and 14.15, respectively). The frequency of severe AEs, SAEs (all assessed as not related), or AEs leading to withdrawal in participants who were SARS-CoV-2 negative was 1.2%, 0.9%, and 0.1%, respectively (Supplemental Table 14.15), while there were no severe AEs, SAEs, or AEs leading to withdrawal in participants who were SARS-CoV-2 positive (Supplemental Table 14.14), supporting previous observations in this study that participants who are SARS-CoV-2 positive at baseline do not report AEs at a higher rate than those who are are negative at baseline (previously reported in 6-month update interim CSR, dated 29 April 2021).

The frequency of at least 1 AE reported in the BNT162b2 group was 6.8% in Hispanic/Latino and 8.6% in non-Hispanic/non-Latino participants (Supplemental Tables 14.16 and 14.17, respectively). The frequency of related AEs, severe AEs, SAEs (all not related), and AEs leading to withdrawal was similar in the Hispanic/Latino and Non-Hispanic/Non-Latino subgroups. Considering that the Hispanic/Latino subgroup (N=132) had fewer participants than the non-Hispanic/non-Latino subgroup (N=997) in the BNT162b2 group, the small numerical differences in these subgroups were not considered clinically meaningful.

The frequency of at least 1 AE reported in the BNT162b2 group was 5.8% to 8.6% across race subgroups (Supplemental Tables 14.18 to 14.20). Related AEs were reported in the BNT162b2 group across race subgroups at frequencies of 1.9% to 5.5%. Low incidences of severe and serious AEs were reported in the BNT162b2 groups across race subgroups (≤1.9%). Considering that some race subgroups had fewer participants than others (within the BNT162b2 groups: White N=970, Black or African American N = 52, and 'All Others' N=109), the small numerical differences in these subgroups were not considered clinically meaningful.

The frequency of at least 1 AE reported in the BNT162b2 group for males and females was 7.4% and 9.4%, respectively, and the corresponding frequency in the placebo group was 9.7% and 10.3%, respectively (Supplemental Tables 14.21 and 14.22, respectively). In the BNT162b2 group, frequencies of at least 1 SAE in male and female participants were 0.5% and 1.2% in the BNT162b2 group and 0.3% and none in the placebo group, respectively.

12.2.1.2. Adverse Events by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

AEs from Dose 1 to the unblinding date during the blinded placebo-controlled follow-up period are presented in Table 19. AEs reported in adolescents were similar in the BNT162b2 and placebo groups (8.4% and 10.0%, respectively). The most frequently reported AEs in the BNT162b2 group included lymphadenopathy (9 [0.8%]), injection site pain (8 [0.7%]), fatigue (8 [0.7%]), pyrexia (6 [0.5%]), depression (6 [0.5%]), nausea (5 [0.4%]), and

headache (5 [0.4%]). Most of these AEs were previously reported in the adolescent interim CSR, dated 14 April 2021.

The number of participants with psychiatric disorder AEs were comparable in the 2 groups, (17 [1.5%] in BNT162b2 group vs. 13 [1.2%] in placebo group) (Table 19). There were 4 participants who were hospitalized with the event of suicidal ideation (3 of these were new after the EUA snapshot (Table 21) and are discussed in Section 12.3.2.1.2; the remaining case that was previously reported in the adolescent interim CSR, dated 14 April 2021 is discussed in Section 12.3.2.1). All participants were in the BNT162b2 group and had an ongoing past medical history of PPD (3 diagnosed within PPD and 1 since PPD) (Appendix 16.2.5.4). Of these 4 participants, 3 had been taking selective serotonin reuptake inhibitors (fluoxetine or sertraline) for their ongoing condition. The fourth participant had their concomitant medication for PPD changed from PPD approximately 22 days before the event of suicidal ideation occurred.

A total of 9 participants reported depression: 6 [0.5%] in the BNT162b2 group and 3 [0.3%] in the placebo group (Table 19), (6 of these were new after the EUA snapshot; 4 in the BNT162b2 group and 2 in the placebo group [Table 21]). Of the 6 participants in the BNT162b2 group, 3 participants had a known past medical history of ongoing depression, and of the 4 newly diagnosed cases in the BNT162b2 group, 3 participants had an ongoing past medical history of attention deficit hyperactivity disorder and the depression for the remaining participant in this group was reported to be due to social events. Within the placebo group, 2 of the 3 participants were newly diagnosed with depression (Table 21 and Table 19, respectively).

The event of conversion disorder (BNT162b2 group) has been previously reported in the adolescent interim CSR dated 14 April 2021 Section 12.4.2.1.1 as an SAE of neuralgia and had been extensively investigated. Further follow-up since the adolescent interim CSR; the participant was continuing with physical therapy and had undergone further neurological examination and investigations including an MRI brain scan with and without contrast that was normal. There has been little change in PPD symptoms, and PPD continues to require treatment.

The 1 participant in the BNT162b2 group who reported a tic had an exacerbation of their known tic disorder (diagnosed since PPD) and was considered to be due to life stressors (as determined by the principal investigator). This event was previously reported in the adolescent interim CSR dated 14 April 2021.

Table 19. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	95 (8.4)	20.8	(16.8, 25.4)	113 (10.0)	25.1	(20.7, 30.1)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	9 (0.8)	2.0	(0.9, 3.7)	2 (0.2)	0.4	(0.1, 1.6)
Lymphadenopathy	9 (0.8)	2.0	(0.9, 3.7)	2 (0.2)	0.4	(0.1, 1.6)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Spine malformation	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
EAR AND LABYRINTH DISORDERS	1 (0.1)	0.2	(0.0, 1.2)	3 (0.3)	0.7	(0.1, 1.9)
Cerumen impaction	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Conductive deafness	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Ear pain	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
EYE DISORDERS	2 (0.2)	0.4	(0.1, 1.6)	1 (0.1)	0.2	(0.0, 1.2)
Eye pain	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Eyelid rash	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Retinal haemorrhage	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
GASTROINTESTINAL DISORDERS	14 (1.2)	3.1	(1.7, 5.1)	8 (0.7)	1.8	(0.8, 3.5)
Abdominal pain	2 (0.2)	0.4	(0.1, 1.6)	1 (0.1)	0.2	(0.0, 1.2)
Aphthous ulcer	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Constipation	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Diarrhoea	3 (0.3)	0.7	(0.1, 1.9)	1 (0.1)	0.2	(0.0, 1.2)
Gastritis	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Lip swelling	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Mouth swelling	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Mouth ulceration	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Nausea	5 (0.4)	1.1	(0.4, 2.6)	3 (0.3)	0.7	(0.1, 1.9)
Oral mucosal blistering	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Rectal prolapse	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Tooth impacted	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Toothache	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Vomiting	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	17 (1.5)	3.7	(2.2, 6.0)	12 (1.1)	2.7	(1.4, 4.6)
Chills	2 (0.2)	0.4	(0.1, 1.6)	1 (0.1)	0.2	(0.0, 1.2)

Table 19. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Fatigue	8 (0.7)	1.7	(0.8, 3.4)	4 (0.4)	0.9	(0.2, 2.3)
Injection site pain	8 (0.7)	1.7	(0.8, 3.4)	8 (0.7)	1.8	(0.8, 3.5)
Injection site swelling	2 (0.2)	0.4	(0.1, 1.6)	0	0.0	(0.0, 0.8)
Nodule	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Oedema peripheral	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Peripheral swelling	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Pyrexia	6 (0.5)	1.3	(0.5, 2.9)	0	0.0	(0.0, 0.8)
Vessel puncture site pain	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
IMMUNE SYSTEM DISORDERS	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
Food allergy	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Seasonal allergy	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
INFECTIONS AND INFESTATIONS	10 (0.9)	2.2	(1.0, 4.0)	9 (0.8)	2.0	(0.9, 3.8)
Anal abscess	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Appendicitis	0	0.0	(0.0, 0.8)	2 (0.2)	0.4	(0.1, 1.6)
Body tinea	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Candida infection	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Cellulitis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Conjunctivitis	0	0.0	(0.0, 0.8)	2 (0.2)	0.4	(0.1, 1.6)
Ear infection	3 (0.3)	0.7	(0.1, 1.9)	0	0.0	(0.0, 0.8)
Focal peritonitis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Infectious mononucleosis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Otitis externa	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Otitis media	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Paronychia	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Pilonidal cyst	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
Subcutaneous abscess	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Tinea capitis	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Vulval abscess	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Vulvovaginal mycotic infection	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	15 (1.3)	3.3	(1.8, 5.4)	25 (2.2)	5.5	(3.6, 8.2)
Accident	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
Ankle fracture	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)

Table 19. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Bone contusion	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Clavicle fracture	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
Concussion	3 (0.3)	0.7	(0.1, 1.9)	4 (0.4)	0.9	(0.2, 2.3)
Contusion	2 (0.2)	0.4	(0.1, 1.6)	2 (0.2)	0.4	(0.1, 1.6)
Fall	2 (0.2)	0.4	(0.1, 1.6)	5 (0.4)	1.1	(0.4, 2.6)
Femur fracture	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Foot fracture	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Hand fracture	1 (0.1)	0.2	(0.0, 1.2)	4 (0.4)	0.9	(0.2, 2.3)
Humerus fracture	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Ligament sprain	1 (0.1)	0.2	(0.0, 1.2)	4 (0.4)	0.9	(0.2, 2.3)
Lip injury	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Meniscus injury	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Muscle strain	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
Patella fracture	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Procedural pain	2 (0.2)	0.4	(0.1, 1.6)	3 (0.3)	0.7	(0.1, 1.9)
Radius fracture	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Skin laceration	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Tibia fracture	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Tooth fracture	0	0.0	(0.0, 0.8)	2 (0.2)	0.4	(0.1, 1.6)
Upper limb fracture	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
INVESTIGATIONS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
SARS-CoV-2 antibody test positive	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	8 (0.7)	1.7	(0.8, 3.4)	14 (1.2)	3.1	(1.7, 5.2)
Arthralgia	2 (0.2)	0.4	(0.1, 1.6)	4 (0.4)	0.9	(0.2, 2.3)
Back pain	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Joint swelling	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Musculoskeletal chest pain	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
Myalgia	3 (0.3)	0.7	(0.1, 1.9)	2 (0.2)	0.4	(0.1, 1.6)
Neck pain	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Osteochondrosis	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Pain in extremity	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Tendonitis	0	0.0	(0.0, 0.8)	4 (0.4)	0.9	(0.2, 2.3)

Table 19. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (0.1)	0.2	(0.0, 1.2)	3 (0.3)	0.7	(0.1, 1.9)
Fibroadenoma of breast	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Hair follicle tumour benign	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Melanocytic naevus	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Skin papilloma	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
NERVOUS SYSTEM DISORDERS	13 (1.1)	2.8	(1.5, 4.9)	13 (1.2)	2.9	(1.5, 4.9)
Dizziness	2 (0.2)	0.4	(0.1, 1.6)	1 (0.1)	0.2	(0.0, 1.2)
Headache	5 (0.4)	1.1	(0.4, 2.6)	7 (0.6)	1.6	(0.6, 3.2)
Migraine	3 (0.3)	0.7	(0.1, 1.9)	0	0.0	(0.0, 0.8)
Paraesthesia	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Presyncope	1 (0.1)	0.2	(0.0, 1.2)	4 (0.4)	0.9	(0.2, 2.3)
Syncope	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
PSYCHIATRIC DISORDERS	17 (1.5)	3.7	(2.2, 6.0)	13 (1.2)	2.9	(1.5, 4.9)
Anxiety	4 (0.4)	0.9	(0.2, 2.2)	6 (0.5)	1.3	(0.5, 2.9)
Attention deficit hyperactivity disorder	2 (0.2)	0.4	(0.1, 1.6)	4 (0.4)	0.9	(0.2, 2.3)
Conversion disorder	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Depression	6 (0.5)	1.3	(0.5, 2.9)	3 (0.3)	0.7	(0.1, 1.9)
Disorientation	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Generalised anxiety disorder	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Obsessive-compulsive disorder	0	0.0	(0.0, 0.8)	2 (0.2)	0.4	(0.1, 1.6)
Panic attack	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Sleep terror	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Suicidal ideation	4 (0.4)	0.9	(0.2, 2.2)	0	0.0	(0.0, 0.8)
Tic	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
RENAL AND URINARY DISORDERS	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Dysuria	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Amenorrhoea	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	3 (0.3)	0.7	(0.1, 1.9)	8 (0.7)	1.8	(0.8, 3.5)
Epistaxis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)

Table 19. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Nasal congestion	2 (0.2)	0.4	(0.1, 1.6)	3 (0.3)	0.7	(0.1, 1.9)
Rhinorrhoea	2 (0.2)	0.4	(0.1, 1.6)	4 (0.4)	0.9	(0.2, 2.3)
Sneezing	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	9 (0.8)	2.0	(0.9, 3.7)	16 (1.4)	3.5	(2.0, 5.8)
Acne	2 (0.2)	0.4	(0.1, 1.6)	3 (0.3)	0.7	(0.1, 1.9)
Dermatitis contact	2 (0.2)	0.4	(0.1, 1.6)	1 (0.1)	0.2	(0.0, 1.2)
Eczema	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Pityriasis rosea	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Rash	3 (0.3)	0.7	(0.1, 1.9)	5 (0.4)	1.1	(0.4, 2.6)
Rash maculo-papular	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Seborrhoeic dermatitis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Urticaria	2 (0.2)	0.4	(0.1, 1.6)	5 (0.4)	1.1	(0.4, 2.6)
SURGICAL AND MEDICAL PROCEDURES	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
Wisdom teeth removal	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_all_unb1_ped6

12.2.1.2.1. Subgroup Analyses

AEs from Dose 1 to the unblinding date by SOC and PT and by subgroup are presented in the following tables:

Baseline SARS-CoV-2 Status: Positive — Supplemental Table 14.23

Baseline SARS-CoV-2 Status: Negative	Supplemental Table 14.24
Ethnicity: Hispanic/Latino	Supplemental Table 14.25
Ethnicity: Non-Hispanic/Non-Latino	Supplemental Table 14.26
Race: White	Supplemental Table 14.27
Race: Black or African American	Supplemental Table 14.28
Race: All Others	Supplemental Table 14.29
Sex: Male	Supplemental Table 14.30
Sex: Female	Supplemental Table 14.31

For the baseline SARS-CoV-2 positive and negative subgroups, AEs by SOC and PT were similar to those in the overall safety population (Supplemental Table 14.23 and 14.24, respectively). Considering that the positive subgroup (N=46) had fewer participants than the negative subgroup (N=1083) in the BNT162b2 group, differences in SOCs were considered not clinically meaningful, and there is no evidence that individuals who are positive at baseline report AEs at a higher frequency than those who are negative at baseline.

For the ethnicity subgroups, AEs by SOC and PT were similar to those in the overall safety population for Hispanic/Latino and non-Hispanic/non-Latino participants (Supplemental Tables 14.25 and 14.26, respectively). Considering that the Hispanic/Latino subgroup (N=132) had fewer participants than non-Hispanic/non-Latino subgroup (N=997) in the BNT162b2 group, differences in AEs by SOC and PT in these subgroups were not clinically meaningful.

For race subgroups, AEs by SOC and PT were similar to those in the overall safety population (Supplemental Tables 14.27 through 14.29). Considering that some race subgroups had fewer participants than others (within the BNT162b2 groups: White N=970, Black or African American N=52, and 'All Others' N=109), differences in AEs by SOC and PT in these subgroups were not clinically meaningful.

For sex subgroups, AEs by SOC and PT were similar to those in the overall safety population (Supplemental Tables 14.30 and 14.31, respectively). There was a slightly higher frequency of any event reported in the BNT162b2 group in female participants compared to males (53 [9.4%], 42 [7.4%] respectively), and of any SAEs 7 (1.2%) females, 3 (0.5%) males (Supplemental Tables 14.51 and 14.50, respectively). Within the placebo group there were 2 (0.3%) SAEs reported in male participants and none in the females. In the BNT162b2 group, lymphadenopathy was reported in 8 (1.4%) male participants and in 1 (0.2%) female participant. AEs in the psychiatric disorders SOC were reported in 12 (2.1%) female participants compared to 5 (0.9%) male participants. Depression was the most frequently reported event in both sexes (4 [0.7%] females and 2 [0.4%] males). Anxiety was reported in 4 (0.7%) females and no males. Suicidal ideation was the next most frequently reported event: in females, 3 [0.5%], 1 (0.2%) in male.

12.2.1.3. Related Adverse Events by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

From Dose 1 to the unblinding date, adolescent participants with AEs assessed as related by the investigator were similar in the BNT162b2 and placebo groups (36 [3.2%] and 24 [2.1%], respectively) (Supplemental Table 14.32). Most related AEs were reactogenicity events and in the SOC of general disorders and administration site conditions, reported by 16 (1.4%) and 10 (0.9%) participants in the BNT162b2 and placebo groups, respectively.

Related events of lymphadenopathy were reported in 7 (0.6%) adolescents in the BNT162b2 group and 1 (0.1%) adolescent in the placebo group (refer to other significant AEs in Section 12.3.4).

12.2.1.4. Immediate Adverse Events – Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

These results were previously reported in the adolescent interim CSR dated 14 April 2021.

Adolescents with immediate AEs were low in frequency (≤0.4%) after either dose of study intervention. 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, most immediate AEs 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.

12.2.1.5. Severe or Life-Threatening Adverse Events – Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

From Dose 1 to the unblinding date, severe AEs were reported in 13 (1.1%) adolescent participants in the BNT162b2 group and 5 (0.4%) participants in the placebo group (Supplemental Table 14.33).

The following severe events in the psychiatric orders SOC were previously reported in the adolescent interim CSR, dated 14 April 2021:

- One participant in the BNT162b2 group reported an SAE each of anxiety and depression (discussed in Section 12.3.2.1)

- One participant in the BNT162b2 group reported 2 SAEs of depression (first SAE discussed in Section 12.3.2.1). The second SAE was a new case not previously reported and occurred after the EUA snapshot (discussed in Section 12.3.2.1.2).

- One participant in the BNT162b2 group reported an SAE of suicidal ideation (discussed in Section 12.3.2.1).

Certain severe events discussed below are new cases which have not been previously reported:

- One participant in the placebo group reported a severe AE of urticaria (discussed in Section 12.2.1.6.4)

- One participant in the BNT162b2 group reported a severe SAE of anal abscess (discussed in Section 12.3.2.1.2).

- One participant in the BNT162b2 group reported an SAE of suicidal ideation (discussed in Section 12.3.2.1.2).

There were 3 participants (2 in the BNT162b2 and 1 in the placebo group) who reported at least 1 life-threatening (or Grade 4) AE from Dose 1 to the unblinding date (Supplemental Table 14.34).

The following life-threatening events were previously reported in the adolescent interim CSR, dated 14 April 2021:

- One participant in the placebo group reported an SAE each of focal peritonitis and appendicitis (discussed in Section 12.3.2.1).

- One participant in the BNT162b2 group reported a Grade 4 AE of pyrexia (40.4°C) on Day 2 after Dose 1, with temperature returning to normal on Day 4. The AE was assessed by the investigator as related to study intervention, resolved, and the participant withdrew from the study (Appendix 16.2.7.2.1).

The life-threatening event below is a new case and has not been previously reported:

- One participant in the BNT162b2 group reported a life-threatening (Grade 4) SAE of suicidal ideation, which was a new event after the EUA snapshot (discussed in Section 12.3.2.1.2)

12.2.1.6. New Adverse Events After the EUA Snapshot – Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

12.2.1.6.1. Summary of New Adverse Events After the EUA Snapshot – Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

The frequency of adolescent participants in the BNT162b2 group with any new AE after the EUA snapshot from Dose 1 to the unblinding date was 2.6%, which was less than the frequency in the placebo group (4.2%) (Table 20). There were 6 (0.5%) participants in the BNT162b2 group with SAEs, and all events were assessed by the investigator as not related to study intervention. No SAEs were reported in the placebo group. There were no withdrawals because of any AEs or deaths.

Table 20. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
Adverse Event	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	29 (2.6)	(1.7, 3.7)	47 (4.2)	(3.1, 5.5)
Related[d]	3 (0.3)	(0.1, 0.8)	3 (0.3)	(0.1, 0.8)
Severe	5 (0.4)	(0.1, 1.0)	2 (0.2)	(0.0, 0.6)
Life-threatening	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Any serious adverse event	6 (0.5)	(0.2, 1.2)	0	(0.0, 0.3)
Related[d]	0	(0.0, 0.3)	0	(0.0, 0.3)
Severe	4 (0.4)	(0.1, 0.9)	0	(0.0, 0.3)
Life-threatening	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Any nonserious adverse event	24 (2.1)	(1.4, 3.1)	47 (4.2)	(3.1, 5.5)
Related[d]	3 (0.3)	(0.1, 0.8)	3 (0.3)	(0.1, 0.8)
Severe	1 (0.1)	(0.0, 0.5)	2 (0.2)	(0.0, 0.6)
Life-threatening	0	(0.0, 0.3)	0	(0.0, 0.3)
Any adverse event leading to withdrawal	0	(0.0, 0.3)	0	(0.0, 0.3)
Related[d]	0	(0.0, 0.3)	0	(0.0, 0.3)
Severe	0	(0.0, 0.3)	0	(0.0, 0.3)
Life-threatening	0	(0.0, 0.3)	0	(0.0, 0.3)
Death	0	(0.0, 0.3)	0	(0.0, 0.3)

Table 20. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
Adverse Event	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])

Abbreviation: EUA = emergency use authorization.
a. N = number of subjects in the specified group, subjects who withdrew from the study before EUA snapshot 25Mar2021 with the cutoff date 13Mar2021 are not included. 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. Exact 2-sided CI based on the Clopper and Pearson method.
d. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:44)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s091_all_unb2_ped6

12.2.1.6.2. New Adverse Events After the EUA Snapshot by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

New AEs after the EUA snapshot from Dose 1 to the unblinding date during the blinded placebo-controlled follow-up period are presented in Table 21.

The most frequently reported AEs in adolescents were in the psychiatric disorders SOC (11 [1.0%] and 9 [0.8%] adolescent participants in the BNT162b2 and placebo groups, respectively). These cases are discussed alongside cumulative cases during this period in Section 12.2.1.2.

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Table 21. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	29 (2.6)	(1.7, 3.7)	47 (4.2)	(3.1, 5.5)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Spine malformation	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
EAR AND LABYRINTH DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Conductive deafness	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
EYE DISORDERS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Eye pain	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
GASTROINTESTINAL DISORDERS	1 (0.1)	(0.0, 0.5)	5 (0.4)	(0.1, 1.0)
Nausea	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Abdominal pain	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Constipation	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Mouth ulceration	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Tooth impacted	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Vomiting	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Injection site pain	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Chills	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Fatigue	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Injection site swelling	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Pyrexia	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
IMMUNE SYSTEM DISORDERS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Seasonal allergy	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
INFECTIONS AND INFESTATIONS	3 (0.3)	(0.1, 0.8)	1 (0.1)	(0.0, 0.5)
Anal abscess	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Cellulitis	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Paronychia	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Pilonidal cyst	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	6 (0.5)	(0.2, 1.2)	13 (1.2)	(0.6, 2.0)
Fall	1 (0.1)	(0.0, 0.5)	4 (0.4)	(0.1, 0.9)
Hand fracture	0	(0.0, 0.3)	4 (0.4)	(0.1, 0.9)

Table 21. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Procedural pain	2 (0.2)	(0.0, 0.6)	1 (0.1)	(0.0, 0.5)
Concussion	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Ligament sprain	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Upper limb fracture	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Ankle fracture	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Bone contusion	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Contusion	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Femur fracture	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Meniscus injury	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Skin laceration	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Tibia fracture	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
INVESTIGATIONS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
SARS-CoV-2 antibody test positive	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (0.1)	(0.0, 0.5)	6 (0.5)	(0.2, 1.2)
Tendonitis	0	(0.0, 0.3)	4 (0.4)	(0.1, 0.9)
Arthralgia	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Back pain	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Musculoskeletal chest pain	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Melanocytic naevus	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
NERVOUS SYSTEM DISORDERS	1 (0.1)	(0.0, 0.5)	6 (0.5)	(0.2, 1.2)
Headache	0	(0.0, 0.3)	3 (0.3)	(0.1, 0.8)
Presyncope	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Migraine	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Syncope	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
PSYCHIATRIC DISORDERS	11 (1.0)	(0.5, 1.7)	9 (0.8)	(0.4, 1.5)
Anxiety	3 (0.3)	(0.1, 0.8)	4 (0.4)	(0.1, 0.9)
Depression	4 (0.4)	(0.1, 0.9)	2 (0.2)	(0.0, 0.6)
Attention deficit hyperactivity disorder	2 (0.2)	(0.0, 0.6)	3 (0.3)	(0.1, 0.8)
Suicidal ideation	3 (0.3)	(0.1, 0.8)	0	(0.0, 0.3)
Obsessive-compulsive disorder	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)

Table 21. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Panic attack	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
RENAL AND URINARY DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Dysuria	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Amenorrhoea	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1 (0.1)	(0.0, 0.5)	4 (0.4)	(0.1, 0.9)
Nasal congestion	1 (0.1)	(0.0, 0.5)	3 (0.3)	(0.1, 0.8)
Epistaxis	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Rhinorrhoea	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Sneezing	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	2 (0.2)	(0.0, 0.6)	3 (0.3)	(0.1, 0.8)
Acne	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Dermatitis contact	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Eczema	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Rash	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Seborrhoeic dermatitis	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Urticaria	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
SURGICAL AND MEDICAL PROCEDURES	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Wisdom teeth removal	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)

Abbreviation: EUA = emergency use authorization.
Note: MedDRA (v24.0) 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, subjects who withdrew from the study before EUA snapshot 25Mar2021 with the cutoff date 13Mar2021 are not included. 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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:47)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_all_unb2_ped6

12.2.1.6.3. New Related Adverse Events After the EUA Snapshot by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

There were few adolescent participants with new related AEs that occurred after the EUA snapshot in either group (3 [0.3%] participants each) (Table 22), and each PT was reported by 1 participant each in either group.

One participant in the BNT162b2 group reported an AE of musculoskeletal chest pain (verbatim term reported was PPD), on Day 3 after Dose 2 (Appendix 16.2.7.2.3). The AE was moderate in severity and resolved the same day. There is no evidence that the investigator had evaluated the participant for cardiac disease.

Table 22. Number (%) of Subjects Reporting at Least 1 New Related Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	3 (0.3)	(0.1, 0.8)	3 (0.3)	(0.1, 0.8)
EAR AND LABYRINTH DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Conductive deafness	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
GASTROINTESTINAL DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Nausea	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Vomiting	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Injection site pain	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Chills	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Fatigue	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Injection site swelling	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Pyrexia	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
INVESTIGATIONS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
SARS-CoV-2 antibody test positive	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Musculoskeletal chest pain	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)

Table 22. Number (%) of Subjects Reporting at Least 1 New Related Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])

Abbreviation: EUA = emergency use authorization.
Note: MedDRA (v24.0) 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, subjects who withdrew from the study before EUA snapshot 25Mar2021 with the cutoff date 13Mar2021 are not included. 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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:48)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_rel_unb2_ped6

12.2.1.6.4. New Severe or Life-Threatening Adverse Events After the EUA Snapshot – Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

New severe AEs after the EUA snapshot were reported in 5 (0.4%) adolescent participants in the BNT162b2 group and 2 (0.2%) participants in the placebo group (Table 23).

Certain severe events are discussed below:

- One participant in the placebo group reported a severe AE of urticaria on Day 55 after Dose 2 with a duration of 8 days, and the AE was assessed by the investigator as not related to study intervention (Appendix 16.2.7.2.3). The participant had a past medical history of PPD The event was nonserious, resolved, and the participant continued in the study, receiving a first dose of BNT162b2 (Appendix 16.1.7) with no further urticaria reported.

- One participant in the BNT162b2 group reported a second severe SAE of depression (previously had a severe SAE and reported in the adolesecent interim CSR, dated 14 April 2021 and discussed in Section 12.3.2.1; second SAE discussed in Section 12.3.2.1.2).

- One participant in the BNT162b2 group reported a severe SAE of suicidal ideation (discussed in Section 12.3.2.1.2).

- One participant in the BNT162b2 group reported a severe SAE of anal abscess (discussed in Section 12.3.2.1.2).

From Dose 1 to the unblinding date, there was 1 participant in the BNT162b2group who reported a life-threatening (or Grade 4) SAE of suicidal ideation (Table 24; discussed in Section 12.3.2.1.2).

All new severe and life-threatening events reported after the EUA snapshot from Dose 1 to the unblinding date were assessed by the investigator as not related to study intervention. Most were resolved as of the data cutoff date (02 September 2021). For additional safety data after the EUA snapshot during blinded placebo-controlled and open-label follow-up periods for original BNT162b2 recipients 12 through 15 years of age, refer to Section 12.2.3.4.

Table 23. Number (%) of Subjects Reporting at Least 1 New Severe Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	5 (0.4)	(0.1, 1.0)	2 (0.2)	(0.0, 0.6)
INFECTIONS AND INFESTATIONS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Anal abscess	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	2 (0.2)	(0.0, 0.6)	1 (0.1)	(0.0, 0.5)
Femur fracture	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Procedural pain	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Upper limb fracture	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
PSYCHIATRIC DISORDERS	2 (0.2)	(0.0, 0.6)	0	(0.0, 0.3)
Depression	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Suicidal ideation	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Urticaria	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)

Table 23. Number (%) of Subjects Reporting at Least 1 New Severe Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])

Abbreviation: EUA = emergency use authorization.
Note: MedDRA (v24.0) 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, subjects who withdrew from the study before EUA snapshot 25Mar2021 with the cutoff date 13Mar2021 are not included. 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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:48)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_sev_unb2_ped6

Table 24. Number (%) of Subjects Reporting at Least 1 New Life-Threatening Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
PSYCHIATRIC DISORDERS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Suicidal ideation	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)

Table 24. Number (%) of Subjects Reporting at Least 1 New Life-Threatening Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])

Abbreviation: EUA = emergency use authorization.
Note: MedDRA (v24.0) 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, subjects who withdrew from the study before EUA snapshot 25Mar2021 with the cutoff date 13Mar2021 are not included. 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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:49)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_lif_unb2_ped6

12.2.2. Open-Label Follow-Up Period From the Unblinding Date to the Data Cutoff Date – Original BNT162b2 Recipients 12 Through 15 Years of Age

12.2.2.1. Summary of Adverse Events – Open-Label Follow-Up Period – Original BNT162b2 Recipients 12 Through 15 Years of Age

An overview of AEs from the unblinding date to the data cutoff date for adolescent participants who originally received BNT162b2 during the open-label follow-up period is presented in Table 25 (Note: Per protocol, AEs are reported through approximately 1 month after Dose 2 and within 48 hours after a blood draw. SAEs are reported to approximately 6 months after the last dose of study intervention.)

There were 18 (1.6%) participants who experienced any AE, including 0.4%, 0.3%, and 0% who experienced related, severe, and life-threatening events, respectively (Table 25). This is markedly reduced relative to AEs from Dose 1 to the unblinding date (8.4% of BNT162b2 participants experienced any AE, including 3.2%, 1.1%, and 0.2% who experienced related, severe, and life-threatening events, respectively [Table 18]). The frequencies of SAEs and AEs leading to withdrawal during the open-label follow-up period (0.4% and 0%, respectively [Table 25]) were similar to those from Dose 1 to the unblinding date (0.9% and 0.1%, respectively [Table 18]). There were no adolescent deaths in the study.

Table 25. Incidence Rates of at Least 1 Adverse Event From Unblinding Date to Data Cutoff Date (02SEP2021) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2 – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1107, TE[b]=3.3)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])
Any event	18 (1.6)	5.4	(3.2, 8.5)
Related[f]	4 (0.4)	1.2	(0.3, 3.1)
Severe	3 (0.3)	0.9	(0.2, 2.6)
Life-threatening	0	0.0	(0.0, 1.1)
Any serious adverse event	4 (0.4)	1.2	(0.3, 3.1)
Related[f]	0	0.0	(0.0, 1.1)
Severe	1 (0.1)	0.3	(0.0, 1.7)
Life-threatening	0	0.0	(0.0, 1.1)
Any nonserious adverse event	14 (1.3)	4.2	(2.3, 7.0)
Related[f]	4 (0.4)	1.2	(0.3, 3.1)
Severe	2 (0.2)	0.6	(0.1, 2.2)
Life-threatening	0	0.0	(0.0, 1.1)
Any adverse event leading to withdrawal	0	0.0	(0.0, 1.1)
Related[f]	0	0.0	(0.0, 1.1)
Severe	0	0.0	(0.0, 1.1)
Life-threatening	0	0.0	(0.0, 1.1)
Death	0	0.0	(0.0, 1.1)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the unblinding date to data cutoff date. 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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s092_ubct1_ped6

12.2.2.2. Adverse Events by System Organ Class and Preferred Term – Open-Label Follow-Up Period – Original BNT162b2 Recipients 12 Through 15 Years of Age

From the unblinding date to the data cutoff date (open-label follow-up period), for adolescent participants who originally received BNT162b2, the number of participants who reported at

least 1 AE was 18 (1.6%) (Supplemental Table 14.35) compared to 95 (8.4%) from Dose 1 to the unblinding date (Table 18).

Overall, the rates in all SOCs after the unblinding date were lower or remained similar to those in the blinded placebo-controlled period.

The frequency for the SOC of nervous system disorders was 6 (0.5%), including the PTs dizziness (2), headache (2), presyncope (2), and syncope (1). (Supplemental Table 14.35). The frequency for the SOC of general disorders and administration site conditions was 4 (0.4%), with injection site pain (3) as the most frequently reported PT.

12.2.2.3. Related Adverse Events by System Organ Class and Preferred Term – Open-Label Follow-Up Period – Original BNT162b2 Recipients 12 Through 15 Years of Age

From the unblinding date to the data cutoff date (open-label follow-up period), for adolescent participants who originally received BNT162b2, the number of participants with AEs assessed as related by the investigator was 4 (0.4%) (Supplemental Table 14.36). The frequencies of related AEs were highest for reactogenicity events and in the SOCs of general disorders and administration site conditions (injection site pain, fatigue, pyrexia, and pain) and nervous system disorders (headache and dizziness) (Supplemental Table 14.36).

12.2.2.4. Severe or Life-Threatening Adverse Events – Open-Label Follow-Up Period – Original BNT162b2 Recipients 12 Through 15 Years of Age

From the unblinding date to the data cutoff date (open-label follow-up period), 3 (0.3%) BNT162b2 participants experienced severe AEs (Supplemental Table 14.37). Two (2) participants experienced pyrexia (general disorders and administration site conditions), a term consistent with reactogenicity.

There were no life-threatening AEs reported from the unblinding date to the data cutoff date (Table 25).

12.2.3. Blinded Placebo-Controlled and Open-Label Follow-Up Periods From Dose 1 to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

12.2.3.1. Summary of Adverse Events – Blinded Placebo-Controlled and Open-Label Follow-Up Periods From Dose 1 to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

There were 1113 adolescent participants who originally received BNT162b2 and had at least 6 months of follow-up time after Dose 2 for the blinded placebo-controlled and open-label follow-up periods (Table 26). There were 98 (8.8%) participants who reported at least 1 AE, and 34 (3.1%) participants reported at least 1 related AE. Severe AEs and SAEs were reported by 13 (1.2%) and 10 (0.9%) participants, respectively. There were no AEs leading to withdrawal, and there were no deaths.

The frequencies of any AEs and related AEs are 70 (6.3%) and 34 (3.1%) through 1 month after Dose 2 compared with 35 (3.1%) and no related AEs from 1 month after Dose 2 to

6 months after Dose 2, respectively (Table 27). From Dose 1 to 1 month after Dose 2, 3 (0.3%) adolescent participants reported SAEs. From 1 month to 6 months after Dose 2, 9 (0.8%) participants reported SAEs. All SAEs were assessed by the investigator as not related to study intervention. There were no AEs leading to withdrawal, and there were no deaths.

Table 26. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2 – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
Adverse Event	**n[b] (%)**	**(95% CI[c])**
Any event	98 (8.8)	(7.2, 10.6)
Related[d]	34 (3.1)	(2.1, 4.2)
Severe	13 (1.2)	(0.6, 2.0)
Life-threatening	0	(0.0, 0.3)
Any serious adverse event	10 (0.9)	(0.4, 1.6)
Related[d]	0	(0.0, 0.3)
Severe	7 (0.6)	(0.3, 1.3)
Life-threatening	0	(0.0, 0.3)
Any nonserious adverse event	91 (8.2)	(6.6, 9.9)
Related[d]	34 (3.1)	(2.1, 4.2)
Severe	6 (0.5)	(0.2, 1.2)
Life-threatening	0	(0.0, 0.3)
Any adverse event leading to withdrawal	0	(0.0, 0.3)
Related[d]	0	(0.0, 0.3)
Severe	0	(0.0, 0.3)
Life-threatening	0	(0.0, 0.3)
Death	0	(0.0, 0.3)

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. Exact 2-sided CI based on the Clopper and Pearson method.
d. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s091_6m1_ped6

Table 27. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
Adverse Event	Dose 1 to 1 Month After Dose 2 n[b] (%)	1 Month After Dose 2 to 6 Months After Dose 2 n[b] (%)
Any event	70 (6.3)	35 (3.1)
Related[c]	34 (3.1)	0
Severe	6 (0.5)	8 (0.7)
Life-threatening	0	0
Any serious adverse event	3 (0.3)	9 (0.8)
Related[c]	0	0
Severe	1 (0.1)	7 (0.6)
Life-threatening	0	0
Any nonserious adverse event	68 (6.1)	28 (2.5)
Related[c]	34 (3.1)	0
Severe	5 (0.4)	1 (0.1)
Life-threatening	0	0
Any adverse event leading to withdrawal	0	0
Related[c]	0	0
Severe	0	0
Life-threatening	0	0
Death	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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s093_6m1_ped6

12.2.3.2. Adverse Events by System Organ Class and Preferred Term – Blinded Placebo-Controlled and Open-Label Follow-Up Periods From Dose 1 to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

There were 98 (8.8%) adolescent participants who originally received BNT162b2, had at least 6 months of follow-up time after Dose 2, and reported AEs from Dose 1 to 6 months

after Dose 2 (Table 28). Frequently reported AEs included reactogenicity events in the following SOCs:

- general disorders and administration site conditions (16 [1.4%])
- musculoskeletal and connective tissue disorders (8 [0.7%])
- nervous system disorders (16 [1.4%])
- gastrointestinal disorders (16 [1.4%])

AEs were reported by 15 (1.3%) participants in the injury, poisoning, and procedural complications SOC; 10 (0.9%) participants in the infections and infestations SOC, and 16 (1.4%) participants in the psychiatric disorders SOC.

When AEs are compared from Dose 1 to 1 month after Dose 2 and from 1 month after Dose 2 to 6 months after Dose 2, the frequencies of AEs by most SOCs were lower or were similar with the additional follow-up time. The overall frequency of any AE for participants from 1 month after Dose 2 to 6 months after Dose 2 (35 [3.1%]) was less compared with the frequency during 1 month follow-up time after Dose 2 (70 [6.3%]) (Table 29). Overall, AEs reported after 1 month post Dose-2 reflect age-appropriate events consistent with the general population.

All lymphadenopathy events were reported from Dose 1 to 1 month after Dose 2, and none were reported from 1 month to 6 months after Dose 2 (Table 29).

AEs in the pyschiatric disorders SOC were reported by 7 (0.6%) participants from Dose 1 to 1 month after Dose 2 and in 11 (1.0%) participants from 1 month to 6 months after Dose 2.

Table 28. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Any event	98 (8.8)	(7.2, 10.6)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	9 (0.8)	(0.4, 1.5)
Lymphadenopathy	9 (0.8)	(0.4, 1.5)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (0.1)	(0.0, 0.5)
Syringomyelia	1 (0.1)	(0.0, 0.5)

Table 28. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
EAR AND LABYRINTH DISORDERS	1 (0.1)	(0.0, 0.5)
Ear pain	1 (0.1)	(0.0, 0.5)
EYE DISORDERS	1 (0.1)	(0.0, 0.5)
Eye pain	1 (0.1)	(0.0, 0.5)
GASTROINTESTINAL DISORDERS	16 (1.4)	(0.8, 2.3)
Nausea	6 (0.5)	(0.2, 1.2)
Diarrhoea	3 (0.3)	(0.1, 0.8)
Abdominal pain	2 (0.2)	(0.0, 0.6)
Aphthous ulcer	2 (0.2)	(0.0, 0.6)
Abdominal pain upper	1 (0.1)	(0.0, 0.5)
Constipation	1 (0.1)	(0.0, 0.5)
Gastritis	1 (0.1)	(0.0, 0.5)
Lip swelling	1 (0.1)	(0.0, 0.5)
Mouth swelling	1 (0.1)	(0.0, 0.5)
Oral mucosal blistering	1 (0.1)	(0.0, 0.5)
Rectal prolapse	1 (0.1)	(0.0, 0.5)
Vomiting	1 (0.1)	(0.0, 0.5)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	16 (1.4)	(0.8, 2.3)
Fatigue	8 (0.7)	(0.3, 1.4)
Injection site pain	8 (0.7)	(0.3, 1.4)
Pyrexia	5 (0.4)	(0.1, 1.0)
Chills	2 (0.2)	(0.0, 0.6)
Injection site swelling	2 (0.2)	(0.0, 0.6)
Nodule	1 (0.1)	(0.0, 0.5)
Peripheral swelling	1 (0.1)	(0.0, 0.5)
IMMUNE SYSTEM DISORDERS	1 (0.1)	(0.0, 0.5)
Seasonal allergy	1 (0.1)	(0.0, 0.5)
INFECTIONS AND INFESTATIONS	10 (0.9)	(0.4, 1.6)
Ear infection	2 (0.2)	(0.0, 0.6)
Anal abscess	1 (0.1)	(0.0, 0.5)

Table 28. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Appendicitis	1 (0.1)	(0.0, 0.5)
Body tinea	1 (0.1)	(0.0, 0.5)
Otitis externa	1 (0.1)	(0.0, 0.5)
Otitis media	1 (0.1)	(0.0, 0.5)
Paronychia	1 (0.1)	(0.0, 0.5)
Pilonidal cyst	1 (0.1)	(0.0, 0.5)
Tinea capitis	1 (0.1)	(0.0, 0.5)
Vulval abscess	1 (0.1)	(0.0, 0.5)
Vulvovaginal mycotic infection	1 (0.1)	(0.0, 0.5)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	15 (1.3)	(0.8, 2.2)
Concussion	3 (0.3)	(0.1, 0.8)
Hand fracture	2 (0.2)	(0.0, 0.6)
Procedural pain	2 (0.2)	(0.0, 0.6)
Accident	1 (0.1)	(0.0, 0.5)
Bone contusion	1 (0.1)	(0.0, 0.5)
Clavicle fracture	1 (0.1)	(0.0, 0.5)
Contusion	1 (0.1)	(0.0, 0.5)
Fall	1 (0.1)	(0.0, 0.5)
Femur fracture	1 (0.1)	(0.0, 0.5)
Ligament sprain	1 (0.1)	(0.0, 0.5)
Meniscus injury	1 (0.1)	(0.0, 0.5)
Muscle strain	1 (0.1)	(0.0, 0.5)
Radius fracture	1 (0.1)	(0.0, 0.5)
Upper limb fracture	1 (0.1)	(0.0, 0.5)
INVESTIGATIONS	1 (0.1)	(0.0, 0.5)
SARS-CoV-2 antibody test positive	1 (0.1)	(0.0, 0.5)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	8 (0.7)	(0.3, 1.4)
Myalgia	3 (0.3)	(0.1, 0.8)
Arthralgia	2 (0.2)	(0.0, 0.6)
Musculoskeletal chest pain	1 (0.1)	(0.0, 0.5)
Osteochondrosis	1 (0.1)	(0.0, 0.5)

Table 28. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Pain in extremity	1 (0.1)	(0.0, 0.5)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (0.1)	(0.0, 0.5)
Hair follicle tumour benign	1 (0.1)	(0.0, 0.5)
NERVOUS SYSTEM DISORDERS	16 (1.4)	(0.8, 2.3)
Headache	5 (0.4)	(0.1, 1.0)
Migraine	3 (0.3)	(0.1, 0.8)
Presyncope	3 (0.3)	(0.1, 0.8)
Dizziness	2 (0.2)	(0.0, 0.6)
Syncope	2 (0.2)	(0.0, 0.6)
Paraesthesia	1 (0.1)	(0.0, 0.5)
PSYCHIATRIC DISORDERS	16 (1.4)	(0.8, 2.3)
Depression	5 (0.4)	(0.1, 1.0)
Anxiety	4 (0.4)	(0.1, 0.9)
Suicidal ideation	3 (0.3)	(0.1, 0.8)
Attention deficit hyperactivity disorder	2 (0.2)	(0.0, 0.6)
Conversion disorder	1 (0.1)	(0.0, 0.5)
Disorientation	1 (0.1)	(0.0, 0.5)
Generalised anxiety disorder	1 (0.1)	(0.0, 0.5)
Panic attack	1 (0.1)	(0.0, 0.5)
Sleep terror	1 (0.1)	(0.0, 0.5)
Tic	1 (0.1)	(0.0, 0.5)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (0.1)	(0.0, 0.5)
Amenorrhoea	1 (0.1)	(0.0, 0.5)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	3 (0.3)	(0.1, 0.8)
Nasal congestion	2 (0.2)	(0.0, 0.6)
Rhinorrhoea	2 (0.2)	(0.0, 0.6)
Sneezing	1 (0.1)	(0.0, 0.5)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	8 (0.7)	(0.3, 1.4)
Acne	2 (0.2)	(0.0, 0.6)
Dermatitis contact	2 (0.2)	(0.0, 0.6)

Table 28. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Rash	2 (0.2)	(0.0, 0.6)
Urticaria	2 (0.2)	(0.0, 0.6)
SURGICAL AND MEDICAL PROCEDURES	1 (0.1)	(0.0, 0.5)
Wisdom teeth removal	1 (0.1)	(0.0, 0.5)

Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_all_6m1_ped6

Table 29. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term and Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1113)			
	Dose 1 to 1 Month After Dose 2		1 Month After Dose 2 to 6 Months After Dose 2	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	70 (6.3)	(4.9, 7.9)	35 (3.1)	(2.2, 4.3)

Table 29. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term and Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1113)			
	Dose 1 to 1 Month After Dose 2		1 Month After Dose 2 to 6 Months After Dose 2	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
BLOOD AND LYMPHATIC SYSTEM DISORDERS	9 (0.8)	(0.4, 1.5)	0	(0.0, 0.3)
Lymphadenopathy	9 (0.8)	(0.4, 1.5)	0	(0.0, 0.3)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Syringomyelia	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
EAR AND LABYRINTH DISORDERS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Ear pain	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
EYE DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Eye pain	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
GASTROINTESTINAL DISORDERS	14 (1.3)	(0.7, 2.1)	3 (0.3)	(0.1, 0.8)
Nausea	5 (0.4)	(0.1, 1.0)	1 (0.1)	(0.0, 0.5)
Diarrhoea	3 (0.3)	(0.1, 0.8)	0	(0.0, 0.3)
Abdominal pain	2 (0.2)	(0.0, 0.6)	1 (0.1)	(0.0, 0.5)
Aphthous ulcer	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Abdominal pain upper	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Constipation	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Gastritis	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Lip swelling	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Mouth swelling	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Oral mucosal blistering	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Rectal prolapse	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Vomiting	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	16 (1.4)	(0.8, 2.3)	0	(0.0, 0.3)
Fatigue	8 (0.7)	(0.3, 1.4)	0	(0.0, 0.3)
Injection site pain	8 (0.7)	(0.3, 1.4)	0	(0.0, 0.3)
Pyrexia	5 (0.4)	(0.1, 1.0)	0	(0.0, 0.3)
Chills	2 (0.2)	(0.0, 0.6)	0	(0.0, 0.3)
Injection site swelling	2 (0.2)	(0.0, 0.6)	0	(0.0, 0.3)
Nodule	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)

Table 29. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term and Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1113)			
	Dose 1 to 1 Month After Dose 2		1 Month After Dose 2 to 6 Months After Dose 2	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Peripheral swelling	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
IMMUNE SYSTEM DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Seasonal allergy	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
INFECTIONS AND INFESTATIONS	6 (0.5)	(0.2, 1.2)	4 (0.4)	(0.1, 0.9)
Ear infection	2 (0.2)	(0.0, 0.6)	0	(0.0, 0.3)
Anal abscess	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Appendicitis	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Body tinea	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Otitis externa	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Otitis media	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Paronychia	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Pilonidal cyst	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Tinea capitis	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Vulval abscess	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Vulvovaginal mycotic infection	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	9 (0.8)	(0.4, 1.5)	6 (0.5)	(0.2, 1.2)
Concussion	3 (0.3)	(0.1, 0.8)	0	(0.0, 0.3)
Hand fracture	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Procedural pain	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Accident	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Bone contusion	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Clavicle fracture	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Contusion	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Fall	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Femur fracture	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Ligament sprain	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Meniscus injury	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Muscle strain	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Radius fracture	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)

Table 29. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term and Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1113)			
	Dose 1 to 1 Month After Dose 2		1 Month After Dose 2 to 6 Months After Dose 2	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Upper limb fracture	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
INVESTIGATIONS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
SARS-CoV-2 antibody test positive	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	8 (0.7)	(0.3, 1.4)	0	(0.0, 0.3)
Myalgia	3 (0.3)	(0.1, 0.8)	0	(0.0, 0.3)
Arthralgia	2 (0.2)	(0.0, 0.6)	0	(0.0, 0.3)
Musculoskeletal chest pain	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Osteochondrosis	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Pain in extremity	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Hair follicle tumour benign	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
NERVOUS SYSTEM DISORDERS	11 (1.0)	(0.5, 1.8)	5 (0.4)	(0.1, 1.0)
Headache	5 (0.4)	(0.1, 1.0)	0	(0.0, 0.3)
Migraine	2 (0.2)	(0.0, 0.6)	1 (0.1)	(0.0, 0.5)
Presyncope	1 (0.1)	(0.0, 0.5)	2 (0.2)	(0.0, 0.6)
Dizziness	2 (0.2)	(0.0, 0.6)	0	(0.0, 0.3)
Syncope	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Paraesthesia	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
PSYCHIATRIC DISORDERS	7 (0.6)	(0.3, 1.3)	11 (1.0)	(0.5, 1.8)
Depression	2 (0.2)	(0.0, 0.6)	4 (0.4)	(0.1, 0.9)
Anxiety	1 (0.1)	(0.0, 0.5)	3 (0.3)	(0.1, 0.8)
Suicidal ideation	0	(0.0, 0.3)	3 (0.3)	(0.1, 0.8)
Attention deficit hyperactivity disorder	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Conversion disorder	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Disorientation	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Generalised anxiety disorder	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Panic attack	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Sleep terror	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)

Table 29. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term and Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1113)			
	Dose 1 to 1 Month After Dose 2		1 Month After Dose 2 to 6 Months After Dose 2	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Tic	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Amenorrhoea	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	2 (0.2)	(0.0, 0.6)	1 (0.1)	(0.0, 0.5)
Nasal congestion	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Rhinorrhoea	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Sneezing	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	6 (0.5)	(0.2, 1.2)	2 (0.2)	(0.0, 0.6)
Acne	2 (0.2)	(0.0, 0.6)	0	(0.0, 0.3)
Dermatitis contact	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Rash	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Urticaria	2 (0.2)	(0.0, 0.6)	0	(0.0, 0.3)
SURGICAL AND MEDICAL PROCEDURES	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Wisdom teeth removal	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)

Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s132_6m1_ped6

12.2.3.3. Related Adverse Events by System Organ Class and Preferred Term – Blinded Placebo-Controlled and Open-Label Follow-Up Periods From Dose 1 to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

From Dose 1 to 6 months after Dose 2, 34 (3.1%) original BNT162b2 adolescent recipients reported AEs assessed by the investigator as related to study intervention (Supplemental

Table 14.38). Most related AEs were reactogenicity events and in the SOC of general disorders and administration site conditions, reported by 15 (1.3%) participants. Related events of lymphadenopathy were reported by 7 (0.6%) adolescents in the BNT162b2 group (refer to other significant AEs in Section 12.3.4.1).

12.2.3.4. New Adverse Events After the EUA Snapshot – Blinded Placebo-Controlled and Open-Label Follow-Up Periods From Dose 1 to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

12.2.3.4.1. Summary of New Adverse Events After the EUA Snapshot – Blinded Placebo-Controlled and Open-Label Follow-Up Periods From Dose 1 to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

From the time after the EUA snapshot for adolescent participants who had at least 6 months of follow-up time after Dose 2 during the blinded placebo-controlled and open-label follow-up periods, there were 36 (3.2%) participants who reported at least 1 AE, and 3 (0.3%) participants reported at least 1 related AE (Table 30). Severe AEs and SAEs were reported by 6 (0.5%) and 7 (0.6%) participants, respectively. There were no AEs leading to withdrawal, and there were no deaths.

When frequencies of new AEs for participants with at least 6 months of follow-up time are examined by time since the second dose, the frequency of any AEs and related AEs is 6 (0.5%) and 3 (0.3%) through 1 month after Dose 2 compared with 32 (2.9%) and no related AEs from 1 month after Dose 2 to 6 months after Dose 2 (Table 31). At 1 month after Dose 2, no adolescent participants reported severe AEs or SAEs. From 1 month to 6 months after Dose 2, the number of participants with severe AEs and SAEs was 6 (0.5%) and 7 (0.6%), respectively. All new SAEs and all AEs reported from 1 month after Dose 2 to 6 months after Dose 2 were assessed by the investigator as not related to study intervention.

Table 30. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2 – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
Adverse Event	n[b] (%)	(95% CI[c])
Any event	36 (3.2)	(2.3, 4.4)
Related[d]	3 (0.3)	(0.1, 0.8)
Severe	6 (0.5)	(0.2, 1.2)
Life-threatening	0	(0.0, 0.3)
Any serious adverse event	7 (0.6)	(0.3, 1.3)

Table 30. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2 – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
Adverse Event	n[b] (%)	(95% CI[c])
Related[d]	0	(0.0, 0.3)
Severe	5 (0.4)	(0.1, 1.0)
Life-threatening	0	(0.0, 0.3)
Any nonserious adverse event	30 (2.7)	(1.8, 3.8)
Related[d]	3 (0.3)	(0.1, 0.8)
Severe	1 (0.1)	(0.0, 0.5)
Life-threatening	0	(0.0, 0.3)
Any adverse event leading to withdrawal	0	(0.0, 0.3)
Related[d]	0	(0.0, 0.3)
Severe	0	(0.0, 0.3)
Life-threatening	0	(0.0, 0.3)
Death	0	(0.0, 0.3)

Abbreviation: EUA = emergency use authorization.
Note: EUA snapshot 25Mar2021 with the cutoff date 13Mar2021.
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. Exact 2-sided CI based on the Clopper and Pearson method.
d. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:49)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s091_6m2_ped6

Table 31. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2, by Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
	Dose 1 to 1 Month After Dose 2	1 Month After Dose 2 to 6 Months After Dose 2
Adverse Event	n[b] (%)	n[b] (%)
Any event	6 (0.5)	32 (2.9)
Related[c]	3 (0.3)	0
Severe	0	6 (0.5)
Life-threatening	0	0
Any serious adverse event	0	7 (0.6)
Related[c]	0	0
Severe	0	5 (0.4)
Life-threatening	0	0
Any nonserious adverse event	6 (0.5)	26 (2.3)
Related[c]	3 (0.3)	0
Severe	0	1 (0.1)
Life-threatening	0	0
Any adverse event leading to withdrawal	0	0
Related[c]	0	0
Severe	0	0
Life-threatening	0	0
Death	0	0

Abbreviation: EUA = emergency use authorization.
Note: EUA snapshot 25Mar2021 with the cutoff date 13Mar2021.
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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:45)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s093_6m2_ped6

12.2.3.4.2. New Adverse Events After the EUA Snapshot by System Organ Class and Preferred Term – Blinded Placebo-Controlled and Open-Label Follow-Up Periods

From Dose 1 to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

Most of the new AEs reported after the EUA snapshot in adolescent participants with at least 6 months of follow-up time after Dose 2 were in the psychiatric disorders SOC (11 [1.0%]) (Table 32).

When AEs are compared from Dose 1 to 1 month after Dose 2 and from 1 month after Dose 2 to 6 months after Dose 2, AEs reported in the psychiatric disorders SOC was 1 (0.1%) and 10 (0.9%) participants, respectively (Table 33). All AEs in this SOC were assessed by the investigator as not related to study intervention (Appendix 16.2.7.2.3).

Table 32. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Any event	36 (3.2)	(2.3, 4.4)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (0.1)	(0.0, 0.5)
Syringomyelia	1 (0.1)	(0.0, 0.5)
EYE DISORDERS	1 (0.1)	(0.0, 0.5)
Eye pain	1 (0.1)	(0.0, 0.5)
GASTROINTESTINAL DISORDERS	3 (0.3)	(0.1, 0.8)
Abdominal pain upper	1 (0.1)	(0.0, 0.5)
Aphthous ulcer	1 (0.1)	(0.0, 0.5)
Constipation	1 (0.1)	(0.0, 0.5)
Nausea	1 (0.1)	(0.0, 0.5)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (0.1)	(0.0, 0.5)
Chills	1 (0.1)	(0.0, 0.5)
Fatigue	1 (0.1)	(0.0, 0.5)
Injection site pain	1 (0.1)	(0.0, 0.5)
Injection site swelling	1 (0.1)	(0.0, 0.5)
Pyrexia	1 (0.1)	(0.0, 0.5)
IMMUNE SYSTEM DISORDERS	1 (0.1)	(0.0, 0.5)
Seasonal allergy	1 (0.1)	(0.0, 0.5)

Table 32. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
INFECTIONS AND INFESTATIONS	4 (0.4)	(0.1, 0.9)
Anal abscess	1 (0.1)	(0.0, 0.5)
Appendicitis	1 (0.1)	(0.0, 0.5)
Paronychia	1 (0.1)	(0.0, 0.5)
Pilonidal cyst	1 (0.1)	(0.0, 0.5)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	6 (0.5)	(0.2, 1.2)
Procedural pain	2 (0.2)	(0.0, 0.6)
Bone contusion	1 (0.1)	(0.0, 0.5)
Femur fracture	1 (0.1)	(0.0, 0.5)
Hand fracture	1 (0.1)	(0.0, 0.5)
Meniscus injury	1 (0.1)	(0.0, 0.5)
Upper limb fracture	1 (0.1)	(0.0, 0.5)
INVESTIGATIONS	1 (0.1)	(0.0, 0.5)
SARS-CoV-2 antibody test positive	1 (0.1)	(0.0, 0.5)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (0.1)	(0.0, 0.5)
Musculoskeletal chest pain	1 (0.1)	(0.0, 0.5)
NERVOUS SYSTEM DISORDERS	4 (0.4)	(0.1, 0.9)
Presyncope	2 (0.2)	(0.0, 0.6)
Migraine	1 (0.1)	(0.0, 0.5)
Syncope	1 (0.1)	(0.0, 0.5)
PSYCHIATRIC DISORDERS	11 (1.0)	(0.5, 1.8)
Anxiety	4 (0.4)	(0.1, 0.9)
Depression	4 (0.4)	(0.1, 0.9)
Attention deficit hyperactivity disorder	2 (0.2)	(0.0, 0.6)
Suicidal ideation	2 (0.2)	(0.0, 0.6)
Panic attack	1 (0.1)	(0.0, 0.5)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (0.1)	(0.0, 0.5)
Amenorrhoea	1 (0.1)	(0.0, 0.5)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1 (0.1)	(0.0, 0.5)
Nasal congestion	1 (0.1)	(0.0, 0.5)

Table 32. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Rhinorrhoea	1 (0.1)	(0.0, 0.5)
Sneezing	1 (0.1)	(0.0, 0.5)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	2 (0.2)	(0.0, 0.6)
Acne	1 (0.1)	(0.0, 0.5)
Dermatitis contact	1 (0.1)	(0.0, 0.5)
SURGICAL AND MEDICAL PROCEDURES	1 (0.1)	(0.0, 0.5)
Wisdom teeth removal	1 (0.1)	(0.0, 0.5)

Abbreviation: EUA = emergency use authorization.
Note: EUA snapshot 25Mar2021 with the cutoff date 13Mar2021.
Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:50)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_all_6m2_ped6

Table 33. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term and Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1113)			
	Dose 1 to 1 Month After Dose 2		1 Month After Dose 2 to 6 Months After Dose 2	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	6 (0.5)	(0.2, 1.2)	32 (2.9)	(2.0, 4.0)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Syringomyelia	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
EYE DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Eye pain	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
GASTROINTESTINAL DISORDERS	0	(0.0, 0.3)	3 (0.3)	(0.1, 0.8)
Abdominal pain upper	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Aphthous ulcer	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Constipation	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Nausea	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Chills	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Fatigue	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Injection site pain	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Injection site swelling	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Pyrexia	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
IMMUNE SYSTEM DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Seasonal allergy	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
INFECTIONS AND INFESTATIONS	0	(0.0, 0.3)	4 (0.4)	(0.1, 0.9)
Anal abscess	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Appendicitis	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Paronychia	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Pilonidal cyst	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	0	(0.0, 0.3)	6 (0.5)	(0.2, 1.2)
Procedural pain	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Bone contusion	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)

Table 33. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term and Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1113)			
	Dose 1 to 1 Month After Dose 2		1 Month After Dose 2 to 6 Months After Dose 2	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Femur fracture	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Hand fracture	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Meniscus injury	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Upper limb fracture	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
INVESTIGATIONS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
SARS-CoV-2 antibody test positive	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Musculoskeletal chest pain	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
NERVOUS SYSTEM DISORDERS	0	(0.0, 0.3)	4 (0.4)	(0.1, 0.9)
Presyncope	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Migraine	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Syncope	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
PSYCHIATRIC DISORDERS	1 (0.1)	(0.0, 0.5)	10 (0.9)	(0.4, 1.6)
Anxiety	1 (0.1)	(0.0, 0.5)	3 (0.3)	(0.1, 0.8)
Depression	0	(0.0, 0.3)	4 (0.4)	(0.1, 0.9)
Attention deficit hyperactivity disorder	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Suicidal ideation	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Panic attack	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Amenorrhoea	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Nasal congestion	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Rhinorrhoea	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Sneezing	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Acne	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)

Table 33. Number (%) of Subjects Reporting at Least 1 New Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term and Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1113)			
	Dose 1 to 1 Month After Dose 2		1 Month After Dose 2 to 6 Months After Dose 2	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Dermatitis contact	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
SURGICAL AND MEDICAL PROCEDURES	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Wisdom teeth removal	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)

Abbreviation: EUA = emergency use authorization.
Note: EUA snapshot 25Mar2021 with the cutoff date 13Mar2021.
Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:45)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s132_6m2_ped6

12.2.3.4.3. New Related Adverse Events After the EUA Snapshot by System Organ Class and Preferred Term – Blinded Placebo-Controlled and Open-Label Follow-Up Periods From Dose 1 to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

There were few new related AEs reported, and most of these events were reactogenicity (Table 34). One (1) participant in the BNT162b2 group reported musculoskeletal chest pain, which is discussed in Section 12.2.1.6.3.

Table 34. Number (%) of Subjects Reporting at Least 1 New Related Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Any event	3 (0.3)	(0.1, 0.8)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (0.1)	(0.0, 0.5)
Chills	1 (0.1)	(0.0, 0.5)
Fatigue	1 (0.1)	(0.0, 0.5)
Injection site pain	1 (0.1)	(0.0, 0.5)
Injection site swelling	1 (0.1)	(0.0, 0.5)
Pyrexia	1 (0.1)	(0.0, 0.5)
INVESTIGATIONS	1 (0.1)	(0.0, 0.5)
SARS-CoV-2 antibody test positive	1 (0.1)	(0.0, 0.5)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (0.1)	(0.0, 0.5)
Musculoskeletal chest pain	1 (0.1)	(0.0, 0.5)

Abbreviation: EUA = emergency use authorization.
Note: EUA snapshot 25Mar2021 with the cutoff date 13Mar2021.
Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:51)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_rel_6m2_ped6

12.2.4. Open-Label Follow-Up Period From Dose 3 to the Data Cutoff Date – Original Placebo Recipients 12 Through 15 Years of Age Who Then Received BNT162b2 After Unblinding

12.2.4.1. Summary of Adverse Events – Open-Label Follow-Up Period – Original Placebo Recipients 12 Through 15 Years of Age Who Then Received BNT162b2 After Unblinding

An overview of AEs for 1,010 original placebo recipients who then were unblinded and received BNT162b2 to the data cutoff date during the open-label follow-up period is presented in Table 35.

The total exposure time is shorter among the original placebo recipients who received BNT162b2 after unblinding than those who originally received BNT162b2 (2.9 per 100 PY vs 4.6 per 100 PY, respectively [Table 35 and Table 18]).

After participants who originally received placebo were unblinded and then received BNT162b2 after unblinding, events related to reactogenicity were not reported using an e-diary but were instead reported as AEs. Because an e-diary was not used after original placebo recipients received open-label BNT162b2, in comparison to participants randomized to BNT162b2 from Dose 1 to the unblinding date, the frequencies for any AE and at least 1 related AE for participants who originally received placebo and then received BNT162b2 are greater (26.2% and 24.0%) than the frequencies (8.4% and 3.2%) for participants who originally received BNT162b2, respectively (Table 35 and Table 18). However, the frequencies for severe, life-threatening AE, SAE, AEs leading to withdrawal and deaths were similar (1.2%, 0%, 0.6%, 0%, 0% [Table 35] versus 1.1%, 0.2%, 0.9%, 0.1%, 0% [Table 18], respectively). There was 1 related SAE of appendicitis for a placebo recipient who was vaccinated with BNT162b2 (see Section 12.3.2.4).

Table 35. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (02SEP2021) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1010, TE[b]=2.9)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])
Any event	265 (26.2)	90.3	(79.7, 101.8)
Related[f]	242 (24.0)	82.5	(72.4, 93.5)
Severe	12 (1.2)	4.1	(2.1, 7.1)
Life-threatening	0	0.0	(0.0, 1.3)
Any serious adverse event	6 (0.6)	2.0	(0.8, 4.4)

Table 35. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (02SEP2021) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1010, TE[b]=2.9)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])
Related[f]	1 (0.1)	0.3	(0.0, 1.9)
Severe	3 (0.3)	1.0	(0.2, 3.0)
Life-threatening	0	0.0	(0.0, 1.3)
Any nonserious adverse event	262 (25.9)	89.3	(78.8, 100.8)
Related[f]	241 (23.9)	82.1	(72.1, 93.2)
Severe	9 (0.9)	3.1	(1.4, 5.8)
Life-threatening	0	0.0	(0.0, 1.3)
Any adverse event leading to withdrawal	0	0.0	(0.0, 1.3)
Related[f]	0	0.0	(0.0, 1.3)
Severe	0	0.0	(0.0, 1.3)
Life-threatening	0	0.0	(0.0, 1.3)
Death	0	0.0	(0.0, 1.3)

Note: Dose 3 = First dose of BNT162b2 (30 µg).
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 3 to data cutoff date. 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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s092_cut1_ped6

12.2.4.2. Adverse Events by System Organ Class and Preferred Term – Open-Label Follow-Up Period – Original Placebo Recipients Who Then Received BNT162b2 After Unblinding – Participants 12 Through 15 Years of Age

From vaccination with BNT162b2 for placebo participants to the data cutoff date (open-label follow-up period), 265 (26.2%) of BNT162b2 participants reported at least 1 AE (Table 36).

Most AEs reported from Dose 3 (first dose of BNT162b2) to the data cutoff date were in SOCs with reactogenicity events.

- general disorders and administration site conditions (225 [22.3%])
- nervous system disorders (75 [7.4%])
- musculoskeletal and connective tissue disorders (48 [4.8%])
- gastrointestinal disorders (20 [2.0%])

As shown in Table 36, the most frequently reported AEs overall were injection site pain (15.5%), fatigue (10.3%), headache (7.0%), pyrexia (6.3%), chills (4.5%), myalgia (3.8%), pain (3.5%), nausea (1.2%), pain in extremity (0.9%), vomiting (0.7%), malaise (0.7%), and injection site erythema (0.5%).

Table 36. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1010, TE[b]=2.9)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Any event	265 (26.2)	90.3	(79.7, 101.8)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	2 (0.2)	0.7	(0.1, 2.5)
Lymphadenitis	1 (0.1)	0.3	(0.0, 1.9)
Lymphadenopathy	1 (0.1)	0.3	(0.0, 1.9)
CARDIAC DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Myocarditis	1 (0.1)	0.3	(0.0, 1.9)
EAR AND LABYRINTH DISORDERS	2 (0.2)	0.7	(0.1, 2.5)
Ear pain	1 (0.1)	0.3	(0.0, 1.9)
Motion sickness	1 (0.1)	0.3	(0.0, 1.9)
ENDOCRINE DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Autoimmune thyroiditis	1 (0.1)	0.3	(0.0, 1.9)
Thyroid mass	1 (0.1)	0.3	(0.0, 1.9)
GASTROINTESTINAL DISORDERS	20 (2.0)	6.8	(4.2, 10.5)
Abdominal pain upper	2 (0.2)	0.7	(0.1, 2.5)
Diarrhoea	1 (0.1)	0.3	(0.0, 1.9)
Nausea	12 (1.2)	4.1	(2.1, 7.1)
Tooth impacted	1 (0.1)	0.3	(0.0, 1.9)
Vomiting	7 (0.7)	2.4	(1.0, 4.9)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	225 (22.3)	76.7	(67.0, 87.4)
Adverse drug reaction	1 (0.1)	0.3	(0.0, 1.9)

Table 36. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1010, TE[b]=2.9)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Axillary pain	1 (0.1)	0.3	(0.0, 1.9)
Chest discomfort	1 (0.1)	0.3	(0.0, 1.9)
Chest pain	1 (0.1)	0.3	(0.0, 1.9)
Chills	45 (4.5)	15.3	(11.2, 20.5)
Fatigue	104 (10.3)	35.4	(29.0, 42.9)
Injection site bruising	3 (0.3)	1.0	(0.2, 3.0)
Injection site erythema	5 (0.5)	1.7	(0.6, 4.0)
Injection site hypoaesthesia	1 (0.1)	0.3	(0.0, 1.9)
Injection site pain	157 (15.5)	53.5	(45.5, 62.5)
Injection site reaction	1 (0.1)	0.3	(0.0, 1.9)
Injection site swelling	4 (0.4)	1.4	(0.4, 3.5)
Malaise	7 (0.7)	2.4	(1.0, 4.9)
Non-cardiac chest pain	1 (0.1)	0.3	(0.0, 1.9)
Pain	35 (3.5)	11.9	(8.3, 16.6)
Pyrexia	64 (6.3)	21.8	(16.8, 27.8)
Thirst	1 (0.1)	0.3	(0.0, 1.9)
IMMUNE SYSTEM DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Food allergy	1 (0.1)	0.3	(0.0, 1.9)
INFECTIONS AND INFESTATIONS	12 (1.2)	4.1	(2.1, 7.1)
Appendicitis	1 (0.1)	0.3	(0.0, 1.9)
Cellulitis	1 (0.1)	0.3	(0.0, 1.9)
Ear infection	2 (0.2)	0.7	(0.1, 2.5)
Hand-foot-and-mouth disease	1 (0.1)	0.3	(0.0, 1.9)
Herpes zoster	1 (0.1)	0.3	(0.0, 1.9)
Otitis externa	1 (0.1)	0.3	(0.0, 1.9)
Otitis media	1 (0.1)	0.3	(0.0, 1.9)
Paronychia	1 (0.1)	0.3	(0.0, 1.9)
Pharyngitis streptococcal	1 (0.1)	0.3	(0.0, 1.9)
Sinusitis	1 (0.1)	0.3	(0.0, 1.9)
Skin candida	1 (0.1)	0.3	(0.0, 1.9)
Tinea infection	1 (0.1)	0.3	(0.0, 1.9)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	11 (1.1)	3.7	(1.9, 6.7)

Table 36. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1010, TE[b]=2.9)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Arthropod bite	1 (0.1)	0.3	(0.0, 1.9)
Concussion	1 (0.1)	0.3	(0.0, 1.9)
Facial bones fracture	1 (0.1)	0.3	(0.0, 1.9)
Hand fracture	1 (0.1)	0.3	(0.0, 1.9)
Hyphaema	1 (0.1)	0.3	(0.0, 1.9)
Joint injury	1 (0.1)	0.3	(0.0, 1.9)
Ligament rupture	1 (0.1)	0.3	(0.0, 1.9)
Ligament sprain	1 (0.1)	0.3	(0.0, 1.9)
Meniscus injury	1 (0.1)	0.3	(0.0, 1.9)
Muscle strain	1 (0.1)	0.3	(0.0, 1.9)
Sports injury	1 (0.1)	0.3	(0.0, 1.9)
Sunburn	1 (0.1)	0.3	(0.0, 1.9)
Traumatic renal injury	1 (0.1)	0.3	(0.0, 1.9)
Wound	1 (0.1)	0.3	(0.0, 1.9)
INVESTIGATIONS	3 (0.3)	1.0	(0.2, 3.0)
Body temperature increased	3 (0.3)	1.0	(0.2, 3.0)
METABOLISM AND NUTRITION DISORDERS	3 (0.3)	1.0	(0.2, 3.0)
Decreased appetite	1 (0.1)	0.3	(0.0, 1.9)
Glucose tolerance impaired	1 (0.1)	0.3	(0.0, 1.9)
Vitamin D deficiency	2 (0.2)	0.7	(0.1, 2.5)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	48 (4.8)	16.4	(12.1, 21.7)
Arthralgia	2 (0.2)	0.7	(0.1, 2.5)
Musculoskeletal chest pain	1 (0.1)	0.3	(0.0, 1.9)
Musculoskeletal stiffness	1 (0.1)	0.3	(0.0, 1.9)
Myalgia	38 (3.8)	12.9	(9.2, 17.8)
Neck pain	1 (0.1)	0.3	(0.0, 1.9)
Pain in extremity	9 (0.9)	3.1	(1.4, 5.8)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (0.1)	0.3	(0.0, 1.9)
Skin papilloma	1 (0.1)	0.3	(0.0, 1.9)
NERVOUS SYSTEM DISORDERS	75 (7.4)	25.6	(20.1, 32.0)
Dizziness	4 (0.4)	1.4	(0.4, 3.5)

Table 36. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1010, TE[b]=2.9)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Epilepsy	1 (0.1)	0.3	(0.0, 1.9)
Headache	71 (7.0)	24.2	(18.9, 30.5)
Somnolence	1 (0.1)	0.3	(0.0, 1.9)
Syncope	1 (0.1)	0.3	(0.0, 1.9)
PSYCHIATRIC DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Major depression	1 (0.1)	0.3	(0.0, 1.9)
RENAL AND URINARY DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Dysuria	1 (0.1)	0.3	(0.0, 1.9)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	3 (0.3)	1.0	(0.2, 3.0)
Cough	1 (0.1)	0.3	(0.0, 1.9)
Nasal congestion	1 (0.1)	0.3	(0.0, 1.9)
Rhinorrhoea	1 (0.1)	0.3	(0.0, 1.9)
Upper-airway cough syndrome	1 (0.1)	0.3	(0.0, 1.9)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	5 (0.5)	1.7	(0.6, 4.0)
Hyperhidrosis	1 (0.1)	0.3	(0.0, 1.9)
Ingrowing nail	2 (0.2)	0.7	(0.1, 2.5)
Photosensitivity reaction	1 (0.1)	0.3	(0.0, 1.9)
Urticaria	1 (0.1)	0.3	(0.0, 1.9)

Note: Dose 3 = First dose of BNT162b2 (30 µg).
Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 3 to data cutoff date. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_cut1_ped6

An analysis was conducted to evaluate if the imbalance in AEs (higher frequencies of some PTs relative to others) observed from Dose 3 to the data cutoff date was attributed to reactogenicity events. The analysis examined the AEs reported within 7 days after each dose (Dose 3 and Dose 4 [first and second dose of BNT162b2 30 µg]), which represented the reactogenicity reporting period.

PTs reported from Dose 3 to 7 days after Dose 3 and from Dose 4 to 7 days after Dose 4 in the SOCs of general disorders and administration site conditions (injection site pain, fatigue, chills, pyrexia, and pain), nervous system disorders (headache), musculoskeletal and connective tissue disorders (myalgia), and gastrointestinal disorders (nausea) represented the majority of PTs reported in those SOCs (Supplemental Tables 14.39 and 14.40).

An SAE of myocarditis was reported in 1 participant within 7 days after Dose 4 (Supplemental Table 14.40 and Appendix 16.2.7.2.1) (previously reported to CBER and discussed by the ACIP). Full details are disussed in Section 12.3.4.1.

In addition to analysis of AEs corresponding to e-diary terms, consideration was given to additional AEs that were reported within 7 days after Dose 3 or Dose 4 such as but not limited to pain in extremity, decreased appetite, malaise, and hyperhidrosis. Similar to the analysis that examined these events 7 days within Dose 1 and Dose 2 of BNT162b2 in blinded placebo-controlled follow-up (adolescent interim CSR, dated 14 April 2021, Section 12.3.2.1.1.1), these events reported in open-label follow-up are interpreted as largely attributable to the experience of local reactions and systemic events after vaccination with Dose 3 and Dose 4 (first and second dose of BNT162b2).

12.2.4.3. Related Adverse Events by System Organ Class and Preferred Term – Open-Label Follow-Up Period – Original Placebo Recipients Who Then Received BNT162b2 – Participants 12 Through 15 Years of Age

From vaccination with BNT162b2 to the data cutoff date (open-label follow-up period) for original placebo recipients who then received BNT162b2 after unblinding, 242 (24.0%) experienced AEs that were assessed as related by the investigator (Supplemental Table 14.41). Related AEs were highest for reactogenicity events and in the SOC of general disorders and administration site conditions (223 [22.1%]) for the following PTs:

- injection site pain (157 [15.5%])
- fatigue (104 [10.3%])
- pyrexia (63 [6.2%])
- chills (45 [4.5%])

Frequently reported related AEs also included PTs of headache 70 (6.9%) and myalgia 37 (3.7%).

Related events of lymphadenitis and appendicitis were reported in 1 participant each:

- One participant experienced a nonserious adverse event of lymphadenitis (right axillary adenitis) on Day 6 after Dose 3. It was moderate in severity, lasted for 24 days, and then resolved (Appendix 16.2.7.2.1).

- See Section 12.3.2.4 for details on related SAE of appendicitis.

12.2.4.4. Immediate Adverse Events – Open-Label Follow-Up Period – Original Placebo Recipients Who Then Received BNT162b2 – Participants 12 Through 15 Years of Age

After vaccination with BNT162b2 (Dose 3/4), 7 (0.7%) placebo adolescent recipients who received BNT162b2 after unblinding reported immediate AEs. Most AEs reported were injection site pain for 6 (0.6%) participants, and 1 (0.1%) participant reported injection site erythema (Supplemental Table 14.42).

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

12.2.4.5. Severe or Life-Threatening Adverse Events – Open-Label Follow-Up Period – Original Placebo Recipients Who Then Received BNT162b2 – Participants 12 Through 15 Years of Age

From vaccination with BNT162b2 to the data cutoff date (open-label follow-up period) for original placebo recipients who then received BNT162b2 after unblinding, 12 (1.2%) reported severe AEs (Supplemental Table 14.43). Three (3) participants reported pyrexia, 2 reported fatigue, and 1 reported malaise (all PTs in the general disorders and administration site conditions SOC), and 1 participant reported myalgia (musculoskeletal and connective tissue disorders SOC), all of which are terms that are consistent with reactogenicity.

One participant experienced a severe SAE of myocarditis (see Section 12.3.2.4).

There were no life-threatening AEs reported from vaccination with BNT162b2 to the data cutoff date (Table 35).

12.3. Deaths, Serious Adverse Events, Safety-Related Participant Withdrawals, and Other Significant Adverse Events – Participants 12 Through 15 Years of Age

12.3.1. Deaths

There were no deaths reported for adolescent participants as of the data cutoff date (02 September 2021) (Appendix 16.2.7.7).

12.3.2. Serious Adverse Events – Participants 12 Through 15 Years of Age

12.3.2.1. Blinded Placebo-Controlled Follow-Up From Dose 1 to the Unblinding Date - Participants 12 Through 15 Years of Age

From Dose 1 to the unblinding date, there were 10 (0.9%) and 2 (0.2%) adolescent participants who reported at least 1 SAE in the BNT162b2 and placebo groups, respectively

(Table 37). All SAEs were assessed by the investigator as not related to study intervention (Table 18).

Certain SAEs discussed below (Appendix 16.2.7.2.1) were previously reported in the adolescent interim CSR, dated 14 April 2021:

- One participant in the placebo group reported a life-threatening (Grade 4) SAE each of focal peritonitis and appendicitis concurrently on Day 19 after Dose 2 with a duration of 2 days, and the event was assessed by the investigator as not related to study intervention. Both events were resolved, and the participant continued in the study.
- PPD
- PPD
-

Table 37. Incidence Rates of at Least 1 Serious Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	10 (0.9)	2.2	(1.0, 4.0)	2 (0.2)	0.4	(0.1, 1.6)
GASTROINTESTINAL DISORDERS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Abdominal pain	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Constipation	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
INFECTIONS AND INFESTATIONS	1 (0.1)	0.2	(0.0, 1.2)	2 (0.2)	0.4	(0.1, 1.6)
Anal abscess	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Appendicitis	0	0.0	(0.0, 0.8)	2 (0.2)	0.4	(0.1, 1.6)
Focal peritonitis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Femur fracture	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
PSYCHIATRIC DISORDERS	8 (0.7)	1.7	(0.8, 3.4)	0	0.0	(0.0, 0.8)
Anxiety	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Conversion disorder	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Depression	3 (0.3)	0.7	(0.1, 1.9)	0	0.0	(0.0, 0.8)
Suicidal ideation	4 (0.4)	0.9	(0.2, 2.2)	0	0.0	(0.0, 0.8)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sae_unb1_ped6

12.3.2.1.1. Subgroup Analyses

There were 10 (0.9%) and 2 (0.2%) adolescent participants who reported at least 1 SAE in the BNT162b2 and placebo groups, respectively (Table 37). Overall, no clinically meaningful differences in frequencies of SAEs were observed by baseline SARS-CoV-2

status, ethnicity, race, or sex subgroups. IRs and frequencies of at least 1 SAE from Dose 1 to the unblinding date by SOC and PT and by subgroup are presented in the following tables:

Baseline SARS-CoV-2 Status: Negative	Supplemental Table 14.44
Ethnicity: Hispanic/Latino	Supplemental Table 14.45
Ethnicity: Non-Hispanic/Non-Latino	Supplemental Table 14.46
Race: White	Supplemental Table 14.47
Race: Black or African American	Supplemental Table 14.48
Race: All Others	Supplemental Table 14.49
Sex: Male	Supplemental Table 14.50
Sex: Female	Supplemental Table 14.51

12.3.2.1.2. New Serious Adverse Events After the EUA Snapshot

There were 6 (0.5%) adolescent participants in the BNT162b2 group who reported an SAE after the EUA snapshot, and none were reported in the placebo group (Table 38).

Certain SAEs are discussed below (Appendix 16.2.7.4):

PPD

PPD

One participant in the BNT162b2 group reported a severe SAE of anal abscess on Day 78 after Dose 2, and the event was recovering/resolving as of the data cutoff date.

Overall, all SAEs occurred long after vaccination.

Table 38. Number (%) of Subjects Reporting at Least 1 New Serious Adverse Event After the EUA Snapshot, From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	6 (0.5)	(0.2, 1.2)	0	(0.0, 0.3)
INFECTIONS AND INFESTATIONS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Anal abscess	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Femur fracture	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
PSYCHIATRIC DISORDERS	4 (0.4)	(0.1, 0.9)	0	(0.0, 0.3)
Suicidal ideation	3 (0.3)	(0.1, 0.8)	0	(0.0, 0.3)
Depression	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)

Abbreviation: EUA = emergency use authorization.
Note: MedDRA (v24.0) 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, subjects who withdrew from the study before EUA snapshot 25Mar2021 with the cutoff date 13Mar2021 are not included. 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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:47)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_sae_unb2_ped6

12.3.2.2. Open-Label Follow-Up Period – Original BNT162b2 Recipients 12 Through 15 Years of Age

From unblinding date to the data cutoff date, 4 (0.4%) original BNT162b2 adolescent participants experienced at least 1 SAE (Supplemental Table 14.52). Of these, 2 participants experienced appendicitis long after vaccination from Dose 2 (Day 148 and Day 177) (infections and infestations SOC); both events were assessed by the investigator as not related (Appendix 16.2.7.4).

12.3.2.3. Blinded Placebo-Controlled and Open-Label Follow-Up Periods From Dose 1 to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

From Dose 1 to 6 months after Dose 2, during the blinded placebo-controlled and open-label follow-up periods, 10 (0.9%) adolescent participants who originally received BNT162b2 reported at least 1 SAE (Table 39).

Comparison of SAEs reported from Dose 1 to 1 month after Dose 2 to SAEs reported from 1 month after Dose 2 to 6 months after Dose 2 shows that the frequency of SAEs was 0.3% and 0.8%, respectively (Table 40). The frequency of SAEs reported in the psychiatric disorders SOC was similar from Dose 1 to 1 month after Dose 2 versus 1 month after Dose 2 to 6 months after Dose 2.

Table 39. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Any event	10 (0.9)	(0.4, 1.6)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (0.1)	(0.0, 0.5)
Syringomyelia	1 (0.1)	(0.0, 0.5)
GASTROINTESTINAL DISORDERS	1 (0.1)	(0.0, 0.5)
Abdominal pain	1 (0.1)	(0.0, 0.5)
Constipation	1 (0.1)	(0.0, 0.5)
INFECTIONS AND INFESTATIONS	2 (0.2)	(0.0, 0.6)
Anal abscess	1 (0.1)	(0.0, 0.5)

Table 39. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Appendicitis	1 (0.1)	(0.0, 0.5)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.1)	(0.0, 0.5)
Femur fracture	1 (0.1)	(0.0, 0.5)
PSYCHIATRIC DISORDERS	6 (0.5)	(0.2, 1.2)
Suicidal ideation	3 (0.3)	(0.1, 0.8)
Depression	2 (0.2)	(0.0, 0.6)
Conversion disorder	1 (0.1)	(0.0, 0.5)

Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_ser_6m1_ped6

Table 40. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term and Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (Na=1113)			
	Dose 1 to 1 Month After Dose 2		1 Month After Dose 2 to 6 Months After Dose 2	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	3 (0.3)	(0.1, 0.8)	9 (0.8)	(0.4, 1.5)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Syringomyelia	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
GASTROINTESTINAL DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Abdominal pain	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Constipation	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
INFECTIONS AND INFESTATIONS	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Anal abscess	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Appendicitis	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Femur fracture	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
PSYCHIATRIC DISORDERS	3 (0.3)	(0.1, 0.8)	4 (0.4)	(0.1, 0.9)
Suicidal ideation	0	(0.0, 0.3)	3 (0.3)	(0.1, 0.8)
Depression	2 (0.2)	(0.0, 0.6)	1 (0.1)	(0.0, 0.5)
Conversion disorder	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)

Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:22)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s132_ser_6m1_ped6

12.3.2.3.1. New Serious Adverse Events After the EUA Snapshot

For original BNT162b2 adolescent recipients with at least 6 months of follow-up time after Dose 2, there were 7 (0.6%) new SAEs reported after the EUA snapshot (Table 41), and all

of the SAEs were reported from 1 month after Dose 2 to 6 months after Dose 2 (Table 42; also discussed in Section 12.2.3.4.1).

Table 41. Number (%) of Subjects Reporting at Least 1 New Serious Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Any event	7 (0.6)	(0.3, 1.3)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (0.1)	(0.0, 0.5)
Syringomyelia	1 (0.1)	(0.0, 0.5)
INFECTIONS AND INFESTATIONS	2 (0.2)	(0.0, 0.6)
Anal abscess	1 (0.1)	(0.0, 0.5)
Appendicitis	1 (0.1)	(0.0, 0.5)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.1)	(0.0, 0.5)
Femur fracture	1 (0.1)	(0.0, 0.5)
PSYCHIATRIC DISORDERS	3 (0.3)	(0.1, 0.8)
Suicidal ideation	2 (0.2)	(0.0, 0.6)
Depression	1 (0.1)	(0.0, 0.5)

Abbreviation: EUA = emergency use authorization.
Note: EUA snapshot 25Mar2021 with the cutoff date 13Mar2021.
Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:50)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_ser_6m2_ped6

Table 42. Number (%) of Subjects Reporting at Least 1 New Serious Adverse Event After the EUA Snapshot, From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term and Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (Na=1113)			
	Dose 1 to 1 Month After Dose 2		1 Month After Dose 2 to 6 Months After Dose 2	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	0	(0.0, 0.3)	7 (0.6)	(0.3, 1.3)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Syringomyelia	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
INFECTIONS AND INFESTATIONS	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Anal abscess	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Appendicitis	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Femur fracture	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
PSYCHIATRIC DISORDERS	0	(0.0, 0.3)	3 (0.3)	(0.1, 0.8)
Suicidal ideation	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Depression	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)

Abbreviation: EUA = emergency use authorization.
Note: EUA snapshot 25Mar2021 with the cutoff date 13Mar2021.
Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:46)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s132_ser_6m2_ped6

12.3.2.4. Open-Label Follow-Up Period – Original Placebo Recipients Who Then Received BNT162b2 After Unblinding

From Dose 3 (first dose of BNT162b2) to the data cutoff date, 6 (0.6%) adolescent participants who originally received placebo then received BNT162b2 after unblinding

reported at least 1 SAE (Table 43). Narratives for participants with reported SAEs are located in Section 14 Narratives.

1 SAE, appendicitis, was assessed by the investigator as related to study intervention (Appendix 16.2.7.4). The event of appendicitis occurred in a 13-year-old PPD (aged 13 years when initially enrolled) on Day 4 after Dose 4 (second dose of BNT162b2), an ultrasound performed in the hospital confirmed the diagnosis, as did macroscopic inspection of the appendix during surgery and the pathology report received post appendectomy. The event lasted for 1 day, as the participant underwent surgery and was considered resolved post surgery.

1 SAE, epilepsy, was assessed by the investigator as not related to study intervention (Appendix 16.2.7.4). This event occurred in a 13-year-old PPD on Day 8 after Dose 4, there was no past medical history of febrile seizures in early childhood, however, there was a positive family history of PPD. The diagnosis of epilepsy was confirmed by electroencephalogram, the participant was not prescribed any medication and remains on neurology follow-up. There have been no further seizures upon continued follow-up with the participant.

An SAE of myocarditis was reported in a 13-year-old PPD participant who experienced chest pain on Day 3 after Dose 2 of BNT162b2 (previously reported to CBER and discussed by ACIP). Full details are discussed in Section 12.3.4.1.

Table 43. Incidence Rates of at Least 1 Serious Adverse Event From Dose 3 to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1010, TE[b]=2.9)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Any event	6 (0.6)	2.0	(0.8, 4.4)
CARDIAC DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Myocarditis	1 (0.1)	0.3	(0.0, 1.9)
INFECTIONS AND INFESTATIONS	1 (0.1)	0.3	(0.0, 1.9)
Appendicitis	1 (0.1)	0.3	(0.0, 1.9)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.1)	0.3	(0.0, 1.9)
Traumatic renal injury	1 (0.1)	0.3	(0.0, 1.9)
NERVOUS SYSTEM DISORDERS	2 (0.2)	0.7	(0.1, 2.5)

Table 43. Incidence Rates of at Least 1 Serious Adverse Event From Dose 3 to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1010, TE[b]=2.9)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Epilepsy	1 (0.1)	0.3	(0.0, 1.9)
Somnolence	1 (0.1)	0.3	(0.0, 1.9)
PSYCHIATRIC DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Major depression	1 (0.1)	0.3	(0.0, 1.9)

Note: Dose 3 = First dose of BNT162b2 (30 µg).
Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 3 to data cutoff date. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_ser_cut1_ped6

12.3.3. Safety-Related Participant Withdrawals

12.3.3.1. Blinded Placebo-Controlled Follow-Up From Dose 1 to the Unblinding Date - Participants 12 Through 15 Years of Age

From Dose 1 to the unblinding date, 1 (0.1%) participant in the BNT162b2 group had an AE of pyrexia leading to withdrawal that was assessed by the investigator as related to study intervention (previously reported in Section 12.3.2.4.1 of the adolescent interim CSR dated 14 April 2021; Supplemental Table 14.53).

12.3.3.2. Open-Label Follow-Up Period – Original BNT162b2 Recipients 12 Through 15 Years of Age

From the unblinding date to the data cutoff date, there were no original BNT162b2 adolescent participants who were withdrawn because of AEs (Table 25).

12.3.3.3. Blinded Placebo-Controlled Follow-Up Period From Dose 1 to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

From Dose 1 to 6 months after Dose 2 during the blinded placebo-controlled and open-label follow-up periods, there were no adolescent participants with at least 6 months of follow-up time after Dose 2 who were withdrawn because of AEs (Table 26).

12.3.3.4. Open-Label Follow-Up Period – Original Placebo Recipients 12 Through 15 Years of Age Who Then Received BNT162b2 After Unblinding

From Dose 3 (first dose of BNT162b2 30 µg) administration to the data cutoff date, there were no original placebo adolescent participants who were withdrawn because of AEs (Table 35).

12.3.4. Other Significant Adverse Events

AEs of clinical interest include AESIs, such as those in the CDC list of AESIs for COVID-19 that include events potentially indicative of severe COVID-19 or autoimmune and neuroinflammatory disorders, were considered, in addition to program-defined TMEs, in the review of reported events for the adolescent group. Narratives were prepared for such events reported in adolescents (12-15 years of age). AEs of clinical interest occurring in the adolescent group were reviewed for the blinded placebo-controlled period.

12.3.4.1. FDA-Requested Adverse Events of Clinical Interest

No cases of anaphylaxis, hypersensitivity, Bell's palsy, or vaccine-related appendicitis were reported as of the data cutoff date (02 September 2021) during the blinded placebo-controlled period. Other events that were reported in the safety database are summarized below.

Lymphadenopathy

Lymphadenopathy is identified as an adverse reaction for BNT162b2 vaccine.

During the blinded placebo-controlled follow-up period, 9 and 2 participants in the BNT162b2 and placebo groups reported AEs of lymphadenopathy, respectively (Table 44). All events were mild or moderate in severity (only 1 moderate AE in the BNT162b2 group). The majority of these events occurred in the arm and neck region. Median onset was 8.0 days (after Dose 1 but before Dose 2) and 3.0 days (after Dose 2) in the BNT162b2 group and none (after Dose 1 but before Dose 2) and 12.5 days (after Dose 2) in the placebo group. The events resolved with median duration of 6.0 days in the BNT162b2 group and 25.5 days in the placebo group.

Table 44. Subjects Reporting an Adverse Event of Lymphadenopathy – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=9) n[b] (%)	Placebo (N[a]=2) n[b] (%)
Severity		
Mild	8 (88.9)	2 (100.0)
Moderate	1 (11.1)	0
Severe	0	0
Life-threatening	0	0
Onset day after Dose 1 and before Dose 2		
n	5	0
Mean (SD)	8.2 (2.28)	NE (NE)
Median	8.0	NE
Min, max	6 - 12	NE - NE
Onset day after Dose 2		
n	4	2
Mean (SD)	9.0 (12.70)	12.5 (3.54)
Median	3.0	12.5
Min, max	2 - 28	10 - 15
Duration (days)		
n	8	2
Mean (SD)	10.8 (11.03)	25.5 (24.75)
Median	6.0	25.5
Min, max	1 - 29	8 - 43
Unknown[c]	1	0

Abbreviation: NE = not estimable.
Note: For each event, the worst severity, earliest onset, and longest duration will be counted.
a. N = number of subjects reporting lymphadenopathy. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the event.
c. Includes those events where the resolution date is partial or missing.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (21:24)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_lym_unb_1

Appendicitis

During the blinded placebo-controlled follow-up period, 2 participants in the placebo group each had an SAE of appendicitis, and both events were assessed by the investigator as not related to study intervention (Appendix 16.2.7.4).

During the open-label follow-up period:

- Two original BNT162b2 recipients each had an SAE of appendicitis long after vaccination from Dose 2 (Day 148 and Day 177), and both events were assessed by the investigator as not related to study intervention (discussed in Section 12.3.2.2).

- One original placebo recipient had an SAE of appendicitis that was assessed by the investigator as related to study intervention (discussed in Section 12.3.2.4).

Myocarditis/pericarditis

One original placebo participant 13 years of age had an SAE of myocarditis on Day 3 after Dose 2 of BNT162b2 (previously reported to CBER and discussed by ACIP). The participant had been participating in a dance class prior to reporting the symptom and attended the ER the same evening where PPD was hospitalized for further investigation and treatment. EKG performed and reviewed by a cardiologist showed diffuse ST elevations, and troponin levels were elevated on serial measurements throughout the admission, (maximum measurement was 0.71 ng/mL [normal range 0 to <0.01 ng/mL]). The chest pain was considered by the investigator to be most likely due to an ongoing viral infection, which could have caused myopericarditis. This conclusion was based on the participant's recent history (one week previously) of a temperature of 100.5°F associated with cough and rhinorrhea, and clinical symptoms at the time of the event (temperature 100.1°F; rhinovirus PCR was positive on a respiratory virus panel, but negative for enterovirus and parvovirus B19, SARS-CoV-2 RNA PCR was negative). The chest pain resolved within 24 hours upon receiving PPD and the participant was discharged home after 2 days hospitalization and treatment. Further continuing cardiology follow-up of this participant confirmed that the condition has resolved, and the participant has resumed gym exercises. The investigator considered the event was not related to study intervention. However, Pfizer considers that there is a reasonable possibility that this event is related to the administration of BNT162b2, considering the prior reports of myocarditis/pericarditis in recipients of mRNA vaccines in younger individuals.

12.3.4.2. Other Adverse Events of Special Interest

Additional AEs of clinical interest, including those on the CDC AESI list, were evaluated based on sponsor agent safety data review. These AEs were identified from the C4591001 study database as of the data cutoff date (02 September 2021). From this analysis, notable pertinent negatives (ie, no cases reported in this population as of the data cutoff for this submission) with regard to the CDC list of AESIs included (but were not limited to): thromboembolic or intravascular coagulation events, autoimmune or demyelination events, meningitis, encephalitis, optic neuritis, Kawasaki disease, MIS-C, or acute respiratory distress syndrome.

An analysis of AEs of clinical interest for potential numerical imbalance (based on risk difference >0) between BNT162b2 and placebo SOC and PT as shown in Table 45, with most PTs showing no numerical difference between the BNT162b2 and placebo groups. SOCs which did include PTs more frequently reported after BNT162b2 compared to placebo, or otherwise considered of particular clinical interest, are summarized below.

Table 45. Incidence Rates of at Least 1 Adverse Event of Special Interest From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)							
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)			Difference	
System Organ Class Preferred Term	n[c]	IR[d]	(95% CI[e])	n[c]	IR[d]	(95% CI[e])	IRD[f]	(95% CI[g])
EYE DISORDERS								
Retinal haemorrhage	0	0.0	(0.0, 0.8)	1	0.2	(0.0, 1.2)	-0.22	(-0.66, 0.21)
GASTROINTESTINAL DISORDERS								
Lip swelling	1	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)	0.22	(-0.21, 0.65)
Mouth swelling	1	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)	0.22	(-0.21, 0.65)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS								
Pyrexia	6	1.3	(0.5, 2.9)	0	0.0	(0.0, 0.8)	1.31	(0.26, 2.36)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS								
Bone contusion	1	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)	0.22	(-0.21, 0.65)
Contusion	2	0.4	(0.1, 1.6)	2	0.4	(0.1, 1.6)	-0.01	(-0.87, 0.86)
INVESTIGATIONS								
SARS-CoV-2 antibody test positive	1	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)	0.22	(-0.21, 0.65)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS								
Arthralgia	2	0.4	(0.1, 1.6)	4	0.9	(0.2, 2.3)	-0.45	(-1.51, 0.61)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS								
Epistaxis	0	0.0	(0.0, 0.8)	1	0.2	(0.0, 1.2)	-0.22	(-0.66, 0.21)
Sneezing	1	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)	0.22	(-0.21, 0.65)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS								
Rash	3	0.7	(0.1, 1.9)	5	1.1	(0.4, 2.6)	-0.45	(-1.68, 0.77)
Urticaria	2	0.4	(0.1, 1.6)	5	1.1	(0.4, 2.6)	-0.67	(-1.82, 0.47)

Table 45. Incidence Rates of at Least 1 Adverse Event of Special Interest From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)							
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.6)			Difference	
System Organ Class Preferred Term	n[c]	IR[d]	(95% CI[e])	n[c]	IR[d]	(95% CI[e])	IRD[f]	(95% CI[g])

Note: MedDRA (v24.0) coding dictionary applied.
Note: The 95% confidence interval quantifies the precision of the incidence rate difference estimate. Confidence intervals are not adjusted for multiplicity. They should only be used to identify potentially important adverse events.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified 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. Difference in incidence rate (BNT162b2 [30 µg] - placebo).
g. 2-sided Wald CI for the incidence rate difference.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:41)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sp_unb1_ped6

General Disorders and Administration Site Conditions

There was a numerical difference for events of pyrexia, which was reported by 6 participants in the BNT162b2 group and none in the placebo group (Table 45). These are recognized as reactogenicity events known to be associated with BNT162b2 vaccination.

Arthralgia

There was no imbalance of arthralgia being reported more frequently in the BNT162b2 group. During the blinded placebo-controlled follow-up period, 2 participants (1 moderate and 1 severe) and 4 participants (2 mild and 2 moderate) in the BNT162b2 and placebo groups reported AEs of arthralgia, respectively (Table 46).

Table 46. Subjects Reporting an Adverse Event of Arthralgia – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=2) n[b] (%)	Placebo (N[a]=4) n[b] (%)
Severity		
Mild	0	2 (50.0)
Moderate	1 (50.0)	2 (50.0)
Severe	1 (50.0)	0
Life-threatening	0	0
Onset day after Dose 1 and before Dose 2		
n	2	3
Mean (SD)	3.0 (2.83)	9.0 (6.24)
Median	3.0	7.0
Min, max	1 - 5	4 - 16
Onset day after Dose 2		
n	0	1
Mean (SD)	NE (NE)	131.0 (NE)
Median	NE	131.0
Min, max	NE - NE	131 - 131
Duration (days)		
n	2	4
Mean (SD)	13.0 (16.97)	14.5 (15.59)
Median	13.0	9.5
Min, max	1 - 25	3 - 36

Abbreviation: NE = not estimable.
Note: For each event, the worst severity, earliest onset, and longest duration will be counted.
a. N = number of subjects reporting arthralgia. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the event.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 10NOV2021 (15:42)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_arth_unb_1

12.3.4.2.1. New Adverse Events of Special Interest After the EUA Snapshot

New AEs of special interest after the EUA snapshot from Dose 1 to the unblinding date during the blinded placebo-controlled follow-up period are presented in Table 47. New AEs reported in adolescents were similar in the BNT162b2 and placebo groups (0.4% each), and PTs were reported in 1 participant each.

Table 47. Number (%) of Subjects Reporting at Least 1 New Adverse Event of Special Interest After the EUA Snapshot, From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=1130)		Placebo (N[a]=1126)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	4 (0.4)	(0.1, 0.9)	5 (0.4)	(0.1, 1.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Pyrexia	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Bone contusion	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
Contusion	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
INVESTIGATIONS	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
SARS-CoV-2 antibody test positive	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Arthralgia	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1 (0.1)	(0.0, 0.5)	1 (0.1)	(0.0, 0.5)
Epistaxis	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Sneezing	1 (0.1)	(0.0, 0.5)	0	(0.0, 0.3)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	0	(0.0, 0.3)	2 (0.2)	(0.0, 0.6)
Rash	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)
Urticaria	0	(0.0, 0.3)	1 (0.1)	(0.0, 0.5)

Abbreviation: EUA = emergency use authorization.
Note: MedDRA (v24.0) 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, subjects who withdrew from the study before EUA snapshot 25Mar2021 with the cutoff date 13Mar2021 are not included. 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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (09:52)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_sp_unb2_ped6

12.3.5. Other Safety Assessments

12.3.5.1. Severe COVID-19 Illness

No AEs were reported that suggested any potential cases of severe COVID-19 among adolescent participants as of the data cutoff date (02 September 2021) (Appendix 16.2.7.4).

12.3.5.2. Pregnancy

No pregnancies were reported in adolescent participants as of the data cutoff date (02 September 2021) (Appendix 16.2.7.7).

12.3.6. Analysis and Discussion of Deaths, Serious Adverse Events, Safety-Related Participant Withdrawals, and Other Significant Adverse Events – Phase 2/3

Overall, there were no deaths (Appendix 16.2.7.6). There was 1 original placebo recipient who received BNT162b2 after unblinding with an SAE of appendicitis that was assessed by the investigator as related to study intervention (Appendix 16.2.7.4; discussed in Section 12.3.2.4). All other SAEs to date were assessed by the investigator as not related to study intervention. During the blinded placebo-controlled follow-up period, only 1 participant in the BNT162b2 group had an AE of pyrexia leading to withdrawal that was assessed by the investigator as related to study intervention (Appendix 16.2.7.5). There were no other AEs leading to withdrawal during the study.

12.4. Safety Conclusions – Participants 12 Through 15 Years of Age

12.4.1. Blinded Placebo-Controlled Follow-Up Period From Dose 1 to the Unblinding Date – Participants 12 Through 15 Years of Age

- Most AEs from Dose 1 to the unblinding date were mild or moderate in severity. The frequency of adolescent participants with AEs was similar in the BNT162b2 and placebo groups (8.4% and 10.0%, respectively).
- SAEs were low in frequency in the BNT162b2 and placebo groups (0.9% and 0.2%, respectively). All SAEs were assessed by the investigator as not related to study intervention. One participant in the BNT162b2 group was withdrawn because of an AE, and there were no deaths.
- AEs assessed as related to BNT162b2 were reactogenicity events and lymphadenopathy.

12.4.2. New Adverse Events After the EUA Snapshot – Original BNT162b2 Recipients 12 Through 15 Years of Age

- No new safety signals or concerns were for new AEs reported after the EUA snapshot. Most new AEs were mild or moderate in severity. All SAEs were assessed by the investigator as not related to study intervention. There were no new AEs leading to withdrawal, and there were no deaths.

12.4.3. Open-Label Follow-Up Period – Original BNT162b2 Participants 12 Through 15 Years of Age

- Most AEs were mild or moderate in severity. The frequency of adolescent participants with AEs in the BNT162b2 group was 1.6%, which was markedly reduced relative to any AEs reported from Dose 1 to the unblinding date (8.4%).
- There were no related SAEs, no withdrawals because of AEs, and no deaths.
- No new safety signals or concerns were identified with additional follow-up.

12.4.4. Blinded Placebo-Controlled and Open-Label Follow-Up Periods to 6 Months After Dose 2 – Original BNT162b2 Recipients 12 Through 15 Years of Age

For the 1113 adolescent participants with at least 6 months of follow-up time:

- Most AEs were mild or moderate in severity. There were 8.8% of participants with any AEs. AE frequencies overall decreased over time from 1 month after the Dose 2 to 6 months after Dose 2.
- SAEs were reported in 0.9% of adolescent participants; all were assessed by the investigator as not related to study intervention. There were no withdrawals because of AEs, and there were no deaths.
- Overall, BNT162b2 at 30 µg was well tolerated with at least 6 months of follow-up after Dose 2.
- No new safety signals or concerns were identified with additional follow-up.

12.4.5. Open-Label Follow-Up Period – Original Placebo Recipients 12 Through 15 Years of Age Who Then Received BNT162b2

For the 1,010 original placebo recipients who then received BNT162b2 after unblinding:

- Most AEs were mild or moderate in severity. There were 26.2% of participants with any AEs, which was greater than the frequency in original BNT162b2 participants (8.4%), due to reactogenicity events being reported as AE rather than e-diary after original placebo recipients received BNT162b2.
- AEs after receipt of BNT162b2 in placebo participants were mostly reactogenicity events.
- There were no withdrawals because of AEs, and there were no deaths.

13. DISCUSSION AND OVERALL CONCLUSIONS

13.1. Discussion – Participants 12 Through 15 Years of Age

In this report, safety data are evaluated from approximately 2200 participants 12-15 years of age, including those with at least 6 months of follow-up after Dose 2 for participants

originally randomized to BNT162b2, comprising the combined blinded and open-label periods.

The long-term AE profile among adolescents reflects age-appropriate events consistent with the general population, with low incidences of severe and/or related events. Lymphadenopathy has been identified as related to BNT162b2 in study participants ≥16 years of age and is also identified as related to BNT162b2 in adolescents. The incidence of SAEs in adolescents was low and similar between the vaccine and placebo groups. Most SAEs, including all SAEs in the psychiatric disorders SOCs, were assessed by the investigator as not related to study intervention. One (1) participant reported an SAE of myocarditis (previously reported to CBER), which was assessed by the investigator as not related to study intervention (Pfizer assessed event as related to study intervention). Refer to Section 12.2.3.4 for additional case details, and refer to Section 2.5.6 of the CO (Module 2.5 Clinical Overview) for the benefit-risk assessment of myocarditis. Only 1 participant was withdrawn from the study because of an AE. No deaths occurred in the adolescent group. Review of AEs, SAEs, and events of clinical interest suggested no clear patterns or additional safety signals or concerns among adolescents.

Similarly, the AE profile of new events after the EUA snapshot were consistent with those observed cumulatively and did not reveal additional safety signals or concerns among adolescents.

As of the safety data cutoff date (02 September 2021), no severe COVID-19 cases were reported in adolescents.

The adolescent interim CSR, dated 14 April 2021, demonstrated that after 2 doses of BNT162b2 30 µg, immune responses in adolescent participants were noninferior to the immune responses in young adults (16-25 years of age), and in fact were statistically greater than that observed in young adults. These data provide reassurance that the vaccine will provide a robust immune response to SARS-CoV-2 in the adolescent population.

Previous descriptive efficacy analyses showed observed VE for the evaluable efficacy population was 100% for adolescent participants (reported in the adolescent interim CSR, dated 14 April 2021). Updated descriptive efficacy analyses for adolescents were consistent with prior analyses. During the blinded placebo-controlled follow-up period, median follow-up time for adolescent participants was 4.4 months. Based on confirmed COVID-19 cases reported from at least 7 days after Dose 2 through the data cutoff date (02 September 2021), observed VE was 100.0% (2-sided 95% CI: 86.8%, 100.0%) for individuals without evidence of prior SARS-CoV-2 infection before and during vaccination regimen, and 100.0% (2-sided 95% CI: 87.5%, 100.0%) for individuals with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen. Sequencing data shows that most variants were neither VOI or VOC except for B.1.1.7 (Alpha), which was found in 23.3% of placebo participants.

In the Dose 1 all-available (modified intention-to-treat) population, 3 participants in the BNT162b2 group and 48 participants in the placebo group had COVID-19 cases occurring after Dose 1, for an observed VE of 94.0% (2-sided 95% CI: 81.3%, 98.8%). All 3 cases in

the BNT162b2 group were SARS-CoV-2 negative at baseline, occurred within the period from after Dose 1 up to <11 days after Dose 1 (prior to Dose 2), after which time the VE was 100.0% for BNT162b2. No severe COVID-19 cases were reported in individuals in the 12-15 years of age group, based on either protocol definition (ie, per FDA criteria) or per CDC criteria for severity.

Taken together, immunogenicity, descriptive efficacy, and available long-term safety data in adolescent participants continue to support the safety, tolerability, and effectiveness of BNT162b2 at 30 µg administered as a 2-dose regimen (21 days apart) to individuals 12 through 15 years of age for the prevention of COVID-19.

13.2. Overall Conclusions – Participants 12 Through 15 Years of Age

- In Phase 2/3, updated descriptive efficacy analysis continues to show that BNT162b2 at 30 µg provided a high level of protection against COVID-19 in participants 12 through 15 years of age with or without evidence of infection with SARS-CoV-2 (100% VE), with no severe cases overall observed in this age group.

- The tolerability and safety profile of BNT162b2 30 µg in participants 12 through 15 years of age at up to 6 months after Dose 2 was acceptable throughout the follow-up period (to the data cutoff date) and consistent with results previously reported.

14. TABLES AND FIGURES

SUPPLEMENTAL TABLES

Conduct of Study

14.1. Demographic Characteristics, by Baseline SARS-CoV-2 Status – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Positive

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=46) n[b] (%)	Placebo (N[a]=50) n[b] (%)	Total (N[a]=96) n[b] (%)
Sex			
Male	21 (45.7)	25 (50.0)	46 (47.9)
Female	25 (54.3)	25 (50.0)	50 (52.1)
Race			
White	39 (84.8)	40 (80.0)	79 (82.3)
Black or African American	6 (13.0)	7 (14.0)	13 (13.5)
All others	1 (2.2)	3 (6.0)	4 (4.2)
American Indian or Alaska Native	0	1 (2.0)	1 (1.0)
Asian	0	1 (2.0)	1 (1.0)
Multiracial	1 (2.2)	0	1 (1.0)
Not reported	0	1 (2.0)	1 (1.0)
Ethnicity			
Hispanic/Latino	7 (15.2)	10 (20.0)	17 (17.7)
Non-Hispanic/non-Latino	39 (84.8)	40 (80.0)	79 (82.3)
Country			
USA	46 (100.0)	50 (100.0)	96 (100.0)
Comorbidities[c]			
Yes	11 (23.9)	12 (24.0)	23 (24.0)
No	35 (76.1)	38 (76.0)	73 (76.0)
Obese[d]			
Yes	6 (13.0)	10 (20.0)	16 (16.7)
No	40 (87.0)	40 (80.0)	80 (83.3)
Age at vaccination (years)			
Mean (SD)	13.5 (1.19)	13.7 (1.07)	13.6 (1.13)
Median	14.0	14.0	14.0
Min, max	(12, 15)	(12, 15)	(12, 15)

14.1. Demographic Characteristics, by Baseline SARS-CoV-2 Status – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Positive

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=46) n[b] (%)	Placebo (N[a]=50) n[b] (%)	Total (N[a]=96) n[b] (%)

Abbreviations: NE = not estimable; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Subjects whose baseline SARS-CoV-2 status cannot be determined because of missing N-binding antibody or NAAT at Visit 1 were not included in the analysis.
Note: Positive = positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
Negative = negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.
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. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥95th percentile.
d. Obese is defined as BMI ≥95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html charts/bmiagerev.htm.
PFIZER CONFIDENTIAL SDTM Creation: 30SEP2021 (10:35) Source Data: adsl Table Generation: 12NOV2021 (15:30)
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14.2. Demographic Characteristics, by Baseline SARS-CoV-2 Status – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Negative

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1083) n[b] (%)	Placebo (N[a]=1078) n[b] (%)	Total (N[a]=2161) n[b] (%)
Sex			
Male	545 (50.3)	560 (51.9)	1105 (51.1)
Female	538 (49.7)	518 (48.1)	1056 (48.9)
Race			
White	929 (85.8)	921 (85.4)	1850 (85.6)
Black or African American	46 (4.2)	50 (4.6)	96 (4.4)
All others	108 (10.0)	107 (9.9)	215 (9.9)
American Indian or Alaska Native	4 (0.4)	2 (0.2)	6 (0.3)
Asian	72 (6.6)	70 (6.5)	142 (6.6)
Native Hawaiian or other Pacific Islander	3 (0.3)	0	3 (0.1)
Multiracial	23 (2.1)	29 (2.7)	52 (2.4)
Not reported	6 (0.6)	6 (0.6)	12 (0.6)
Racial designation			
Japanese	5 (0.5)	2 (0.2)	7 (0.3)
Ethnicity			
Hispanic/Latino	125 (11.5)	120 (11.1)	245 (11.3)
Non-Hispanic/non-Latino	956 (88.3)	955 (88.6)	1911 (88.4)
Not reported	2 (0.2)	3 (0.3)	5 (0.2)
Country			
USA	1083 (100.0)	1078 (100.0)	2161 (100.0)
Comorbidities[c]			
Yes	238 (22.0)	230 (21.3)	468 (21.7)
No	845 (78.0)	848 (78.7)	1693 (78.3)
Obese[d]			
Yes	137 (12.7)	118 (10.9)	255 (11.8)
No	946 (87.3)	960 (89.1)	1906 (88.2)
Age at vaccination (years)			
Mean (SD)	13.6 (1.10)	13.6 (1.11)	13.6 (1.11)
Median	14.0	14.0	14.0
Min, max	(12, 15)	(12, 15)	(12, 15)

14.2. Demographic Characteristics, by Baseline SARS-CoV-2 Status – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Negative

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1083) n[b] (%)	Placebo (N[a]=1078) n[b] (%)	Total (N[a]=2161) n[b] (%)

Abbreviations: NE = not estimable; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Subjects whose baseline SARS-CoV-2 status cannot be determined because of missing N-binding antibody or NAAT at Visit 1 were not included in the analysis.
Note: Positive = positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
Negative = negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.
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. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥95th percentile.
d. Obese is defined as BMI ≥95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html charts/bmiagerev.htm.
PFIZER CONFIDENTIAL SDTM Creation: 30SEP2021 (10:35) Source Data: adsl Table Generation: 12NOV2021 (15:30)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adsl_s005_base1_ped6_saf

14.3. Medical History – Phase 2/3 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] (%)
Any medical history	850 (75.2)	832 (73.7)
Blood and lymphatic system disorders	3 (0.3)	8 (0.7)
Anaemia	0	1 (0.1)
Immune thrombocytopenia	3 (0.3)	1 (0.1)
Iron deficiency anaemia	0	3 (0.3)
Lymphadenopathy	0	2 (0.2)
Thrombocytopenia	0	1 (0.1)
Cardiac disorders	5 (0.4)	3 (0.3)
Aortic valve disease	2 (0.2)	0
Arrhythmia	1 (0.1)	0
Postural orthostatic tachycardia syndrome	1 (0.1)	1 (0.1)
Pulmonary valve stenosis	1 (0.1)	0
Supraventricular tachycardia	0	1 (0.1)
Ventricular extrasystoles	0	1 (0.1)
Congenital, familial and genetic disorders	29 (2.6)	45 (4.0)
Adenomatous polyposis coli	0	1 (0.1)
Ankyloglossia congenital	0	1 (0.1)
Anorectal malformation	0	1 (0.1)
Atrial septal defect	1 (0.1)	2 (0.2)
Bicuspid aortic valve	2 (0.2)	2 (0.2)
Birth mark	0	2 (0.2)
Cerebral cavernous malformation	0	1 (0.1)
Cerebral palsy	0	1 (0.1)
Chondrodystrophy	1 (0.1)	0
Cleft lip and palate	1 (0.1)	0
Cleft palate	1 (0.1)	1 (0.1)
Colour blindness	1 (0.1)	0
Congenital anomaly	1 (0.1)	0
Congenital diaphragmatic hernia	1 (0.1)	0
Congenital flat feet	1 (0.1)	0
Congenital megacolon	0	1 (0.1)
Congenital nystagmus	2 (0.2)	0
Congenital skin dimples	0	1 (0.1)
Cryptorchism	1 (0.1)	0
Cystic fibrosis	0	2 (0.2)

14.3. Medical History – Phase 2/3 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] (%)
Developmental hip dysplasia	0	1 (0.1)
Ehlers-Danlos syndrome	0	1 (0.1)
Factor V Leiden carrier	1 (0.1)	1 (0.1)
Factor V Leiden mutation	0	1 (0.1)
Gilbert's syndrome	0	1 (0.1)
Hemivertebra	0	1 (0.1)
Hereditary motor and sensory neuropathy	0	1 (0.1)
Hereditary spherocytosis	0	1 (0.1)
Hypoplastic left heart syndrome	0	1 (0.1)
Hypospadias	0	1 (0.1)
Imperforate hymen	0	1 (0.1)
Malformation venous	1 (0.1)	0
Metabolic myopathy	1 (0.1)	0
Microgenia	0	1 (0.1)
Multiple epiphyseal dysplasia	0	1 (0.1)
Naevus flammeus	0	1 (0.1)
Neurofibromatosis	0	2 (0.2)
Oculoauriculovertebral dysplasia	0	1 (0.1)
Otospondylomegaepiphyseal dysplasia	1 (0.1)	0
Pectus carinatum	0	1 (0.1)
Pectus excavatum	2 (0.2)	1 (0.1)
Phimosis	1 (0.1)	1 (0.1)
Polydactyly	1 (0.1)	0
Renal dysplasia	0	1 (0.1)
Sickle cell anaemia	1 (0.1)	0
Sickle cell trait	0	3 (0.3)
Spina bifida occulta	1 (0.1)	0
Strabismus congenital	1 (0.1)	0
Talipes	1 (0.1)	0
Thalassaemia beta	2 (0.2)	0
Thalassaemia minor	0	1 (0.1)
Thyroglossal cyst	1 (0.1)	0
Tourette's disorder	2 (0.2)	2 (0.2)
Transposition of the great vessels	0	1 (0.1)
Ventricular septal defect	0	1 (0.1)
Von Willebrand's disease	1 (0.1)	2 (0.2)
Ear and labyrinth disorders	11 (1.0)	10 (0.9)
Auditory disorder	1 (0.1)	0
Deafness	2 (0.2)	0

14.3. Medical History – Phase 2/3 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] (%)
Deafness bilateral	1 (0.1)	0
Deafness unilateral	1 (0.1)	1 (0.1)
Ear pain	0	1 (0.1)
Eustachian tube disorder	1 (0.1)	0
Eustachian tube dysfunction	2 (0.2)	0
Hypoacusis	1 (0.1)	2 (0.2)
Middle ear adhesions	0	1 (0.1)
Motion sickness	0	1 (0.1)
Tinnitus	1 (0.1)	2 (0.2)
Tympanic membrane perforation	1 (0.1)	1 (0.1)
Vestibular disorder	0	1 (0.1)
Endocrine disorders	7 (0.6)	7 (0.6)
Autoimmune thyroiditis	0	1 (0.1)
Growth hormone deficiency	1 (0.1)	3 (0.3)
Hypopituitarism	1 (0.1)	0
Hypothyroidism	3 (0.3)	1 (0.1)
Precocious puberty	2 (0.2)	2 (0.2)
Eye disorders	46 (4.1)	59 (5.2)
Amblyopia	1 (0.1)	2 (0.2)
Amblyopia strabismic	1 (0.1)	0
Anisometropia	1 (0.1)	0
Astigmatism	1 (0.1)	6 (0.5)
Blepharitis	2 (0.2)	0
Blindness unilateral	0	1 (0.1)
Cataract	1 (0.1)	0
Chalazion	0	1 (0.1)
Conjunctivitis allergic	1 (0.1)	0
Dacryostenosis acquired	0	1 (0.1)
Eyelid ptosis	1 (0.1)	0
Hypermetropia	5 (0.4)	7 (0.6)
Myopia	20 (1.8)	27 (2.4)
Optic atrophy	0	1 (0.1)
Optic nerve cupping	0	1 (0.1)
Presbyopia	1 (0.1)	0
Punctate keratitis	1 (0.1)	0
Pupils unequal	0	1 (0.1)
Recession of chamber angle of eye	0	1 (0.1)
Refractive amblyopia	0	1 (0.1)

14.3. Medical History – Phase 2/3 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] (%)
Strabismus	4 (0.4)	4 (0.4)
Visual acuity reduced	8 (0.7)	12 (1.1)
Gastrointestinal disorders	43 (3.8)	44 (3.9)
Abdominal hernia	1 (0.1)	0
Abdominal migraine	2 (0.2)	1 (0.1)
Abdominal pain	1 (0.1)	3 (0.3)
Abdominal pain upper	1 (0.1)	1 (0.1)
Coeliac disease	4 (0.4)	4 (0.4)
Constipation	10 (0.9)	11 (1.0)
Cyclic vomiting syndrome	1 (0.1)	0
Diarrhoea	1 (0.1)	2 (0.2)
Dyspepsia	3 (0.3)	0
Dysphagia	0	1 (0.1)
Enterocolitis	1 (0.1)	0
Eosinophilic oesophagitis	1 (0.1)	3 (0.3)
Gastrooesophageal reflux disease	12 (1.1)	14 (1.2)
Hiatus hernia	0	1 (0.1)
Inguinal hernia	1 (0.1)	1 (0.1)
Intussusception	2 (0.2)	0
Irritable bowel syndrome	2 (0.2)	2 (0.2)
Malabsorption	1 (0.1)	0
Oesophagitis	1 (0.1)	0
Oral pain	0	1 (0.1)
Tooth impacted	0	1 (0.1)
Toothache	0	1 (0.1)
Umbilical hernia	2 (0.2)	3 (0.3)
General disorders and administration site conditions	10 (0.9)	10 (0.9)
Adverse food reaction	1 (0.1)	0
Cyst	1 (0.1)	1 (0.1)
Developmental delay	0	2 (0.2)
Drug intolerance	1 (0.1)	2 (0.2)
Medical device pain	1 (0.1)	1 (0.1)
Pain	5 (0.4)	3 (0.3)
Peripheral swelling	1 (0.1)	0
Pyrexia	0	1 (0.1)
Hepatobiliary disorders	4 (0.4)	0
Cholelithiasis	2 (0.2)	0

14.3. Medical History – Phase 2/3 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] (%)
Hepatic steatosis	1 (0.1)	0
Non-alcoholic steatohepatitis	1 (0.1)	0
Immune system disorders	399 (35.3)	391 (34.6)
Allergy to animal	24 (2.1)	19 (1.7)
Allergy to arthropod bite	1 (0.1)	2 (0.2)
Allergy to arthropod sting	2 (0.2)	4 (0.4)
Allergy to chemicals	1 (0.1)	0
Allergy to metals	0	2 (0.2)
Allergy to plants	4 (0.4)	2 (0.2)
Anaphylactic reaction	1 (0.1)	0
Cockroach allergy	1 (0.1)	1 (0.1)
Drug hypersensitivity	130 (11.5)	97 (8.6)
Food allergy	32 (2.8)	40 (3.5)
Hypersensitivity	22 (1.9)	16 (1.4)
Milk allergy	3 (0.3)	5 (0.4)
Mite allergy	1 (0.1)	4 (0.4)
Multiple allergies	0	1 (0.1)
Mycotic allergy	0	1 (0.1)
Oral allergy syndrome	0	4 (0.4)
Perennial allergy	2 (0.2)	3 (0.3)
Perfume sensitivity	1 (0.1)	0
Reaction to colouring	1 (0.1)	0
Reaction to food additive	0	1 (0.1)
Rubber sensitivity	6 (0.5)	5 (0.4)
Seasonal allergy	241 (21.3)	247 (21.9)
Selective IgA immunodeficiency	0	1 (0.1)
Serum sickness	1 (0.1)	0
Infections and infestations	72 (6.4)	52 (4.6)
Abscess limb	0	1 (0.1)
Adenoiditis	11 (1.0)	6 (0.5)
Appendicitis	6 (0.5)	9 (0.8)
Body tinea	1 (0.1)	0
Cellulitis	1 (0.1)	0
Chronic sinusitis	2 (0.2)	1 (0.1)
Chronic tonsillitis	2 (0.2)	3 (0.3)
Conjunctivitis	1 (0.1)	1 (0.1)
Croup infectious	1 (0.1)	1 (0.1)
Dermatophytosis of nail	1 (0.1)	0

14.3. Medical History – Phase 2/3 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] (%)
Ear infection	12 (1.1)	8 (0.7)
Gastrointestinal viral infection	1 (0.1)	0
Herpes simplex	1 (0.1)	0
Histoplasmosis	1 (0.1)	0
Impetigo	1 (0.1)	0
Infectious mononucleosis	0	1 (0.1)
Kidney infection	1 (0.1)	0
Lyme disease	2 (0.2)	0
Meningitis	1 (0.1)	0
Meningitis viral	1 (0.1)	0
Molluscum contagiosum	0	1 (0.1)
Nail infection	1 (0.1)	0
Oral herpes	1 (0.1)	0
Osteomyelitis	2 (0.2)	0
Otitis media	3 (0.3)	1 (0.1)
Otitis media acute	1 (0.1)	0
Otitis media chronic	1 (0.1)	2 (0.2)
Paronychia	1 (0.1)	0
Pharyngeal abscess	0	1 (0.1)
Pharyngitis	2 (0.2)	0
Pharyngitis streptococcal	1 (0.1)	3 (0.3)
Pneumonia	6 (0.5)	4 (0.4)
Respiratory syncytial virus bronchiolitis	0	1 (0.1)
Respiratory syncytial virus infection	1 (0.1)	0
Rhinitis	1 (0.1)	1 (0.1)
Rotavirus infection	0	1 (0.1)
Scarlet fever	1 (0.1)	1 (0.1)
Sinusitis	4 (0.4)	1 (0.1)
Staphylococcal scalded skin syndrome	1 (0.1)	0
Tinea infection	0	1 (0.1)
Tonsillitis	11 (1.0)	8 (0.7)
Urinary tract infection	0	2 (0.2)
Viral infection	1 (0.1)	0
Vulvovaginal mycotic infection	1 (0.1)	0
Injury, poisoning and procedural complications	58 (5.1)	48 (4.3)
Ankle fracture	5 (0.4)	1 (0.1)
Chest injury	1 (0.1)	0
Chillblains	1 (0.1)	1 (0.1)
Clavicle fracture	2 (0.2)	3 (0.3)

14.3. Medical History – Phase 2/3 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] (%)
Concussion	5 (0.4)	3 (0.3)
Contusion	1 (0.1)	0
Epiphyseal fracture	1 (0.1)	0
Facial bones fracture	1 (0.1)	2 (0.2)
Fall	1 (0.1)	0
Femur fracture	0	1 (0.1)
Fibula fracture	1 (0.1)	0
Foot fracture	8 (0.7)	3 (0.3)
Foreign body in ear	0	1 (0.1)
Hand fracture	8 (0.7)	5 (0.4)
Humerus fracture	0	1 (0.1)
Jaw fracture	0	1 (0.1)
Joint dislocation	0	1 (0.1)
Joint injury	0	2 (0.2)
Ligament injury	1 (0.1)	0
Ligament rupture	1 (0.1)	0
Ligament sprain	0	2 (0.2)
Limb fracture	2 (0.2)	0
Limb injury	1 (0.1)	0
Lower limb fracture	1 (0.1)	1 (0.1)
Meniscus injury	2 (0.2)	0
Muscle strain	4 (0.4)	1 (0.1)
Nasal injury	0	1 (0.1)
Post concussion syndrome	0	1 (0.1)
Radius fracture	5 (0.4)	1 (0.1)
Skin laceration	0	1 (0.1)
Stress fracture	1 (0.1)	2 (0.2)
Tibia fracture	3 (0.3)	5 (0.4)
Torus fracture	0	2 (0.2)
Upper limb fracture	12 (1.1)	11 (1.0)
VIIth nerve injury	1 (0.1)	0
Wrist fracture	10 (0.9)	6 (0.5)
Investigations	14 (1.2)	8 (0.7)
Blood pressure increased	1 (0.1)	2 (0.2)
Body height decreased	1 (0.1)	0
Cardiac murmur	9 (0.8)	4 (0.4)
Endoscopy	1 (0.1)	0
Endoscopy upper gastrointestinal tract	0	1 (0.1)
Menstruation normal	1 (0.1)	1 (0.1)

14.3. Medical History – Phase 2/3 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] (%)
Serum ferritin decreased	1 (0.1)	0
Weight decreased	1 (0.1)	0
Metabolism and nutrition disorders	39 (3.4)	51 (4.5)
Calcium deficiency	0	1 (0.1)
Dairy intolerance	1 (0.1)	1 (0.1)
Decreased appetite	2 (0.2)	1 (0.1)
Dehydration	1 (0.1)	0
Dyslipidaemia	1 (0.1)	2 (0.2)
Food intolerance	2 (0.2)	2 (0.2)
Fructose intolerance	1 (0.1)	1 (0.1)
Glucose tolerance impaired	1 (0.1)	0
Gluten sensitivity	0	2 (0.2)
Hyperglycaemia	1 (0.1)	0
Hyperlipidaemia	4 (0.4)	0
Hypertriglyceridaemia	1 (0.1)	1 (0.1)
Iron deficiency	0	2 (0.2)
Lactose intolerance	5 (0.4)	7 (0.6)
Obesity	15 (1.3)	20 (1.8)
Overweight	1 (0.1)	4 (0.4)
Type 1 diabetes mellitus	2 (0.2)	5 (0.4)
Underweight	1 (0.1)	0
Vitamin D deficiency	4 (0.4)	6 (0.5)
Musculoskeletal and connective tissue disorders	58 (5.1)	49 (4.3)
Arthralgia	12 (1.1)	8 (0.7)
Back pain	1 (0.1)	1 (0.1)
Discoid meniscus	0	1 (0.1)
Exostosis	1 (0.1)	0
Foot deformity	2 (0.2)	2 (0.2)
Growing pains	1 (0.1)	0
Growth retardation	1 (0.1)	0
Hypermobility syndrome	0	1 (0.1)
Joint instability	1 (0.1)	0
Juvenile idiopathic arthritis	0	2 (0.2)
Knee deformity	2 (0.2)	0
Kyphosis	2 (0.2)	1 (0.1)
Lordosis	1 (0.1)	0
Myalgia	1 (0.1)	5 (0.4)
Neck pain	1 (0.1)	0

14.3. Medical History – Phase 2/3 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] (%)
Osteitis	1 (0.1)	1 (0.1)
Osteochondrosis	3 (0.3)	4 (0.4)
Pain in extremity	2 (0.2)	3 (0.3)
Pain in jaw	1 (0.1)	0
Patellofemoral pain syndrome	0	2 (0.2)
Plantar fascial fibromatosis	0	1 (0.1)
Rotator cuff syndrome	1 (0.1)	0
Scoliosis	21 (1.9)	12 (1.1)
Short stature	6 (0.5)	2 (0.2)
Shoulder deformity	0	1 (0.1)
Synovial cyst	0	1 (0.1)
Temporomandibular joint syndrome	2 (0.2)	1 (0.1)
Tendon disorder	0	1 (0.1)
Tendonitis	1 (0.1)	3 (0.3)
Toe walking	1 (0.1)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	10 (0.9)	14 (1.2)
Benign ear neoplasm	1 (0.1)	0
Cholesteatoma	0	1 (0.1)
Eyelid haemangioma	1 (0.1)	0
Fibroadenoma of breast	0	1 (0.1)
Fibroma	0	1 (0.1)
Haemangioma	1 (0.1)	0
Lipoma	0	1 (0.1)
Melanocytic naevus	1 (0.1)	3 (0.3)
Nephroblastoma	0	1 (0.1)
Skin papilloma	6 (0.5)	6 (0.5)
Nervous system disorders	94 (8.3)	68 (6.0)
Apraxia	1 (0.1)	0
Arachnoid cyst	1 (0.1)	0
Benign rolandic epilepsy	1 (0.1)	0
Convulsion in childhood	1 (0.1)	0
Disturbance in attention	4 (0.4)	0
Dizziness	2 (0.2)	0
Dysgraphia	0	2 (0.2)
Dyslexia	1 (0.1)	6 (0.5)
Epilepsy	4 (0.4)	1 (0.1)
Febrile convulsion	3 (0.3)	0
Headache	38 (3.4)	30 (2.7)

14.3. Medical History – Phase 2/3 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] (%)
Hydrocephalus	0	1 (0.1)
Idiopathic intracranial hypertension	0	1 (0.1)
Mental impairment	2 (0.2)	0
Migraine	30 (2.7)	25 (2.2)
Migraine with aura	2 (0.2)	1 (0.1)
Migraine without aura	0	2 (0.2)
Nystagmus	1 (0.1)	0
Ophthalmic migraine	0	1 (0.1)
Retinal migraine	1 (0.1)	0
Seizure	1 (0.1)	1 (0.1)
Sensory disturbance	0	1 (0.1)
Sensory processing disorder	1 (0.1)	1 (0.1)
Speech disorder	2 (0.2)	0
Syncope	1 (0.1)	1 (0.1)
Tension headache	1 (0.1)	0
Tethered cord syndrome	1 (0.1)	0
Pregnancy, puerperium and perinatal conditions	2 (0.2)	1 (0.1)
Premature baby	2 (0.2)	1 (0.1)
Product issues	0	1 (0.1)
Device breakage	0	1 (0.1)
Psychiatric disorders	293 (25.9)	285 (25.2)
Adjustment disorder with depressed mood	1 (0.1)	1 (0.1)
Adjustment disorder with mixed anxiety and depressed mood	0	1 (0.1)
Aggression	1 (0.1)	1 (0.1)
Anger	0	1 (0.1)
Anxiety	107 (9.5)	96 (8.5)
Anxiety disorder	4 (0.4)	3 (0.3)
Attention deficit hyperactivity disorder	182 (16.1)	166 (14.7)
Autism spectrum disorder	10 (0.9)	10 (0.9)
Behaviour disorder	2 (0.2)	1 (0.1)
Bipolar disorder	2 (0.2)	0
Childhood depression	1 (0.1)	0
Chronic tic disorder	0	2 (0.2)
Depression	51 (4.5)	46 (4.1)
Depressive symptom	0	1 (0.1)
Disruptive mood dysregulation disorder	3 (0.3)	2 (0.2)
Eating disorder	1 (0.1)	2 (0.2)

14.3. Medical History – Phase 2/3 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] (%)
Enuresis	3 (0.3)	2 (0.2)
Gender dysphoria	2 (0.2)	0
Generalised anxiety disorder	8 (0.7)	14 (1.2)
Hallucination, auditory	1 (0.1)	0
Impulse-control disorder	2 (0.2)	0
Impulsive behaviour	0	1 (0.1)
Insomnia	27 (2.4)	29 (2.6)
Learning disorder	0	1 (0.1)
Major depression	5 (0.4)	6 (0.5)
Neurodevelopmental disorder	1 (0.1)	0
Nightmare	1 (0.1)	0
Obsessive-compulsive disorder	5 (0.4)	9 (0.8)
Oppositional defiant disorder	2 (0.2)	3 (0.3)
Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection	0	1 (0.1)
Persistent depressive disorder	1 (0.1)	0
Post-traumatic stress disorder	4 (0.4)	5 (0.4)
Reactive attachment disorder of infancy or early childhood	0	1 (0.1)
Reading disorder	0	1 (0.1)
Separation anxiety disorder	1 (0.1)	0
Sleep disorder	0	3 (0.3)
Social anxiety disorder	0	1 (0.1)
Speech sound disorder	1 (0.1)	0
Suicidal ideation	1 (0.1)	1 (0.1)
Tic	3 (0.3)	2 (0.2)
Renal and urinary disorders	5 (0.4)	6 (0.5)
Dysuria	0	1 (0.1)
Haematuria	1 (0.1)	1 (0.1)
Hydronephrosis	1 (0.1)	0
Nephrolithiasis	1 (0.1)	0
Renal cyst	0	1 (0.1)
Renal disorder	1 (0.1)	0
Single functional kidney	0	1 (0.1)
Urinary retention	0	1 (0.1)
Urinary tract disorder	1 (0.1)	0
Vesicoureteric reflux	1 (0.1)	1 (0.1)
Reproductive system and breast disorders	32 (2.8)	35 (3.1)
Abnormal uterine bleeding	2 (0.2)	1 (0.1)

14.3. Medical History – Phase 2/3 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] (%)
Breast cyst	1 (0.1)	0
Dysmenorrhoea	11 (1.0)	15 (1.3)
Epididymal cyst	1 (0.1)	0
Gynaecomastia	0	1 (0.1)
Heavy menstrual bleeding	7 (0.6)	9 (0.8)
Intermenstrual bleeding	0	1 (0.1)
Menstruation irregular	4 (0.4)	6 (0.5)
Ovulation disorder	1 (0.1)	0
Polycystic ovaries	3 (0.3)	1 (0.1)
Premenstrual dysphoric disorder	0	2 (0.2)
Testicular torsion	1 (0.1)	0
Vaginal disorder	1 (0.1)	0
Varicocele	1 (0.1)	1 (0.1)
Respiratory, thoracic and mediastinal disorders	179 (15.8)	179 (15.9)
Adenoidal hypertrophy	1 (0.1)	0
Asthma	108 (9.5)	110 (9.7)
Asthma exercise induced	11 (1.0)	16 (1.4)
Bronchial hyperreactivity	6 (0.5)	4 (0.4)
Bronchitis chronic	0	1 (0.1)
Bronchospasm	0	1 (0.1)
Epistaxis	6 (0.5)	5 (0.4)
Nasal inflammation	1 (0.1)	0
Nasal polyps	0	1 (0.1)
Nasal septum deviation	1 (0.1)	1 (0.1)
Nasal turbinate hypertrophy	3 (0.3)	0
Oropharyngeal pain	1 (0.1)	1 (0.1)
Rhinitis allergic	41 (3.6)	46 (4.1)
Rhinitis perennial	1 (0.1)	0
Sleep apnoea syndrome	5 (0.4)	3 (0.3)
Snoring	2 (0.2)	0
Tonsillar hypertrophy	2 (0.2)	1 (0.1)
Tonsillolith	1 (0.1)	0
Tracheomalacia	0	1 (0.1)
Vasomotor rhinitis	1 (0.1)	0
Vocal cord disorder	1 (0.1)	0
Vocal cord thickening	1 (0.1)	0
Wheezing	2 (0.2)	0
Skin and subcutaneous tissue disorders	170 (15.0)	182 (16.1)

14.3. Medical History – Phase 2/3 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] (%)
Acanthosis nigricans	0	1 (0.1)
Acne	96 (8.5)	99 (8.8)
Acne cosmetica	1 (0.1)	0
Acne cystic	0	1 (0.1)
Actinic keratosis	1 (0.1)	1 (0.1)
Alopecia	1 (0.1)	0
Alopecia areata	1 (0.1)	0
Blister	1 (0.1)	0
Dermatitis	4 (0.4)	1 (0.1)
Dermatitis allergic	0	1 (0.1)
Dermatitis atopic	10 (0.9)	12 (1.1)
Dermatitis contact	5 (0.4)	4 (0.4)
Drug eruption	0	3 (0.3)
Dry skin	0	2 (0.2)
Eczema	35 (3.1)	44 (3.9)
Hand dermatitis	8 (0.7)	2 (0.2)
Hirsutism	0	1 (0.1)
Hyperhidrosis	1 (0.1)	3 (0.3)
Hyperkeratosis	1 (0.1)	0
Idiopathic urticaria	2 (0.2)	0
Ingrowing nail	1 (0.1)	1 (0.1)
Keratosis pilaris	1 (0.1)	2 (0.2)
Miliaria	1 (0.1)	0
Nail psoriasis	1 (0.1)	0
Pityriasis alba	0	1 (0.1)
Pityriasis rosea	0	1 (0.1)
Psoriasis	6 (0.5)	7 (0.6)
Rash	0	2 (0.2)
Rosacea	1 (0.1)	1 (0.1)
Seborrhoea	1 (0.1)	0
Spider naevus	0	1 (0.1)
Urticaria	8 (0.7)	2 (0.2)
Vitiligo	0	2 (0.2)
Social circumstances	104 (9.2)	95 (8.4)
Corrective lens user	8 (0.7)	10 (0.9)
Menarche	11 (1.0)	16 (1.4)
Premenarche	88 (7.8)	69 (6.1)
Vegan	1 (0.1)	0
Vegetarian	2 (0.2)	6 (0.5)

14.3. Medical History – Phase 2/3 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] (%)
Woman of childbearing potential	0	1 (0.1)
Surgical and medical procedures	111 (9.8)	117 (10.4)
Abdominal hernia repair	1 (0.1)	0
Abscess drainage	0	2 (0.2)
Adenoidectomy	33 (2.9)	22 (1.9)
Adenotonsillectomy	1 (0.1)	2 (0.2)
Ankle operation	0	1 (0.1)
Anorectal operation	0	1 (0.1)
Appendicectomy	9 (0.8)	10 (0.9)
Arterial switch operation	0	1 (0.1)
Atrial septal defect repair	1 (0.1)	1 (0.1)
Bone operation	1 (0.1)	1 (0.1)
Cardiac ablation	0	1 (0.1)
Cardiac operation	0	1 (0.1)
Cataract operation	0	1 (0.1)
Cautery to nose	1 (0.1)	1 (0.1)
Central venous catheterisation	1 (0.1)	0
Cerebral cyst excision	1 (0.1)	0
Cholecystectomy	1 (0.1)	0
Chondroplasty	1 (0.1)	0
Circumcision	2 (0.2)	4 (0.4)
Colon operation	0	1 (0.1)
Dacryocystorhinostomy	0	1 (0.1)
Ear operation	0	1 (0.1)
Ear tube insertion	12 (1.1)	10 (0.9)
Ear tube removal	1 (0.1)	1 (0.1)
Elbow operation	0	1 (0.1)
Epiphyseal surgery	1 (0.1)	0
Epiphysiodesis	1 (0.1)	0
Eye operation	2 (0.2)	4 (0.4)
Facial lesion excision	1 (0.1)	1 (0.1)
Finger amputation	1 (0.1)	1 (0.1)
Foot operation	0	1 (0.1)
Fracture treatment	3 (0.3)	5 (0.4)
Hernia diaphragmatic repair	1 (0.1)	1 (0.1)
Hernia repair	2 (0.2)	0
Hip surgery	0	1 (0.1)
Hydrocele operation	1 (0.1)	0
Hymenectomy	1 (0.1)	0

14.3. Medical History – Phase 2/3 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] (%)
Inguinal hernia repair	1 (0.1)	1 (0.1)
Intestinal operation	1 (0.1)	0
Intrauterine contraception	2 (0.2)	0
Jaw operation	1 (0.1)	0
Joint stabilisation	0	1 (0.1)
Knee operation	2 (0.2)	0
Lacrimal duct procedure	0	1 (0.1)
Ligament operation	1 (0.1)	0
Limb operation	3 (0.3)	1 (0.1)
Limb reconstructive surgery	0	1 (0.1)
Lipoma excision	0	1 (0.1)
Liposuction	0	1 (0.1)
Lymphadenectomy	0	1 (0.1)
Mass excision	1 (0.1)	0
Mastoidectomy	1 (0.1)	0
Medical device change	0	1 (0.1)
Medical diet	1 (0.1)	0
Meniscus operation	1 (0.1)	0
Middle ear operation	1 (0.1)	0
Mole excision	0	1 (0.1)
Myringotomy	11 (1.0)	8 (0.7)
Nail operation	1 (0.1)	0
Nephrectomy	0	1 (0.1)
Oesophagogastric fundoplasty	0	1 (0.1)
Open reduction of fracture	2 (0.2)	1 (0.1)
Orchidopexy	1 (0.1)	0
Ostectomy	1 (0.1)	0
Pharyngeal reconstruction	0	1 (0.1)
Pilonidal sinus repair	0	1 (0.1)
Portal shunt procedure	0	1 (0.1)
Removal of foreign body from external ear	0	1 (0.1)
Rhinoplasty	0	1 (0.1)
Scoliosis surgery	1 (0.1)	1 (0.1)
Scrotal cystectomy	0	1 (0.1)
Sinuplasty	0	1 (0.1)
Skin lesion removal	1 (0.1)	0
Spinal fusion surgery	2 (0.2)	1 (0.1)
Strabismus correction	2 (0.2)	2 (0.2)
Suture insertion	1 (0.1)	0
Temporomandibular joint surgery	0	1 (0.1)

14.3. Medical History – Phase 2/3 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] (%)
Testes exploration	1 (0.1)	0
Testicular operation	1 (0.1)	0
Thyroglossal cyst excision	1 (0.1)	0
Toe operation	1 (0.1)	0
Tonsillectomy	33 (2.9)	31 (2.7)
Tooth extraction	1 (0.1)	1 (0.1)
Transgender hormonal therapy	0	1 (0.1)
Turbinectomy	1 (0.1)	0
Turbinoplasty	1 (0.1)	0
Tympanoplasty	1 (0.1)	0
Umbilical hernia repair	2 (0.2)	3 (0.3)
Urethral repair	1 (0.1)	1 (0.1)
Urinary tract operation	0	1 (0.1)
Vitrectomy	0	1 (0.1)
Wisdom teeth removal	2 (0.2)	5 (0.4)
Vascular disorders	3 (0.3)	2 (0.2)
Hypertension	0	1 (0.1)
Hypotension	1 (0.1)	1 (0.1)
Peripheral venous disease	1 (0.1)	0
Raynaud's phenomenon	1 (0.1)	0

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic. Subjects with multiple occurrences of the same preferred term are counted only once.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:33) Source Data: admh Table Generation: 03NOV2021 (10:03)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/admh_s002_all1_ped6

14.4. Baseline Charlson Comorbidities – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)	
Charlson Comorbidity Index Category	BNT162b2 (30 µg) (N[a]=1131) n[b] (%)	Placebo (N[a]=1129) n[b] (%)
Subjects with any Charlson comorbidity	123 (10.9)	136 (12.0)
Any malignancy	0	1 (0.1)
Chronic pulmonary disease	119 (10.5)	127 (11.2)
Diabetes without chronic complication	2 (0.2)	5 (0.4)
Hemiplegia or paraplegia	0	1 (0.1)
Mild liver disease	2 (0.2)	0
Rheumatic disease	0	2 (0.2)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic. Subjects with multiple occurrences within each category are counted only once. For "Subjects with any Charlson comorbidity," n = number of subjects reporting at least 1 occurrence of any Charlson comorbidity.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:33) Source Data: admh Table Generation: 03NOV2021 (10:03)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/admh_s002_risk1_ped6

14.5. Demographic Characteristics – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=1113) n[b] (%)
Sex	
Male	553 (49.7)
Female	560 (50.3)
Race	
White	955 (85.8)
Black or African American	51 (4.6)
All others	107 (9.6)
American Indian or Alaska Native	4 (0.4)
Asian	70 (6.3)
Native Hawaiian or other Pacific Islander	3 (0.3)
Multiracial	24 (2.2)
Not reported	6 (0.5)
Racial designation	
Japanese	5 (0.4)
Ethnicity	
Hispanic/Latino	130 (11.7)
Non-Hispanic/non-Latino	981 (88.1)
Not reported	2 (0.2)
Country	
USA	1113 (100.0)
Baseline SARS-CoV-2 status	
Positive[c]	45 (4.0)
Negative[d]	1066 (95.8)
Missing	2 (0.2)
Comorbidities[e]	
Yes	243 (21.8)
No	870 (78.2)
Obese[f]	
Yes	140 (12.6)
No	973 (87.4)
Age at vaccination (years)	
Mean (SD)	13.6 (1.11)
Median	14.0
Min, max	(12, 15)

14.5. Demographic Characteristics – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=1113) n[b] (%)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
a. N = number of subjects in the specified group. 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. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥95th percentile.
f. Obese is defined as BMI ≥95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.
PFIZER CONFIDENTIAL SDTM Creation: 30SEP2021 (10:35) Source Data: adsl Table Generation: 08NOV2021 (03:38)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adsl_s005_6m1_ped6_saf

14.6. Demographic Characteristics – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=1010) n[b] (%)
Sex	
Male	518 (51.3)
Female	492 (48.7)
Race	
White	866 (85.7)
Black or African American	48 (4.8)
All others	96 (9.5)
American Indian or Alaska Native	2 (0.2)
Asian	62 (6.1)
Multiracial	26 (2.6)
Not reported	6 (0.6)
Racial designation	
Japanese	2 (0.2)
Ethnicity	
Hispanic/Latino	115 (11.4)
Non-Hispanic/non-Latino	892 (88.3)
Not reported	3 (0.3)
Country	
USA	1010 (100.0)
Baseline SARS-CoV-2 status	
Positive[c]	43 (4.3)
Negative[d]	966 (95.6)
Missing	1 (0.1)
Comorbidities[e]	
Yes	215 (21.3)
No	795 (78.7)
Obese[f]	
Yes	116 (11.5)
No	894 (88.5)
Age at vaccination (years)	
Mean (SD)	13.6 (1.11)
Median	14.0
Min, max	(12, 15)

14.6. Demographic Characteristics – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=1010) n[b] (%)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
a. N = number of subjects in the specified group. 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. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥95th percentile.
f. Obese is defined as BMI ≥95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.
PFIZER CONFIDENTIAL SDTM Creation: 30SEP2021 (10:35) Source Data: adsl Table Generation: 08NOV2021 (03:38)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adsl_s005_cr1_ped6_saf

14.7. Demographic Characteristics – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=1057) n[b] (%)	Placebo (N[a]=1030) n[b] (%)	Total (N[a]=2087) n[b] (%)
Sex			
Male	530 (50.1)	533 (51.7)	1063 (50.9)
Female	527 (49.9)	497 (48.3)	1024 (49.1)
Race			
White	909 (86.0)	874 (84.9)	1783 (85.4)
Black or African American	44 (4.2)	50 (4.9)	94 (4.5)
All others	104 (9.8)	106 (10.3)	210 (10.1)
American Indian or Alaska Native	4 (0.4)	2 (0.2)	6 (0.3)
Asian	68 (6.4)	69 (6.7)	137 (6.6)
Native Hawaiian or other Pacific Islander	3 (0.3)	0	3 (0.1)
Multiracial	23 (2.2)	29 (2.8)	52 (2.5)
Not reported	6 (0.6)	6 (0.6)	12 (0.6)
Ethnicity			
Hispanic/Latino	121 (11.4)	113 (11.0)	234 (11.2)
Non-Hispanic/non-Latino	934 (88.4)	914 (88.7)	1848 (88.5)
Not reported	2 (0.2)	3 (0.3)	5 (0.2)
Country			
USA	1057 (100.0)	1030 (100.0)	2087 (100.0)
Comorbidities[c]			
Yes	233 (22.0)	216 (21.0)	449 (21.5)
No	824 (78.0)	814 (79.0)	1638 (78.5)
Obese[d]			
Yes	135 (12.8)	111 (10.8)	246 (11.8)
No	922 (87.2)	919 (89.2)	1841 (88.2)
Age at vaccination (years)			
Mean (SD)	13.6 (1.10)	13.6 (1.11)	13.6 (1.11)
Median	14.0	14.0	14.0
Min, max	(12, 15)	(12, 15)	(12, 15)

14.7. Demographic Characteristics – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=1057) n[b] (%)	Placebo (N[a]=1030) n[b] (%)	Total (N[a]=2087) n[b] (%)

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. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥95th percentile.
d. Obese is defined as BMI ≥95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.
PFIZER CONFIDENTIAL SDTM Creation: 30SEP2021 (11:35) Source Data: adsl Table Generation: 03NOV2021 (11:38)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adsl_demo_7d_peds_eval_eff

14.8. Demographic Characteristics – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=1131) n[b] (%)	Placebo (N[a]=1129) n[b] (%)	Total (N[a]=2260) n[b] (%)
Sex			
Male	567 (50.1)	585 (51.8)	1152 (51.0)
Female	564 (49.9)	544 (48.2)	1108 (49.0)
Race			
White	970 (85.8)	962 (85.2)	1932 (85.5)
Black or African American	52 (4.6)	57 (5.0)	109 (4.8)
All others	109 (9.6)	110 (9.7)	219 (9.7)
American Indian or Alaska Native	4 (0.4)	3 (0.3)	7 (0.3)
Asian	72 (6.4)	71 (6.3)	143 (6.3)
Native Hawaiian or other Pacific Islander	3 (0.3)	0	3 (0.1)
Multiracial	24 (2.1)	29 (2.6)	53 (2.3)
Not reported	6 (0.5)	7 (0.6)	13 (0.6)
Ethnicity			
Hispanic/Latino	132 (11.7)	130 (11.5)	262 (11.6)
Non-Hispanic/non-Latino	997 (88.2)	996 (88.2)	1993 (88.2)
Not reported	2 (0.2)	3 (0.3)	5 (0.2)
Country			
USA	1131 (100.0)	1129 (100.0)	2260 (100.0)
Comorbidities[c]			
Yes	249 (22.0)	242 (21.4)	491 (21.7)
No	882 (78.0)	887 (78.6)	1769 (78.3)
Obese[d]			
Yes	143 (12.6)	128 (11.3)	271 (12.0)
No	988 (87.4)	1001 (88.7)	1989 (88.0)
Baseline SARS-CoV-2 status			
Positive[e]	46 (4.1)	50 (4.4)	96 (4.2)
Negative[f]	1083 (95.8)	1078 (95.5)	2161 (95.6)
Unknown	2 (0.2)	1 (0.1)	3 (0.1)
Age at vaccination (years)			
Mean (SD)	13.6 (1.11)	13.6 (1.11)	13.6 (1.11)
Median	14.0	14.0	14.0
Min, max	(12, 15)	(12, 15)	(12, 15)

14.8. Demographic Characteristics – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=1131) n[b] (%)	Placebo (N[a]=1129) n[b] (%)	Total (N[a]=2260) n[b] (%)

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. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥95th percentile.
d. Obese is defined as BMI ≥95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.
e. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
f. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.
PFIZER CONFIDENTIAL SDTM Creation: 30SEP2021 (11:35) Source Data: adsl Table Generation: 03NOV2021 (11:38)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adsl_demo_d1_peds_aai

14.9. Demographic Characteristics – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=1119) n[b] (%)	Placebo (N[a]=1109) n[b] (%)	Total (N[a]=2228) n[b] (%)
Sex			
Male	559 (50.0)	573 (51.7)	1132 (50.8)
Female	560 (50.0)	536 (48.3)	1096 (49.2)
Race			
White	961 (85.9)	943 (85.0)	1904 (85.5)
Black or African American	50 (4.5)	57 (5.1)	107 (4.8)
All others	108 (9.7)	109 (9.8)	217 (9.7)
American Indian or Alaska Native	4 (0.4)	2 (0.2)	6 (0.3)
Asian	71 (6.3)	71 (6.4)	142 (6.4)
Native Hawaiian or other Pacific Islander	3 (0.3)	0	3 (0.1)
Multiracial	24 (2.1)	29 (2.6)	53 (2.4)
Not reported	6 (0.5)	7 (0.6)	13 (0.6)
Ethnicity			
Hispanic/Latino	131 (11.7)	127 (11.5)	258 (11.6)
Non-Hispanic/non-Latino	986 (88.1)	979 (88.3)	1965 (88.2)
Not reported	2 (0.2)	3 (0.3)	5 (0.2)
Country			
USA	1119 (100.0)	1109 (100.0)	2228 (100.0)
Comorbidities[c]			
Yes	244 (21.8)	236 (21.3)	480 (21.5)
No	875 (78.2)	873 (78.7)	1748 (78.5)
Obese[d]			
Yes	141 (12.6)	125 (11.3)	266 (11.9)
No	978 (87.4)	984 (88.7)	1962 (88.1)
Baseline SARS-CoV-2 status			
Positive[e]	46 (4.1)	49 (4.4)	95 (4.3)
Negative[f]	1071 (95.7)	1059 (95.5)	2130 (95.6)
Unknown	2 (0.2)	1 (0.1)	3 (0.1)
Age at vaccination (years)			
Mean (SD)	13.6 (1.11)	13.6 (1.11)	13.6 (1.11)
Median	14.0	14.0	14.0
Min, max	(12, 15)	(12, 15)	(12, 15)

14.9. Demographic Characteristics – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=1119) n[b] (%)	Placebo (N[a]=1109) n[b] (%)	Total (N[a]=2228) n[b] (%)

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. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥95th percentile.
d. Obese is defined as BMI ≥95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.
e. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
f. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.
PFIZER CONFIDENTIAL SDTM Creation: 30SEP2021 (11:35) Source Data: adsl Table Generation: 03NOV2021 (11:38)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adsl_demo_7d_wwo_peds_eval_eff

14.10. Concomitant Vaccines Received After Dose 1 – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

Vaccine[b]	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1131) n[c] (%)	Placebo (N[a]=1129) n[c] (%)
Any concomitant vaccine	32 (2.8)	31 (2.7)
DIPHTHERIA VACCINE TOXOID;PERTUSSIS VACCINE ACELLULAR;TETANUS VACCINE TOXOID	3 (0.3)	0
HPV VACCINE	3 (0.3)	10 (0.9)
HPV VACCINE VLP RL1 4V (YEAST)	4 (0.4)	2 (0.2)
INFLUENZA VACCINE	12 (1.1)	5 (0.4)
INFLUENZA VACCINE INACT SPLIT 4V	2 (0.2)	1 (0.1)
MENINGOCOCCAL VACCINE	3 (0.3)	7 (0.6)
MENINGOCOCCAL VACCINE A/C/Y/W	1 (0.1)	1 (0.1)
MENINGOCOCCAL VACCINE A/C/Y/W CONJ (DIP TOX)	3 (0.3)	4 (0.4)
MENINGOCOCCAL VACCINE B	1 (0.1)	0
MENINGOCOCCAL VACCINE B RFHBP/NADA/NHBA OMV	1 (0.1)	0
MENINGOCOCCAL VACCINE B RFHBPA/FHBPB	0	2 (0.2)
MENINGOCOCCAL VACCINE CONJ	1 (0.1)	1 (0.1)
POLIO VACCINE	0	1 (0.1)
RABIES VACCINE	1 (0.1)	0
TETANUS VACCINE	0	1 (0.1)

Note: WHODDG B3 v202103 coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. Subjects are counted only once for each preferred term.
c. n = Number of subjects with the specified characteristic.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adcm Table Generation: 03NOV2021 (10:23)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adcm_s001_1_ped6

Efficacy

14.11. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and Without Evidence of Infection Prior to 7 Days After Dose 2 – Dose 2 All-Available Efficacy Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=1061)		Placebo (N[a]=1037)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence from 7 days after Dose 2	0	0.345 (1047)	29	0.325 (1026)	100.0	(87.2, 100.0)
≥7 days after Dose 2 to <2 Months after Dose 2	0	0.139 (1047)	15	0.134 (1026)	100.0	(73.1, 100.0)
≥2 Months after Dose 2 to <4 Months after Dose 2	0	0.148 (1012)	10	0.140 (964)	100.0	(57.9, 100.0)
≥4 Months after Dose 2	0	0.058 (726)	4	0.051 (688)	100.0	(-34.2, 100.0)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2, and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2) were included in the analysis.
a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period for the overall row and from start to the end of the range stated for each time interval.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adc19ef Table Generation: 05NOV2021 (11:01)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adc19ef_ve_cov_7pd2_peds_wo_aai2

14.12. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=1119)		Placebo (N[a]=1109)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence from 7 days after Dose 2						
Overall	0	0.362 (1098)	30	0.345 (1088)	100.0	(87.5, 100.0)
Sex						
Male	0	0.183 (550)	18	0.177 (561)	100.0	(78.0, 100.0)
Female	0	0.179 (548)	12	0.169 (527)	100.0	(66.1, 100.0)
Race						
White	0	0.309 (945)	28	0.291 (926)	100.0	(86.8, 100.0)
Black or African American	0	0.019 (47)	2	0.021 (56)	100.0	(-492.9, 100.0)
Ethnicity						
Hispanic/Latino	0	0.045 (127)	7	0.040 (125)	100.0	(37.8, 100.0)
Non-Hispanic/non-Latino	0	0.317 (969)	23	0.304 (960)	100.0	(83.3, 100.0)
Country						
USA	0	0.362 (1098)	30	0.345 (1088)	100.0	(87.5, 100.0)
Comorbidities[f]						
Yes	0	0.082 (241)	11	0.073 (228)	100.0	(64.6, 100.0)
No	0	0.280 (857)	19	0.273 (860)	100.0	(79.2, 100.0)
Obese[g]						
Yes	0	0.048 (140)	7	0.039 (122)	100.0	(43.1, 100.0)
No	0	0.314 (958)	23	0.306 (966)	100.0	(83.1, 100.0)
Prior SARS-CoV-2 Status						
Negative at baseline but positive prior to 7 days after Dose 2[h]	0	0.001 (3)	2	0.004 (11)	100.0	(-1374.1, 100.0)
Negative prior to 7 days after Dose 2[i]	0	0.343 (1043)	28	0.322 (1019)	100.0	(86.8, 100.0)

14.12. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=1119)		Placebo (N[a]=1109)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. Comorbidities are defined as having at least one of the Charlson comorbidity index category or obesity (BMI ≥95th percentile).
g. Obese is defined as BMI ≥95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.
h. Negative N-binding antibody result and negative NAAT result at Visit 1, positive NAAT result at Visit 2 or at unscheduled visit, if any, prior to 7 days after Dose 2.
i. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1 and Visit 2, and negative NAAT result at unscheduled visit, if any, prior to 7 days after Dose 2.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:31) Source Data: adc19ef Table Generation: 08DEC2021 (16:13)
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14.13. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Subjects 12 Through 15 Years of Age – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=1131)		Placebo (N[a]=1129)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence after Dose 1						
Overall	3	0.450 (1109)	48	0.434 (1114)	94.0	(81.3, 98.8)
Sex						
Male	3	0.227 (557)	26	0.223 (575)	88.7	(63.0, 97.8)
Female	0	0.223 (552)	22	0.211 (539)	100.0	(82.7, 100.0)
Race						
White	2	0.384 (953)	45	0.367 (951)	95.8	(83.8, 99.5)
Black or African American	0	0.024 (49)	2	0.026 (56)	100.0	(-479.7, 100.0)
All others	1	0.042 (107)	1	0.042 (107)	1.4	(-7638.0, 98.7)
American Indian or Alaska native	0	0.002 (4)	1	0.001 (3)	100.0	(-1965.1, 100.0)
Asian	1	0.027 (70)	0	0.027 (69)	UND	(NA, NA)
Ethnicity						
Hispanic/Latino	1	0.055 (128)	11	0.051 (130)	91.6	(42.3, 99.8)
Non-Hispanic/non-Latino	2	0.394 (979)	37	0.382 (981)	94.8	(79.7, 99.4)
Country						
USA	3	0.450 (1109)	48	0.434 (1114)	94.0	(81.3, 98.8)
Comorbidities[f]						
Yes	1	0.102 (246)	18	0.092 (238)	95.0	(68.3, 99.9)
No	2	0.348 (863)	30	0.342 (876)	93.4	(74.2, 99.2)
Obese[g]						
Yes	0	0.060 (142)	11	0.049 (127)	100.0	(67.0, 100.0)
No	3	0.391 (967)	37	0.385 (987)	92.0	(74.8, 98.4)
Baseline SARS-CoV-2 status						
Positive[h]	0	0.019 (45)	1	0.021 (50)	100.0	(-4202.3, 100.0)
Positive NAAT only	0	0.002 (6)	1	0.004 (10)	100.0	(-5725.9, 100.0)
Negative[i]	3	0.431 (1062)	47	0.413 (1063)	93.9	(81.0, 98.8)

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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=1131)		Placebo (N[a]=1129)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; UND=Undefined; VE = vaccine efficacy.
a. N = number of subjects in the specified group.
b. n1 = Number of subjects meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
d. n2 = Number of subjects at risk for the endpoint.
e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
f. Comorbidities are defined as having at least one of the Charlson comorbidity index category or obesity (BMI ≥95th percentile).
g. Obese is defined as BMI ≥95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.
h. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
i. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:31) Source Data: adc19ef Table Generation: 08DEC2021 (16:16)
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Adverse Events

14.14. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Baseline SARS-CoV-2 Status – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Positive

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=46, TE[b]=0.2)			Placebo (N[a]=50, TE[b]=0.2)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	4 (8.7)	20.8	(5.7, 53.3)	4 (8.0)	19.2	(5.2, 49.1)
Related[f]	1 (2.2)	5.2	(0.1, 29.0)	2 (4.0)	9.6	(1.2, 34.6)
Severe	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Life-threatening	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Any serious adverse event	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Related[f]	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Severe	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Life-threatening	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Any nonserious adverse event	4 (8.7)	20.8	(5.7, 53.3)	4 (8.0)	19.2	(5.2, 49.1)
Related[f]	1 (2.2)	5.2	(0.1, 29.0)	2 (4.0)	9.6	(1.2, 34.6)
Severe	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Life-threatening	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Any adverse event leading to withdrawal	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Related[f]	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Severe	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Life-threatening	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)
Death	0	0.0	(0.0, 19.2)	0	0.0	(0.0, 17.7)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Subjects whose baseline SARS-CoV-2 status cannot be determined because of missing N-binding antibody or NAAT at Visit 1 were not included in the analysis.
Note: Positive = positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19. Negative = negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. 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: 05OCT2021 (17:29) Source Data: adae Table Generation: 12NOV2021 (15:47)
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14.15. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Baseline SARS-CoV-2 Status – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Negative

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1083, TE[b]=4.4)			Placebo (N[a]=1078, TE[b]=4.3)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	91 (8.4)	20.8	(16.8, 25.6)	109 (10.1)	25.4	(20.8, 30.6)
Related[f]	35 (3.2)	8.0	(5.6, 11.1)	22 (2.0)	5.1	(3.2, 7.8)
Severe	13 (1.2)	3.0	(1.6, 5.1)	5 (0.5)	1.2	(0.4, 2.7)
Life-threatening	2 (0.2)	0.5	(0.1, 1.7)	1 (0.1)	0.2	(0.0, 1.3)
Any serious adverse event	10 (0.9)	2.3	(1.1, 4.2)	2 (0.2)	0.5	(0.1, 1.7)
Related[f]	0	0.0	(0.0, 0.8)	0	0.0	(0.0, 0.9)
Severe	7 (0.6)	1.6	(0.6, 3.3)	1 (0.1)	0.2	(0.0, 1.3)
Life-threatening	1 (0.1)	0.2	(0.0, 1.3)	1 (0.1)	0.2	(0.0, 1.3)
Any nonserious adverse event	85 (7.8)	19.4	(15.5, 24.0)	107 (9.9)	24.9	(20.4, 30.1)
Related[f]	35 (3.2)	8.0	(5.6, 11.1)	22 (2.0)	5.1	(3.2, 7.8)
Severe	6 (0.6)	1.4	(0.5, 3.0)	4 (0.4)	0.9	(0.3, 2.4)
Life-threatening	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Any adverse event leading to withdrawal	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Related[f]	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Severe	0	0.0	(0.0, 0.8)	0	0.0	(0.0, 0.9)
Life-threatening	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Death	0	0.0	(0.0, 0.8)	0	0.0	(0.0, 0.9)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Subjects whose baseline SARS-CoV-2 status cannot be determined because of missing N-binding antibody or NAAT at Visit 1 were not included in the analysis.
Note: Positive = positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19. Negative = negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. 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: 05OCT2021 (17:29) Source Data: adae Table Generation: 12NOV2021 (15:47)
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14.16. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Ethnicity – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Ethnicity: Hispanic/Latino

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=132, TE[b]=0.6)			Placebo (N[a]=130, TE[b]=0.5)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	9 (6.8)	16.0	(7.3, 30.3)	16 (12.3)	29.8	(17.0, 48.4)
Related[f]	3 (2.3)	5.3	(1.1, 15.6)	4 (3.1)	7.5	(2.0, 19.1)
Severe	2 (1.5)	3.6	(0.4, 12.8)	0	0.0	(0.0, 6.9)
Life-threatening	0	0.0	(0.0, 6.6)	0	0.0	(0.0, 6.9)
Any serious adverse event	2 (1.5)	3.6	(0.4, 12.8)	0	0.0	(0.0, 6.9)
Related[f]	0	0.0	(0.0, 6.6)	0	0.0	(0.0, 6.9)
Severe	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Life-threatening	0	0.0	(0.0, 6.6)	0	0.0	(0.0, 6.9)
Any nonserious adverse event	8 (6.1)	14.2	(6.1, 28.0)	16 (12.3)	29.8	(17.0, 48.4)
Related[f]	3 (2.3)	5.3	(1.1, 15.6)	4 (3.1)	7.5	(2.0, 19.1)
Severe	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Life-threatening	0	0.0	(0.0, 6.6)	0	0.0	(0.0, 6.9)
Any adverse event leading to withdrawal	0	0.0	(0.0, 6.6)	0	0.0	(0.0, 6.9)
Related[f]	0	0.0	(0.0, 6.6)	0	0.0	(0.0, 6.9)
Severe	0	0.0	(0.0, 6.6)	0	0.0	(0.0, 6.9)
Life-threatening	0	0.0	(0.0, 6.6)	0	0.0	(0.0, 6.9)
Death	0	0.0	(0.0, 6.6)	0	0.0	(0.0, 6.9)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. 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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (16:17)
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14.17. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Ethnicity – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Ethnicity: Non-Hispanic/Non-Latino

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=997, TE[b]=4.0)			Placebo (N[a]=996, TE[b]=4.0)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	86 (8.6)	21.5	(17.2, 26.5)	96 (9.6)	24.2	(19.6, 29.6)
Related[f]	33 (3.3)	8.2	(5.7, 11.6)	20 (2.0)	5.1	(3.1, 7.8)
Severe	11 (1.1)	2.7	(1.4, 4.9)	5 (0.5)	1.3	(0.4, 2.9)
Life-threatening	2 (0.2)	0.5	(0.1, 1.8)	1 (0.1)	0.3	(0.0, 1.4)
Any serious adverse event	8 (0.8)	2.0	(0.9, 3.9)	2 (0.2)	0.5	(0.1, 1.8)
Related[f]	0	0.0	(0.0, 0.9)	0	0.0	(0.0, 0.9)
Severe	6 (0.6)	1.5	(0.6, 3.3)	1 (0.1)	0.3	(0.0, 1.4)
Life-threatening	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)
Any nonserious adverse event	81 (8.1)	20.2	(16.1, 25.2)	94 (9.4)	23.7	(19.2, 29.0)
Related[f]	33 (3.3)	8.2	(5.7, 11.6)	20 (2.0)	5.1	(3.1, 7.8)
Severe	5 (0.5)	1.2	(0.4, 2.9)	4 (0.4)	1.0	(0.3, 2.6)
Life-threatening	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Any adverse event leading to withdrawal	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Related[f]	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Severe	0	0.0	(0.0, 0.9)	0	0.0	(0.0, 0.9)
Life-threatening	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Death	0	0.0	(0.0, 0.9)	0	0.0	(0.0, 0.9)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. 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: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (16:17)
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14.18. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: White

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=970, TE[b]=3.9)			Placebo (N[a]=962, TE[b]=3.8)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	83 (8.6)	21.3	(17.0, 26.4)	100 (10.4)	26.2	(21.3, 31.9)
Related[f]	29 (3.0)	7.5	(5.0, 10.7)	19 (2.0)	5.0	(3.0, 7.8)
Severe	10 (1.0)	2.6	(1.2, 4.7)	5 (0.5)	1.3	(0.4, 3.1)
Life-threatening	2 (0.2)	0.5	(0.1, 1.9)	1 (0.1)	0.3	(0.0, 1.5)
Any serious adverse event	7 (0.7)	1.8	(0.7, 3.7)	2 (0.2)	0.5	(0.1, 1.9)
Related[f]	0	0.0	(0.0, 0.9)	0	0.0	(0.0, 1.0)
Severe	5 (0.5)	1.3	(0.4, 3.0)	1 (0.1)	0.3	(0.0, 1.5)
Life-threatening	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
Any nonserious adverse event	79 (8.1)	20.3	(16.1, 25.3)	98 (10.2)	25.7	(20.8, 31.3)
Related[f]	29 (3.0)	7.5	(5.0, 10.7)	19 (2.0)	5.0	(3.0, 7.8)
Severe	5 (0.5)	1.3	(0.4, 3.0)	4 (0.4)	1.0	(0.3, 2.7)
Life-threatening	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Any adverse event leading to withdrawal	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Related[f]	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Severe	0	0.0	(0.0, 0.9)	0	0.0	(0.0, 1.0)
Life-threatening	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Death	0	0.0	(0.0, 0.9)	0	0.0	(0.0, 1.0)

Note: All Others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. 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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
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14.19. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: Black or African American

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=52, TE[b]=0.2)			Placebo (N[a]=57, TE[b]=0.3)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	3 (5.8)	12.1	(2.5, 35.4)	3 (5.3)	11.5	(2.4, 33.6)
Related[f]	1 (1.9)	4.0	(0.1, 22.5)	3 (5.3)	11.5	(2.4, 33.6)
Severe	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
Life-threatening	0	0.0	(0.0, 14.9)	0	0.0	(0.0, 14.1)
Any serious adverse event	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
Related[f]	0	0.0	(0.0, 14.9)	0	0.0	(0.0, 14.1)
Severe	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
Life-threatening	0	0.0	(0.0, 14.9)	0	0.0	(0.0, 14.1)
Any nonserious adverse event	3 (5.8)	12.1	(2.5, 35.4)	3 (5.3)	11.5	(2.4, 33.6)
Related[f]	1 (1.9)	4.0	(0.1, 22.5)	3 (5.3)	11.5	(2.4, 33.6)
Severe	0	0.0	(0.0, 14.9)	0	0.0	(0.0, 14.1)
Life-threatening	0	0.0	(0.0, 14.9)	0	0.0	(0.0, 14.1)
Any adverse event leading to withdrawal	0	0.0	(0.0, 14.9)	0	0.0	(0.0, 14.1)
Related[f]	0	0.0	(0.0, 14.9)	0	0.0	(0.0, 14.1)
Severe	0	0.0	(0.0, 14.9)	0	0.0	(0.0, 14.1)
Life-threatening	0	0.0	(0.0, 14.9)	0	0.0	(0.0, 14.1)
Death	0	0.0	(0.0, 14.9)	0	0.0	(0.0, 14.1)

Note: All Others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. 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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
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14.20. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: All Others

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=109, TE[b]=0.4)			Placebo (N[a]=110, TE[b]=0.4)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	9 (8.3)	20.8	(9.5, 39.4)	10 (9.1)	23.3	(11.2, 42.9)
Related[f]	6 (5.5)	13.8	(5.1, 30.1)	2 (1.8)	4.7	(0.6, 16.9)
Severe	2 (1.8)	4.6	(0.6, 16.7)	0	0.0	(0.0, 8.6)
Life-threatening	0	0.0	(0.0, 8.5)	0	0.0	(0.0, 8.6)
Any serious adverse event	2 (1.8)	4.6	(0.6, 16.7)	0	0.0	(0.0, 8.6)
Related[f]	0	0.0	(0.0, 8.5)	0	0.0	(0.0, 8.6)
Severe	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
Life-threatening	0	0.0	(0.0, 8.5)	0	0.0	(0.0, 8.6)
Any nonserious adverse event	7 (6.4)	16.1	(6.5, 33.3)	10 (9.1)	23.3	(11.2, 42.9)
Related[f]	6 (5.5)	13.8	(5.1, 30.1)	2 (1.8)	4.7	(0.6, 16.9)
Severe	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
Life-threatening	0	0.0	(0.0, 8.5)	0	0.0	(0.0, 8.6)
Any adverse event leading to withdrawal	0	0.0	(0.0, 8.5)	0	0.0	(0.0, 8.6)
Related[f]	0	0.0	(0.0, 8.5)	0	0.0	(0.0, 8.6)
Severe	0	0.0	(0.0, 8.5)	0	0.0	(0.0, 8.6)
Life-threatening	0	0.0	(0.0, 8.5)	0	0.0	(0.0, 8.6)
Death	0	0.0	(0.0, 8.5)	0	0.0	(0.0, 8.6)

Note: All Others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. 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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
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14.21. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Sex – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Sex: Male

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=567, TE[b]=2.3)			Placebo (N[a]=585, TE[b]=2.3)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	42 (7.4)	18.2	(13.1, 24.5)	57 (9.7)	24.4	(18.5, 31.7)
Related[f]	21 (3.7)	9.1	(5.6, 13.9)	12 (2.1)	5.1	(2.7, 9.0)
Severe	5 (0.9)	2.2	(0.7, 5.0)	4 (0.7)	1.7	(0.5, 4.4)
Life-threatening	1 (0.2)	0.4	(0.0, 2.4)	1 (0.2)	0.4	(0.0, 2.4)
Any serious adverse event	3 (0.5)	1.3	(0.3, 3.8)	2 (0.3)	0.9	(0.1, 3.1)
Related[f]	0	0.0	(0.0, 1.6)	0	0.0	(0.0, 1.6)
Severe	3 (0.5)	1.3	(0.3, 3.8)	1 (0.2)	0.4	(0.0, 2.4)
Life-threatening	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Any nonserious adverse event	39 (6.9)	16.9	(12.0, 23.1)	55 (9.4)	23.6	(17.8, 30.7)
Related[f]	21 (3.7)	9.1	(5.6, 13.9)	12 (2.1)	5.1	(2.7, 9.0)
Severe	2 (0.4)	0.9	(0.1, 3.1)	3 (0.5)	1.3	(0.3, 3.8)
Life-threatening	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Any adverse event leading to withdrawal	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Related[f]	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Severe	0	0.0	(0.0, 1.6)	0	0.0	(0.0, 1.6)
Life-threatening	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Death	0	0.0	(0.0, 1.6)	0	0.0	(0.0, 1.6)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. 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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
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14.22. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by Sex – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Sex: Female

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=564, TE[b]=2.3)			Placebo (N[a]=544, TE[b]=2.2)		
Adverse Event	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	53 (9.4)	23.5	(17.6, 30.7)	56 (10.3)	25.7	(19.4, 33.4)
Related[f]	15 (2.7)	6.6	(3.7, 11.0)	12 (2.2)	5.5	(2.8, 9.6)
Severe	8 (1.4)	3.5	(1.5, 7.0)	1 (0.2)	0.5	(0.0, 2.6)
Life-threatening	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Any serious adverse event	7 (1.2)	3.1	(1.2, 6.4)	0	0.0	(0.0, 1.7)
Related[f]	0	0.0	(0.0, 1.6)	0	0.0	(0.0, 1.7)
Severe	4 (0.7)	1.8	(0.5, 4.5)	0	0.0	(0.0, 1.7)
Life-threatening	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Any nonserious adverse event	50 (8.9)	22.1	(16.4, 29.2)	56 (10.3)	25.7	(19.4, 33.4)
Related[f]	15 (2.7)	6.6	(3.7, 11.0)	12 (2.2)	5.5	(2.8, 9.6)
Severe	4 (0.7)	1.8	(0.5, 4.5)	1 (0.2)	0.5	(0.0, 2.6)
Life-threatening	0	0.0	(0.0, 1.6)	0	0.0	(0.0, 1.7)
Any adverse event leading to withdrawal	0	0.0	(0.0, 1.6)	0	0.0	(0.0, 1.7)
Related[f]	0	0.0	(0.0, 1.6)	0	0.0	(0.0, 1.7)
Severe	0	0.0	(0.0, 1.6)	0	0.0	(0.0, 1.7)
Life-threatening	0	0.0	(0.0, 1.6)	0	0.0	(0.0, 1.7)
Death	0	0.0	(0.0, 1.6)	0	0.0	(0.0, 1.7)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. 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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s092_unb_sex1_ped6

14.23. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Baseline SARS-CoV-2 Status – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Positive

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=46, TE[b]=0.2)			Placebo (N[a]=50, TE[b]=0.2)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	4 (8.7)	20.8	(5.7, 53.3)	4 (8.0)	19.2	(5.2, 49.1)
GASTROINTESTINAL DISORDERS	2 (4.3)	10.4	(1.3, 37.6)	0	0.0	(0.0, 17.7)
Diarrhoea	1 (2.2)	5.2	(0.1, 29.0)	0	0.0	(0.0, 17.7)
Nausea	1 (2.2)	5.2	(0.1, 29.0)	0	0.0	(0.0, 17.7)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	0	0.0	(0.0, 19.2)	1 (2.0)	4.8	(0.1, 26.7)
Fatigue	0	0.0	(0.0, 19.2)	1 (2.0)	4.8	(0.1, 26.7)
INFECTIONS AND INFESTATIONS	1 (2.2)	5.2	(0.1, 29.0)	0	0.0	(0.0, 17.7)
Ear infection	1 (2.2)	5.2	(0.1, 29.0)	0	0.0	(0.0, 17.7)
Otitis externa	1 (2.2)	5.2	(0.1, 29.0)	0	0.0	(0.0, 17.7)
Otitis media	1 (2.2)	5.2	(0.1, 29.0)	0	0.0	(0.0, 17.7)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	0	0.0	(0.0, 19.2)	2 (4.0)	9.6	(1.2, 34.6)
Musculoskeletal chest pain	0	0.0	(0.0, 19.2)	1 (2.0)	4.8	(0.1, 26.7)
Myalgia	0	0.0	(0.0, 19.2)	1 (2.0)	4.8	(0.1, 26.7)
NERVOUS SYSTEM DISORDERS	2 (4.3)	10.4	(1.3, 37.6)	1 (2.0)	4.8	(0.1, 26.7)
Dizziness	1 (2.2)	5.2	(0.1, 29.0)	1 (2.0)	4.8	(0.1, 26.7)
Syncope	1 (2.2)	5.2	(0.1, 29.0)	0	0.0	(0.0, 17.7)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	0	0.0	(0.0, 19.2)	1 (2.0)	4.8	(0.1, 26.7)
Rash	0	0.0	(0.0, 19.2)	1 (2.0)	4.8	(0.1, 26.7)

14.23. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Baseline SARS-CoV-2 Status – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Positive

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=46, TE[b]=0.2)			Placebo (N[a]=50, TE[b]=0.2)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: MedDRA (v24.0) coding dictionary applied.
Note: Subjects whose baseline SARS-CoV-2 status cannot be determined because of missing N-binding antibody or NAAT at Visit 1 were not included in the analysis.
Note: Positive = positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19. Negative = negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
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14.24. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Baseline SARS-CoV-2 Status – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Negative

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1083, TE[b]=4.4)			Placebo (N[a]=1078, TE[b]=4.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	91 (8.4)	20.8	(16.8, 25.6)	109 (10.1)	25.4	(20.8, 30.6)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	9 (0.8)	2.1	(0.9, 3.9)	2 (0.2)	0.5	(0.1, 1.7)
Lymphadenopathy	9 (0.8)	2.1	(0.9, 3.9)	2 (0.2)	0.5	(0.1, 1.7)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Spine malformation	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
EAR AND LABYRINTH DISORDERS	1 (0.1)	0.2	(0.0, 1.3)	3 (0.3)	0.7	(0.1, 2.0)
Cerumen impaction	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Conductive deafness	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Ear pain	1 (0.1)	0.2	(0.0, 1.3)	1 (0.1)	0.2	(0.0, 1.3)
EYE DISORDERS	2 (0.2)	0.5	(0.1, 1.7)	1 (0.1)	0.2	(0.0, 1.3)
Eye pain	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Eyelid rash	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Retinal haemorrhage	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
GASTROINTESTINAL DISORDERS	12 (1.1)	2.7	(1.4, 4.8)	8 (0.7)	1.9	(0.8, 3.7)
Abdominal pain	2 (0.2)	0.5	(0.1, 1.7)	1 (0.1)	0.2	(0.0, 1.3)
Aphthous ulcer	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Constipation	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Diarrhoea	2 (0.2)	0.5	(0.1, 1.7)	1 (0.1)	0.2	(0.0, 1.3)
Gastritis	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Lip swelling	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Mouth swelling	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Mouth ulceration	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Nausea	4 (0.4)	0.9	(0.2, 2.3)	3 (0.3)	0.7	(0.1, 2.0)
Oral mucosal blistering	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Rectal prolapse	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Tooth impacted	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Toothache	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Vomiting	1 (0.1)	0.2	(0.0, 1.3)	1 (0.1)	0.2	(0.0, 1.3)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	17 (1.6)	3.9	(2.3, 6.2)	11 (1.0)	2.6	(1.3, 4.6)
Chills	2 (0.2)	0.5	(0.1, 1.7)	1 (0.1)	0.2	(0.0, 1.3)
Fatigue	8 (0.7)	1.8	(0.8, 3.6)	3 (0.3)	0.7	(0.1, 2.0)
Injection site pain	8 (0.7)	1.8	(0.8, 3.6)	8 (0.7)	1.9	(0.8, 3.7)
Injection site swelling	2 (0.2)	0.5	(0.1, 1.7)	0	0.0	(0.0, 0.9)
Nodule	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)

14.24. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Baseline SARS-CoV-2 Status – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Negative

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1083, TE[b]=4.4)			Placebo (N[a]=1078, TE[b]=4.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Oedema peripheral	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Peripheral swelling	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Pyrexia	6 (0.6)	1.4	(0.5, 3.0)	0	0.0	(0.0, 0.9)
Vessel puncture site pain	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
IMMUNE SYSTEM DISORDERS	1 (0.1)	0.2	(0.0, 1.3)	1 (0.1)	0.2	(0.0, 1.3)
Food allergy	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Seasonal allergy	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
INFECTIONS AND INFESTATIONS	9 (0.8)	2.1	(0.9, 3.9)	9 (0.8)	2.1	(1.0, 4.0)
Anal abscess	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Appendicitis	0	0.0	(0.0, 0.8)	2 (0.2)	0.5	(0.1, 1.7)
Body tinea	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Candida infection	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Cellulitis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Conjunctivitis	0	0.0	(0.0, 0.8)	2 (0.2)	0.5	(0.1, 1.7)
Ear infection	2 (0.2)	0.5	(0.1, 1.7)	0	0.0	(0.0, 0.9)
Focal peritonitis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Infectious mononucleosis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Paronychia	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Pilonidal cyst	1 (0.1)	0.2	(0.0, 1.3)	1 (0.1)	0.2	(0.0, 1.3)
Subcutaneous abscess	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Tinea capitis	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Vulval abscess	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Vulvovaginal mycotic infection	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	15 (1.4)	3.4	(1.9, 5.7)	25 (2.3)	5.8	(3.8, 8.6)
Accident	1 (0.1)	0.2	(0.0, 1.3)	1 (0.1)	0.2	(0.0, 1.3)
Ankle fracture	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Bone contusion	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Clavicle fracture	1 (0.1)	0.2	(0.0, 1.3)	1 (0.1)	0.2	(0.0, 1.3)
Concussion	3 (0.3)	0.7	(0.1, 2.0)	4 (0.4)	0.9	(0.3, 2.4)
Contusion	2 (0.2)	0.5	(0.1, 1.7)	2 (0.2)	0.5	(0.1, 1.7)
Fall	2 (0.2)	0.5	(0.1, 1.7)	5 (0.5)	1.2	(0.4, 2.7)
Femur fracture	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Foot fracture	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Hand fracture	1 (0.1)	0.2	(0.0, 1.3)	4 (0.4)	0.9	(0.3, 2.4)
Humerus fracture	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Ligament sprain	1 (0.1)	0.2	(0.0, 1.3)	4 (0.4)	0.9	(0.3, 2.4)

14.24. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Baseline SARS-CoV-2 Status – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Negative

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1083, TE[b]=4.4)			Placebo (N[a]=1078, TE[b]=4.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Lip injury	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Meniscus injury	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Muscle strain	1 (0.1)	0.2	(0.0, 1.3)	1 (0.1)	0.2	(0.0, 1.3)
Patella fracture	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Procedural pain	2 (0.2)	0.5	(0.1, 1.7)	3 (0.3)	0.7	(0.1, 2.0)
Radius fracture	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Skin laceration	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Tibia fracture	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Tooth fracture	0	0.0	(0.0, 0.8)	2 (0.2)	0.5	(0.1, 1.7)
Upper limb fracture	1 (0.1)	0.2	(0.0, 1.3)	1 (0.1)	0.2	(0.0, 1.3)
INVESTIGATIONS	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
SARS-CoV-2 antibody test positive	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	8 (0.7)	1.8	(0.8, 3.6)	12 (1.1)	2.8	(1.4, 4.9)
Arthralgia	2 (0.2)	0.5	(0.1, 1.7)	4 (0.4)	0.9	(0.3, 2.4)
Back pain	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Joint swelling	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Musculoskeletal chest pain	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Myalgia	3 (0.3)	0.7	(0.1, 2.0)	1 (0.1)	0.2	(0.0, 1.3)
Neck pain	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Osteochondrosis	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Pain in extremity	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Tendonitis	0	0.0	(0.0, 0.8)	4 (0.4)	0.9	(0.3, 2.4)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (0.1)	0.2	(0.0, 1.3)	3 (0.3)	0.7	(0.1, 2.0)
Fibroadenoma of breast	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Hair follicle tumour benign	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Melanocytic naevus	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Skin papilloma	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
NERVOUS SYSTEM DISORDERS	11 (1.0)	2.5	(1.3, 4.5)	12 (1.1)	2.8	(1.4, 4.9)
Dizziness	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Headache	5 (0.5)	1.1	(0.4, 2.7)	7 (0.6)	1.6	(0.7, 3.4)
Migraine	3 (0.3)	0.7	(0.1, 2.0)	0	0.0	(0.0, 0.9)
Paraesthesia	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Presyncope	1 (0.1)	0.2	(0.0, 1.3)	4 (0.4)	0.9	(0.3, 2.4)
Syncope	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
PSYCHIATRIC DISORDERS	17 (1.6)	3.9	(2.3, 6.2)	13 (1.2)	3.0	(1.6, 5.2)

14.24. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Baseline SARS-CoV-2 Status – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Negative

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1083, TE[b]=4.4)			Placebo (N[a]=1078, TE[b]=4.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Anxiety	4 (0.4)	0.9	(0.2, 2.3)	6 (0.6)	1.4	(0.5, 3.0)
Attention deficit hyperactivity disorder	2 (0.2)	0.5	(0.1, 1.7)	4 (0.4)	0.9	(0.3, 2.4)
Conversion disorder	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Depression	6 (0.6)	1.4	(0.5, 3.0)	3 (0.3)	0.7	(0.1, 2.0)
Disorientation	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Generalised anxiety disorder	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Obsessive-compulsive disorder	0	0.0	(0.0, 0.8)	2 (0.2)	0.5	(0.1, 1.7)
Panic attack	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Sleep terror	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Suicidal ideation	4 (0.4)	0.9	(0.2, 2.3)	0	0.0	(0.0, 0.9)
Tic	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
RENAL AND URINARY DISORDERS	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Dysuria	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Amenorrhoea	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	3 (0.3)	0.7	(0.1, 2.0)	8 (0.7)	1.9	(0.8, 3.7)
Epistaxis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Nasal congestion	2 (0.2)	0.5	(0.1, 1.7)	3 (0.3)	0.7	(0.1, 2.0)
Rhinorrhoea	2 (0.2)	0.5	(0.1, 1.7)	4 (0.4)	0.9	(0.3, 2.4)
Sneezing	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	9 (0.8)	2.1	(0.9, 3.9)	15 (1.4)	3.5	(2.0, 5.8)
Acne	2 (0.2)	0.5	(0.1, 1.7)	3 (0.3)	0.7	(0.1, 2.0)
Dermatitis contact	2 (0.2)	0.5	(0.1, 1.7)	1 (0.1)	0.2	(0.0, 1.3)
Eczema	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Pityriasis rosea	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Rash	3 (0.3)	0.7	(0.1, 2.0)	4 (0.4)	0.9	(0.3, 2.4)
Rash maculo-papular	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Seborrhoeic dermatitis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
Urticaria	2 (0.2)	0.5	(0.1, 1.7)	5 (0.5)	1.2	(0.4, 2.7)
SURGICAL AND MEDICAL PROCEDURES	1 (0.1)	0.2	(0.0, 1.3)	1 (0.1)	0.2	(0.0, 1.3)
Wisdom teeth removal	1 (0.1)	0.2	(0.0, 1.3)	1 (0.1)	0.2	(0.0, 1.3)

14.24. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Baseline SARS-CoV-2 Status – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Negative

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1083, TE[b]=4.4)			Placebo (N[a]=1078, TE[b]=4.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: MedDRA (v24.0) coding dictionary applied.
Note: Subjects whose baseline SARS-CoV-2 status cannot be determined because of missing N-binding antibody or NAAT at Visit 1 were not included in the analysis.
Note: Positive = positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19. Negative = negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 12NOV2021 (15:38)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_unb_base1_ped6

14.25. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Ethnicity – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Ethnicity: Hispanic/Latino

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=132, TE[b]=0.6)			Placebo (N[a]=130, TE[b]=0.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	9 (6.8)	16.0	(7.3, 30.3)	16 (12.3)	29.8	(17.0, 48.4)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Lymphadenopathy	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
EAR AND LABYRINTH DISORDERS	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
Conductive deafness	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
GASTROINTESTINAL DISORDERS	2 (1.5)	3.6	(0.4, 12.8)	1 (0.8)	1.9	(0.0, 10.4)
Abdominal pain	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Constipation	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Diarrhoea	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Gastritis	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Nausea	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
Vomiting	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (0.8)	1.8	(0.0, 9.9)	1 (0.8)	1.9	(0.0, 10.4)
Injection site pain	1 (0.8)	1.8	(0.0, 9.9)	1 (0.8)	1.9	(0.0, 10.4)
Vessel puncture site pain	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
INFECTIONS AND INFESTATIONS	3 (2.3)	5.3	(1.1, 15.6)	0	0.0	(0.0, 6.9)
Body tinea	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Paronychia	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Vulval abscess	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	0	0.0	(0.0, 6.6)	3 (2.3)	5.6	(1.2, 16.3)
Accident	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
Ankle fracture	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
Contusion	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
Fall	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
Hand fracture	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
Lip injury	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
Tooth fracture	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	0	0.0	(0.0, 6.6)	3 (2.3)	5.6	(1.2, 16.3)
Arthralgia	0	0.0	(0.0, 6.6)	2 (1.5)	3.7	(0.5, 13.5)
Musculoskeletal chest pain	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)

14.25. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Ethnicity – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Ethnicity: Hispanic/Latino

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=132, TE[b]=0.6)			Placebo (N[a]=130, TE[b]=0.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Melanocytic naevus	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
NERVOUS SYSTEM DISORDERS	2 (1.5)	3.6	(0.4, 12.8)	3 (2.3)	5.6	(1.2, 16.3)
Headache	1 (0.8)	1.8	(0.0, 9.9)	3 (2.3)	5.6	(1.2, 16.3)
Paraesthesia	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
PSYCHIATRIC DISORDERS	2 (1.5)	3.6	(0.4, 12.8)	1 (0.8)	1.9	(0.0, 10.4)
Anxiety	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Conversion disorder	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Obsessive-compulsive disorder	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
Suicidal ideation	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (0.8)	1.8	(0.0, 9.9)	6 (4.6)	11.2	(4.1, 24.3)
Acne	0	0.0	(0.0, 6.6)	2 (1.5)	3.7	(0.5, 13.5)
Dermatitis contact	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Rash	0	0.0	(0.0, 6.6)	3 (2.3)	5.6	(1.2, 16.3)
Seborrhoeic dermatitis	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)
Urticaria	0	0.0	(0.0, 6.6)	1 (0.8)	1.9	(0.0, 10.4)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (16:25)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_unb_eth1_ped6

14.26. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Ethnicity – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Ethnicity: Non-Hispanic/Non-Latino

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=997, TE[b]=4.0)			Placebo (N[a]=996, TE[b]=4.0)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	86 (8.6)	21.5	(17.2, 26.5)	96 (9.6)	24.2	(19.6, 29.6)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	8 (0.8)	2.0	(0.9, 3.9)	2 (0.2)	0.5	(0.1, 1.8)
Lymphadenopathy	8 (0.8)	2.0	(0.9, 3.9)	2 (0.2)	0.5	(0.1, 1.8)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Spine malformation	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
EAR AND LABYRINTH DISORDERS	1 (0.1)	0.2	(0.0, 1.4)	2 (0.2)	0.5	(0.1, 1.8)
Cerumen impaction	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Ear pain	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)
EYE DISORDERS	2 (0.2)	0.5	(0.1, 1.8)	1 (0.1)	0.3	(0.0, 1.4)
Eye pain	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Eyelid rash	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Retinal haemorrhage	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
GASTROINTESTINAL DISORDERS	12 (1.2)	3.0	(1.5, 5.2)	7 (0.7)	1.8	(0.7, 3.6)
Abdominal pain	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)
Aphthous ulcer	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Diarrhoea	2 (0.2)	0.5	(0.1, 1.8)	1 (0.1)	0.3	(0.0, 1.4)
Lip swelling	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Mouth swelling	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Mouth ulceration	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Nausea	5 (0.5)	1.2	(0.4, 2.9)	2 (0.2)	0.5	(0.1, 1.8)
Oral mucosal blistering	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Rectal prolapse	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Tooth impacted	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Toothache	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Vomiting	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	16 (1.6)	4.0	(2.3, 6.5)	11 (1.1)	2.8	(1.4, 5.0)
Chills	2 (0.2)	0.5	(0.1, 1.8)	1 (0.1)	0.3	(0.0, 1.4)
Fatigue	8 (0.8)	2.0	(0.9, 3.9)	4 (0.4)	1.0	(0.3, 2.6)
Injection site pain	7 (0.7)	1.7	(0.7, 3.6)	7 (0.7)	1.8	(0.7, 3.6)
Injection site swelling	2 (0.2)	0.5	(0.1, 1.8)	0	0.0	(0.0, 0.9)
Nodule	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Oedema peripheral	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Peripheral swelling	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Pyrexia	6 (0.6)	1.5	(0.6, 3.3)	0	0.0	(0.0, 0.9)

14.26. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Ethnicity – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Ethnicity: Non-Hispanic/Non-Latino

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=997, TE[b]=4.0)			Placebo (N[a]=996, TE[b]=4.0)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
IMMUNE SYSTEM DISORDERS	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)
Food allergy	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Seasonal allergy	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
INFECTIONS AND INFESTATIONS	7 (0.7)	1.7	(0.7, 3.6)	9 (0.9)	2.3	(1.0, 4.3)
Anal abscess	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Appendicitis	0	0.0	(0.0, 0.9)	2 (0.2)	0.5	(0.1, 1.8)
Candida infection	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Cellulitis	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Conjunctivitis	0	0.0	(0.0, 0.9)	2 (0.2)	0.5	(0.1, 1.8)
Ear infection	3 (0.3)	0.7	(0.2, 2.2)	0	0.0	(0.0, 0.9)
Focal peritonitis	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Infectious mononucleosis	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Otitis externa	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Otitis media	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Pilonidal cyst	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)
Subcutaneous abscess	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Tinea capitis	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Vulvovaginal mycotic infection	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	15 (1.5)	3.7	(2.1, 6.2)	22 (2.2)	5.6	(3.5, 8.4)
Accident	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Bone contusion	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Clavicle fracture	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)
Concussion	3 (0.3)	0.7	(0.2, 2.2)	4 (0.4)	1.0	(0.3, 2.6)
Contusion	2 (0.2)	0.5	(0.1, 1.8)	1 (0.1)	0.3	(0.0, 1.4)
Fall	2 (0.2)	0.5	(0.1, 1.8)	4 (0.4)	1.0	(0.3, 2.6)
Femur fracture	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Foot fracture	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Hand fracture	1 (0.1)	0.2	(0.0, 1.4)	3 (0.3)	0.8	(0.2, 2.2)
Humerus fracture	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Ligament sprain	1 (0.1)	0.2	(0.0, 1.4)	4 (0.4)	1.0	(0.3, 2.6)
Meniscus injury	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Muscle strain	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)
Patella fracture	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Procedural pain	2 (0.2)	0.5	(0.1, 1.8)	3 (0.3)	0.8	(0.2, 2.2)
Radius fracture	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Skin laceration	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)

14.26. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Ethnicity – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Ethnicity: Non-Hispanic/Non-Latino

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=997, TE[b]=4.0)			Placebo (N[a]=996, TE[b]=4.0)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Tibia fracture	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Tooth fracture	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Upper limb fracture	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)
INVESTIGATIONS	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
SARS-CoV-2 antibody test positive	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	8 (0.8)	2.0	(0.9, 3.9)	11 (1.1)	2.8	(1.4, 5.0)
Arthralgia	2 (0.2)	0.5	(0.1, 1.8)	2 (0.2)	0.5	(0.1, 1.8)
Back pain	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Joint swelling	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Musculoskeletal chest pain	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Myalgia	3 (0.3)	0.7	(0.2, 2.2)	2 (0.2)	0.5	(0.1, 1.8)
Neck pain	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Osteochondrosis	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Pain in extremity	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Tendonitis	0	0.0	(0.0, 0.9)	4 (0.4)	1.0	(0.3, 2.6)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (0.1)	0.2	(0.0, 1.4)	2 (0.2)	0.5	(0.1, 1.8)
Fibroadenoma of breast	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Hair follicle tumour benign	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Skin papilloma	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
NERVOUS SYSTEM DISORDERS	11 (1.1)	2.7	(1.4, 4.9)	10 (1.0)	2.5	(1.2, 4.6)
Dizziness	2 (0.2)	0.5	(0.1, 1.8)	1 (0.1)	0.3	(0.0, 1.4)
Headache	4 (0.4)	1.0	(0.3, 2.6)	4 (0.4)	1.0	(0.3, 2.6)
Migraine	3 (0.3)	0.7	(0.2, 2.2)	0	0.0	(0.0, 0.9)
Presyncope	1 (0.1)	0.2	(0.0, 1.4)	4 (0.4)	1.0	(0.3, 2.6)
Syncope	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)
PSYCHIATRIC DISORDERS	15 (1.5)	3.7	(2.1, 6.2)	12 (1.2)	3.0	(1.6, 5.3)
Anxiety	3 (0.3)	0.7	(0.2, 2.2)	6 (0.6)	1.5	(0.6, 3.3)
Attention deficit hyperactivity disorder	2 (0.2)	0.5	(0.1, 1.8)	4 (0.4)	1.0	(0.3, 2.6)
Depression	6 (0.6)	1.5	(0.6, 3.3)	3 (0.3)	0.8	(0.2, 2.2)
Disorientation	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Generalised anxiety disorder	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Obsessive-compulsive disorder	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Panic attack	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Sleep terror	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Suicidal ideation	3 (0.3)	0.7	(0.2, 2.2)	0	0.0	(0.0, 0.9)

14.26. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Ethnicity – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Ethnicity: Non-Hispanic/Non-Latino

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=997, TE[b]=4.0)			Placebo (N[a]=996, TE[b]=4.0)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Tic	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
RENAL AND URINARY DISORDERS	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Dysuria	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Amenorrhoea	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	3 (0.3)	0.7	(0.2, 2.2)	8 (0.8)	2.0	(0.9, 4.0)
Epistaxis	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Nasal congestion	2 (0.2)	0.5	(0.1, 1.8)	3 (0.3)	0.8	(0.2, 2.2)
Rhinorrhoea	2 (0.2)	0.5	(0.1, 1.8)	4 (0.4)	1.0	(0.3, 2.6)
Sneezing	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	8 (0.8)	2.0	(0.9, 3.9)	9 (0.9)	2.3	(1.0, 4.3)
Acne	2 (0.2)	0.5	(0.1, 1.8)	1 (0.1)	0.3	(0.0, 1.4)
Dermatitis contact	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)
Eczema	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Rash	3 (0.3)	0.7	(0.2, 2.2)	2 (0.2)	0.5	(0.1, 1.8)
Rash maculo-papular	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
Urticaria	2 (0.2)	0.5	(0.1, 1.8)	4 (0.4)	1.0	(0.3, 2.6)
SURGICAL AND MEDICAL PROCEDURES	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)
Wisdom teeth removal	1 (0.1)	0.2	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.4)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (16:25)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_unb_eth1_ped6

14.27. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: White

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=970, TE[b]=3.9)			Placebo (N[a]=962, TE[b]=3.8)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	83 (8.6)	21.3	(17.0, 26.4)	100 (10.4)	26.2	(21.3, 31.9)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	6 (0.6)	1.5	(0.6, 3.4)	1 (0.1)	0.3	(0.0, 1.5)
Lymphadenopathy	6 (0.6)	1.5	(0.6, 3.4)	1 (0.1)	0.3	(0.0, 1.5)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Spine malformation	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
EAR AND LABYRINTH DISORDERS	1 (0.1)	0.3	(0.0, 1.4)	2 (0.2)	0.5	(0.1, 1.9)
Cerumen impaction	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Ear pain	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
EYE DISORDERS	2 (0.2)	0.5	(0.1, 1.9)	1 (0.1)	0.3	(0.0, 1.5)
Eye pain	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Eyelid rash	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Retinal haemorrhage	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
GASTROINTESTINAL DISORDERS	13 (1.3)	3.3	(1.8, 5.7)	7 (0.7)	1.8	(0.7, 3.8)
Abdominal pain	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
Aphthous ulcer	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Constipation	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Diarrhoea	3 (0.3)	0.8	(0.2, 2.3)	0	0.0	(0.0, 1.0)
Gastritis	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Lip swelling	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Mouth swelling	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Mouth ulceration	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Nausea	5 (0.5)	1.3	(0.4, 3.0)	3 (0.3)	0.8	(0.2, 2.3)
Oral mucosal blistering	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Rectal prolapse	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Tooth impacted	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Toothache	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Vomiting	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	15 (1.5)	3.9	(2.2, 6.4)	10 (1.0)	2.6	(1.3, 4.8)
Chills	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
Fatigue	7 (0.7)	1.8	(0.7, 3.7)	4 (0.4)	1.0	(0.3, 2.7)
Injection site pain	7 (0.7)	1.8	(0.7, 3.7)	6 (0.6)	1.6	(0.6, 3.4)
Injection site swelling	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Nodule	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)

14.27. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: White

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=970, TE[b]=3.9)			Placebo (N[a]=962, TE[b]=3.8)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Oedema peripheral	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Pyrexia	5 (0.5)	1.3	(0.4, 3.0)	0	0.0	(0.0, 1.0)
Vessel puncture site pain	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
IMMUNE SYSTEM DISORDERS	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
Food allergy	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Seasonal allergy	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
INFECTIONS AND INFESTATIONS	9 (0.9)	2.3	(1.1, 4.4)	7 (0.7)	1.8	(0.7, 3.8)
Anal abscess	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Appendicitis	0	0.0	(0.0, 0.9)	2 (0.2)	0.5	(0.1, 1.9)
Candida infection	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Conjunctivitis	0	0.0	(0.0, 0.9)	2 (0.2)	0.5	(0.1, 1.9)
Ear infection	3 (0.3)	0.8	(0.2, 2.3)	0	0.0	(0.0, 1.0)
Focal peritonitis	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Infectious mononucleosis	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Otitis externa	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Otitis media	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Paronychia	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Pilonidal cyst	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
Tinea capitis	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Vulval abscess	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Vulvovaginal mycotic infection	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	14 (1.4)	3.6	(2.0, 6.0)	24 (2.5)	6.3	(4.0, 9.4)
Accident	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
Ankle fracture	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Bone contusion	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Clavicle fracture	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
Concussion	3 (0.3)	0.8	(0.2, 2.3)	4 (0.4)	1.0	(0.3, 2.7)
Contusion	1 (0.1)	0.3	(0.0, 1.4)	2 (0.2)	0.5	(0.1, 1.9)
Fall	1 (0.1)	0.3	(0.0, 1.4)	5 (0.5)	1.3	(0.4, 3.1)
Femur fracture	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Foot fracture	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Hand fracture	1 (0.1)	0.3	(0.0, 1.4)	3 (0.3)	0.8	(0.2, 2.3)
Humerus fracture	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Ligament sprain	1 (0.1)	0.3	(0.0, 1.4)	4 (0.4)	1.0	(0.3, 2.7)
Lip injury	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Meniscus injury	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)

14.27. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: White

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=970, TE[b]=3.9)			Placebo (N[a]=962, TE[b]=3.8)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Muscle strain	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
Patella fracture	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Procedural pain	2 (0.2)	0.5	(0.1, 1.9)	3 (0.3)	0.8	(0.2, 2.3)
Radius fracture	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Skin laceration	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Tibia fracture	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Tooth fracture	0	0.0	(0.0, 0.9)	2 (0.2)	0.5	(0.1, 1.9)
Upper limb fracture	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
INVESTIGATIONS	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
SARS-CoV-2 antibody test positive	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	8 (0.8)	2.1	(0.9, 4.1)	13 (1.4)	3.4	(1.8, 5.8)
Arthralgia	2 (0.2)	0.5	(0.1, 1.9)	4 (0.4)	1.0	(0.3, 2.7)
Back pain	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Joint swelling	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Musculoskeletal chest pain	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Myalgia	3 (0.3)	0.8	(0.2, 2.3)	2 (0.2)	0.5	(0.1, 1.9)
Neck pain	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Osteochondrosis	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Pain in extremity	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Tendonitis	0	0.0	(0.0, 0.9)	4 (0.4)	1.0	(0.3, 2.7)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (0.1)	0.3	(0.0, 1.4)	2 (0.2)	0.5	(0.1, 1.9)
Hair follicle tumour benign	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Melanocytic naevus	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Skin papilloma	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
NERVOUS SYSTEM DISORDERS	11 (1.1)	2.8	(1.4, 5.1)	12 (1.2)	3.1	(1.6, 5.5)
Dizziness	2 (0.2)	0.5	(0.1, 1.9)	1 (0.1)	0.3	(0.0, 1.5)
Headache	5 (0.5)	1.3	(0.4, 3.0)	6 (0.6)	1.6	(0.6, 3.4)
Migraine	2 (0.2)	0.5	(0.1, 1.9)	0	0.0	(0.0, 1.0)
Presyncope	1 (0.1)	0.3	(0.0, 1.4)	4 (0.4)	1.0	(0.3, 2.7)
Syncope	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
PSYCHIATRIC DISORDERS	14 (1.4)	3.6	(2.0, 6.0)	13 (1.4)	3.4	(1.8, 5.8)
Anxiety	3 (0.3)	0.8	(0.2, 2.3)	6 (0.6)	1.6	(0.6, 3.4)
Attention deficit hyperactivity disorder	2 (0.2)	0.5	(0.1, 1.9)	4 (0.4)	1.0	(0.3, 2.7)
Conversion disorder	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Depression	4 (0.4)	1.0	(0.3, 2.6)	3 (0.3)	0.8	(0.2, 2.3)

14.27. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: White

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=970, TE[b]=3.9)			Placebo (N[a]=962, TE[b]=3.8)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Disorientation	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Generalised anxiety disorder	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Obsessive-compulsive disorder	0	0.0	(0.0, 0.9)	2 (0.2)	0.5	(0.1, 1.9)
Panic attack	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Sleep terror	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Suicidal ideation	3 (0.3)	0.8	(0.2, 2.3)	0	0.0	(0.0, 1.0)
Tic	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
RENAL AND URINARY DISORDERS	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Dysuria	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Amenorrhoea	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	3 (0.3)	0.8	(0.2, 2.3)	7 (0.7)	1.8	(0.7, 3.8)
Epistaxis	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Nasal congestion	2 (0.2)	0.5	(0.1, 1.9)	3 (0.3)	0.8	(0.2, 2.3)
Rhinorrhoea	2 (0.2)	0.5	(0.1, 1.9)	3 (0.3)	0.8	(0.2, 2.3)
Sneezing	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	9 (0.9)	2.3	(1.1, 4.4)	13 (1.4)	3.4	(1.8, 5.8)
Acne	2 (0.2)	0.5	(0.1, 1.9)	2 (0.2)	0.5	(0.1, 1.9)
Dermatitis contact	2 (0.2)	0.5	(0.1, 1.9)	1 (0.1)	0.3	(0.0, 1.5)
Eczema	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Rash	3 (0.3)	0.8	(0.2, 2.3)	4 (0.4)	1.0	(0.3, 2.7)
Rash maculo-papular	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Seborrhoeic dermatitis	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
Urticaria	2 (0.2)	0.5	(0.1, 1.9)	5 (0.5)	1.3	(0.4, 3.1)
SURGICAL AND MEDICAL PROCEDURES	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)
Wisdom teeth removal	1 (0.1)	0.3	(0.0, 1.4)	1 (0.1)	0.3	(0.0, 1.5)

14.27. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: White

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=970, TE[b]=3.9)			Placebo (N[a]=962, TE[b]=3.8)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])

Note: MedDRA (v24.0) coding dictionary applied.
Note: All Others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_unb_race1_ped6

14.28. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: Black or African American

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=52, TE[b]=0.2)			Placebo (N[a]=57, TE[b]=0.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	3 (5.8)	12.1	(2.5, 35.4)	3 (5.3)	11.5	(2.4, 33.6)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	0	0.0	(0.0, 14.9)	1 (1.8)	3.8	(0.1, 21.3)
Lymphadenopathy	0	0.0	(0.0, 14.9)	1 (1.8)	3.8	(0.1, 21.3)
EAR AND LABYRINTH DISORDERS	0	0.0	(0.0, 14.9)	1 (1.8)	3.8	(0.1, 21.3)
Conductive deafness	0	0.0	(0.0, 14.9)	1 (1.8)	3.8	(0.1, 21.3)
GASTROINTESTINAL DISORDERS	0	0.0	(0.0, 14.9)	1 (1.8)	3.8	(0.1, 21.3)
Diarrhoea	0	0.0	(0.0, 14.9)	1 (1.8)	3.8	(0.1, 21.3)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
Peripheral swelling	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
INFECTIONS AND INFESTATIONS	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
Body tinea	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
Contusion	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
Fall	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
PSYCHIATRIC DISORDERS	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
Anxiety	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
Depression	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	0	0.0	(0.0, 14.9)	1 (1.8)	3.8	(0.1, 21.3)
Rhinorrhoea	0	0.0	(0.0, 14.9)	1 (1.8)	3.8	(0.1, 21.3)

Note: MedDRA (v24.0) coding dictionary applied.
Note: All Others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
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14.29. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: All Others

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=109, TE[b]=0.4)			Placebo (N[a]=110, TE[b]=0.4)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	9 (8.3)	20.8	(9.5, 39.4)	10 (9.1)	23.3	(11.2, 42.9)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	3 (2.8)	6.9	(1.4, 20.2)	0	0.0	(0.0, 8.6)
Lymphadenopathy	3 (2.8)	6.9	(1.4, 20.2)	0	0.0	(0.0, 8.6)
GASTROINTESTINAL DISORDERS	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
Abdominal pain	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (0.9)	2.3	(0.1, 12.8)	2 (1.8)	4.7	(0.6, 16.9)
Chills	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
Fatigue	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
Injection site pain	1 (0.9)	2.3	(0.1, 12.8)	2 (1.8)	4.7	(0.6, 16.9)
Injection site swelling	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
Pyrexia	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
INFECTIONS AND INFESTATIONS	0	0.0	(0.0, 8.5)	2 (1.8)	4.7	(0.6, 16.9)
Cellulitis	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)
Subcutaneous abscess	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)
Hand fracture	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)
Musculoskeletal chest pain	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)
Fibroadenoma of breast	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)
NERVOUS SYSTEM DISORDERS	2 (1.8)	4.6	(0.6, 16.7)	1 (0.9)	2.3	(0.1, 13.0)
Headache	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)
Migraine	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
Paraesthesia	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
PSYCHIATRIC DISORDERS	2 (1.8)	4.6	(0.6, 16.7)	0	0.0	(0.0, 8.6)
Depression	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
Suicidal ideation	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	0	0.0	(0.0, 8.5)	3 (2.7)	7.0	(1.4, 20.5)
Acne	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)
Pityriasis rosea	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)
Rash	0	0.0	(0.0, 8.5)	1 (0.9)	2.3	(0.1, 13.0)

14.29. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: All Others

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=109, TE[b]=0.4)			Placebo (N[a]=110, TE[b]=0.4)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])

Note: MedDRA (v24.0) coding dictionary applied.
Note: All Others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_unb_race1_ped6

14.30. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Sex – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Sex: Male

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=567, TE[b]=2.3)			Placebo (N[a]=585, TE[b]=2.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	42 (7.4)	18.2	(13.1, 24.5)	57 (9.7)	24.4	(18.5, 31.7)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	8 (1.4)	3.5	(1.5, 6.8)	0	0.0	(0.0, 1.6)
Lymphadenopathy	8 (1.4)	3.5	(1.5, 6.8)	0	0.0	(0.0, 1.6)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Spine malformation	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
EAR AND LABYRINTH DISORDERS	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Ear pain	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
EYE DISORDERS	2 (0.4)	0.9	(0.1, 3.1)	1 (0.2)	0.4	(0.0, 2.4)
Eye pain	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Eyelid rash	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Retinal haemorrhage	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
GASTROINTESTINAL DISORDERS	6 (1.1)	2.6	(1.0, 5.6)	3 (0.5)	1.3	(0.3, 3.8)
Aphthous ulcer	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Diarrhoea	2 (0.4)	0.9	(0.1, 3.1)	1 (0.2)	0.4	(0.0, 2.4)
Lip swelling	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Mouth swelling	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Nausea	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Oral mucosal blistering	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Tooth impacted	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Toothache	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Vomiting	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	10 (1.8)	4.3	(2.1, 8.0)	7 (1.2)	3.0	(1.2, 6.2)
Fatigue	5 (0.9)	2.2	(0.7, 5.0)	2 (0.3)	0.9	(0.1, 3.1)
Injection site pain	5 (0.9)	2.2	(0.7, 5.0)	4 (0.7)	1.7	(0.5, 4.4)
Injection site swelling	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Nodule	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Oedema peripheral	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Pyrexia	3 (0.5)	1.3	(0.3, 3.8)	0	0.0	(0.0, 1.6)
IMMUNE SYSTEM DISORDERS	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Food allergy	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
INFECTIONS AND INFESTATIONS	3 (0.5)	1.3	(0.3, 3.8)	7 (1.2)	3.0	(1.2, 6.2)
Anal abscess	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)

14.30. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Sex – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Sex: Male

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=567, TE[b]=2.3)			Placebo (N[a]=585, TE[b]=2.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Appendicitis	0	0.0	(0.0, 1.6)	2 (0.3)	0.9	(0.1, 3.1)
Candida infection	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Cellulitis	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Conjunctivitis	0	0.0	(0.0, 1.6)	2 (0.3)	0.9	(0.1, 3.1)
Ear infection	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Focal peritonitis	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Paronychia	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Pilonidal cyst	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	8 (1.4)	3.5	(1.5, 6.8)	13 (2.2)	5.6	(3.0, 9.5)
Accident	1 (0.2)	0.4	(0.0, 2.4)	1 (0.2)	0.4	(0.0, 2.4)
Bone contusion	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Clavicle fracture	1 (0.2)	0.4	(0.0, 2.4)	1 (0.2)	0.4	(0.0, 2.4)
Concussion	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Contusion	1 (0.2)	0.4	(0.0, 2.4)	1 (0.2)	0.4	(0.0, 2.4)
Fall	1 (0.2)	0.4	(0.0, 2.4)	2 (0.3)	0.9	(0.1, 3.1)
Hand fracture	0	0.0	(0.0, 1.6)	2 (0.3)	0.9	(0.1, 3.1)
Humerus fracture	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Ligament sprain	0	0.0	(0.0, 1.6)	2 (0.3)	0.9	(0.1, 3.1)
Lip injury	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Meniscus injury	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Muscle strain	1 (0.2)	0.4	(0.0, 2.4)	1 (0.2)	0.4	(0.0, 2.4)
Patella fracture	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Procedural pain	0	0.0	(0.0, 1.6)	2 (0.3)	0.9	(0.1, 3.1)
Radius fracture	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Skin laceration	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Tibia fracture	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Tooth fracture	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Upper limb fracture	1 (0.2)	0.4	(0.0, 2.4)	1 (0.2)	0.4	(0.0, 2.4)
INVESTIGATIONS	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
SARS-CoV-2 antibody test positive	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	4 (0.7)	1.7	(0.5, 4.4)	8 (1.4)	3.4	(1.5, 6.8)
Arthralgia	1 (0.2)	0.4	(0.0, 2.4)	2 (0.3)	0.9	(0.1, 3.1)
Joint swelling	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Myalgia	2 (0.4)	0.9	(0.1, 3.1)	1 (0.2)	0.4	(0.0, 2.4)
Neck pain	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)

14.30. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Sex – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Sex: Male

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=567, TE[b]=2.3)			Placebo (N[a]=585, TE[b]=2.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Pain in extremity	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Tendonitis	0	0.0	(0.0, 1.6)	3 (0.5)	1.3	(0.3, 3.8)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Hair follicle tumour benign	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
NERVOUS SYSTEM DISORDERS	5 (0.9)	2.2	(0.7, 5.0)	5 (0.9)	2.1	(0.7, 5.0)
Dizziness	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Headache	2 (0.4)	0.9	(0.1, 3.1)	2 (0.3)	0.9	(0.1, 3.1)
Paraesthesia	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Presyncope	1 (0.2)	0.4	(0.0, 2.4)	1 (0.2)	0.4	(0.0, 2.4)
Syncope	1 (0.2)	0.4	(0.0, 2.4)	1 (0.2)	0.4	(0.0, 2.4)
PSYCHIATRIC DISORDERS	5 (0.9)	2.2	(0.7, 5.0)	3 (0.5)	1.3	(0.3, 3.8)
Anxiety	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Depression	2 (0.4)	0.9	(0.1, 3.1)	2 (0.3)	0.9	(0.1, 3.1)
Disorientation	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Obsessive-compulsive disorder	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Panic attack	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Suicidal ideation	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1 (0.2)	0.4	(0.0, 2.4)	2 (0.3)	0.9	(0.1, 3.1)
Nasal congestion	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Rhinorrhoea	1 (0.2)	0.4	(0.0, 2.4)	1 (0.2)	0.4	(0.0, 2.4)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	3 (0.5)	1.3	(0.3, 3.8)	11 (1.9)	4.7	(2.4, 8.4)
Acne	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Dermatitis contact	1 (0.2)	0.4	(0.0, 2.4)	1 (0.2)	0.4	(0.0, 2.4)
Eczema	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Pityriasis rosea	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Rash	2 (0.4)	0.9	(0.1, 3.1)	3 (0.5)	1.3	(0.3, 3.8)
Rash maculo-papular	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
Urticaria	0	0.0	(0.0, 1.6)	4 (0.7)	1.7	(0.5, 4.4)

14.30. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Sex – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Sex: Male

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=567, TE[b]=2.3)			Placebo (N[a]=585, TE[b]=2.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_unb_sex1_ped6

14.31. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Sex – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Sex: Female

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=564, TE[b]=2.3)			Placebo (N[a]=544, TE[b]=2.2)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	53 (9.4)	23.5	(17.6, 30.7)	56 (10.3)	25.7	(19.4, 33.4)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.2)	0.4	(0.0, 2.5)	2 (0.4)	0.9	(0.1, 3.3)
Lymphadenopathy	1 (0.2)	0.4	(0.0, 2.5)	2 (0.4)	0.9	(0.1, 3.3)
EAR AND LABYRINTH DISORDERS	1 (0.2)	0.4	(0.0, 2.5)	2 (0.4)	0.9	(0.1, 3.3)
Cerumen impaction	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Conductive deafness	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Ear pain	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
GASTROINTESTINAL DISORDERS	8 (1.4)	3.5	(1.5, 7.0)	5 (0.9)	2.3	(0.7, 5.4)
Abdominal pain	2 (0.4)	0.9	(0.1, 3.2)	1 (0.2)	0.5	(0.0, 2.6)
Constipation	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Diarrhoea	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Gastritis	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Mouth ulceration	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Nausea	4 (0.7)	1.8	(0.5, 4.5)	3 (0.6)	1.4	(0.3, 4.0)
Rectal prolapse	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Vomiting	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	7 (1.2)	3.1	(1.2, 6.4)	5 (0.9)	2.3	(0.7, 5.4)
Chills	2 (0.4)	0.9	(0.1, 3.2)	1 (0.2)	0.5	(0.0, 2.6)
Fatigue	3 (0.5)	1.3	(0.3, 3.9)	2 (0.4)	0.9	(0.1, 3.3)
Injection site pain	3 (0.5)	1.3	(0.3, 3.9)	4 (0.7)	1.8	(0.5, 4.7)
Injection site swelling	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Peripheral swelling	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Pyrexia	3 (0.5)	1.3	(0.3, 3.9)	0	0.0	(0.0, 1.7)
Vessel puncture site pain	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
IMMUNE SYSTEM DISORDERS	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Seasonal allergy	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
INFECTIONS AND INFESTATIONS	7 (1.2)	3.1	(1.2, 6.4)	2 (0.4)	0.9	(0.1, 3.3)
Body tinea	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Ear infection	2 (0.4)	0.9	(0.1, 3.2)	0	0.0	(0.0, 1.7)
Infectious mononucleosis	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Otitis externa	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Otitis media	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Pilonidal cyst	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Subcutaneous abscess	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Tinea capitis	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)

14.31. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Sex – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Sex: Female

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=564, TE[b]=2.3)			Placebo (N[a]=544, TE[b]=2.2)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Vulval abscess	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Vulvovaginal mycotic infection	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	7 (1.2)	3.1	(1.2, 6.4)	12 (2.2)	5.5	(2.8, 9.6)
Ankle fracture	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Concussion	2 (0.4)	0.9	(0.1, 3.2)	4 (0.7)	1.8	(0.5, 4.7)
Contusion	1 (0.2)	0.4	(0.0, 2.5)	1 (0.2)	0.5	(0.0, 2.6)
Fall	1 (0.2)	0.4	(0.0, 2.5)	3 (0.6)	1.4	(0.3, 4.0)
Femur fracture	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Foot fracture	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Hand fracture	1 (0.2)	0.4	(0.0, 2.5)	2 (0.4)	0.9	(0.1, 3.3)
Ligament sprain	1 (0.2)	0.4	(0.0, 2.5)	2 (0.4)	0.9	(0.1, 3.3)
Procedural pain	2 (0.4)	0.9	(0.1, 3.2)	1 (0.2)	0.5	(0.0, 2.6)
Tooth fracture	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	4 (0.7)	1.8	(0.5, 4.5)	6 (1.1)	2.8	(1.0, 6.0)
Arthralgia	1 (0.2)	0.4	(0.0, 2.5)	2 (0.4)	0.9	(0.1, 3.3)
Back pain	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Musculoskeletal chest pain	1 (0.2)	0.4	(0.0, 2.5)	1 (0.2)	0.5	(0.0, 2.6)
Myalgia	1 (0.2)	0.4	(0.0, 2.5)	1 (0.2)	0.5	(0.0, 2.6)
Osteochondrosis	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Tendonitis	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	0	0.0	(0.0, 1.6)	3 (0.6)	1.4	(0.3, 4.0)
Fibroadenoma of breast	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Melanocytic naevus	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Skin papilloma	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
NERVOUS SYSTEM DISORDERS	8 (1.4)	3.5	(1.5, 7.0)	8 (1.5)	3.7	(1.6, 7.2)
Dizziness	2 (0.4)	0.9	(0.1, 3.2)	0	0.0	(0.0, 1.7)
Headache	3 (0.5)	1.3	(0.3, 3.9)	5 (0.9)	2.3	(0.7, 5.4)
Migraine	3 (0.5)	1.3	(0.3, 3.9)	0	0.0	(0.0, 1.7)
Presyncope	0	0.0	(0.0, 1.6)	3 (0.6)	1.4	(0.3, 4.0)
PSYCHIATRIC DISORDERS	12 (2.1)	5.3	(2.7, 9.3)	10 (1.8)	4.6	(2.2, 8.5)
Anxiety	4 (0.7)	1.8	(0.5, 4.5)	5 (0.9)	2.3	(0.7, 5.4)
Attention deficit hyperactivity disorder	2 (0.4)	0.9	(0.1, 3.2)	4 (0.7)	1.8	(0.5, 4.7)
Conversion disorder	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Depression	4 (0.7)	1.8	(0.5, 4.5)	1 (0.2)	0.5	(0.0, 2.6)

14.31. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Sex – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Sex: Female

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=564, TE[b]=2.3)			Placebo (N[a]=544, TE[b]=2.2)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Generalised anxiety disorder	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Obsessive-compulsive disorder	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Sleep terror	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Suicidal ideation	3 (0.5)	1.3	(0.3, 3.9)	0	0.0	(0.0, 1.7)
Tic	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
RENAL AND URINARY DISORDERS	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Dysuria	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Amenorrhoea	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	2 (0.4)	0.9	(0.1, 3.2)	6 (1.1)	2.8	(1.0, 6.0)
Epistaxis	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Nasal congestion	2 (0.4)	0.9	(0.1, 3.2)	2 (0.4)	0.9	(0.1, 3.3)
Rhinorrhoea	1 (0.2)	0.4	(0.0, 2.5)	3 (0.6)	1.4	(0.3, 4.0)
Sneezing	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	6 (1.1)	2.7	(1.0, 5.8)	5 (0.9)	2.3	(0.7, 5.4)
Acne	2 (0.4)	0.9	(0.1, 3.2)	2 (0.4)	0.9	(0.1, 3.3)
Dermatitis contact	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Rash	1 (0.2)	0.4	(0.0, 2.5)	2 (0.4)	0.9	(0.1, 3.3)
Seborrhoeic dermatitis	0	0.0	(0.0, 1.6)	1 (0.2)	0.5	(0.0, 2.6)
Urticaria	2 (0.4)	0.9	(0.1, 3.2)	1 (0.2)	0.5	(0.0, 2.6)
SURGICAL AND MEDICAL PROCEDURES	1 (0.2)	0.4	(0.0, 2.5)	1 (0.2)	0.5	(0.0, 2.6)
Wisdom teeth removal	1 (0.2)	0.4	(0.0, 2.5)	1 (0.2)	0.5	(0.0, 2.6)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_unb_sex1_ped6

14.32. Incidence Rates of at Least 1 Related Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	36 (3.2)	7.9	(5.5, 10.9)	24 (2.1)	5.3	(3.4, 7.9)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	7 (0.6)	1.5	(0.6, 3.2)	1 (0.1)	0.2	(0.0, 1.2)
Lymphadenopathy	7 (0.6)	1.5	(0.6, 3.2)	1 (0.1)	0.2	(0.0, 1.2)
EAR AND LABYRINTH DISORDERS	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Conductive deafness	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
EYE DISORDERS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Eyelid rash	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
GASTROINTESTINAL DISORDERS	11 (1.0)	2.4	(1.2, 4.3)	2 (0.2)	0.4	(0.1, 1.6)
Abdominal pain	2 (0.2)	0.4	(0.1, 1.6)	0	0.0	(0.0, 0.8)
Diarrhoea	2 (0.2)	0.4	(0.1, 1.6)	1 (0.1)	0.2	(0.0, 1.2)
Lip swelling	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Mouth swelling	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Nausea	5 (0.4)	1.1	(0.4, 2.6)	1 (0.1)	0.2	(0.0, 1.2)
Oral mucosal blistering	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Vomiting	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	16 (1.4)	3.5	(2.0, 5.7)	10 (0.9)	2.2	(1.1, 4.1)
Chills	2 (0.2)	0.4	(0.1, 1.6)	1 (0.1)	0.2	(0.0, 1.2)
Fatigue	8 (0.7)	1.7	(0.8, 3.4)	3 (0.3)	0.7	(0.1, 1.9)
Injection site pain	8 (0.7)	1.7	(0.8, 3.4)	8 (0.7)	1.8	(0.8, 3.5)
Injection site swelling	2 (0.2)	0.4	(0.1, 1.6)	0	0.0	(0.0, 0.8)
Peripheral swelling	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Pyrexia	6 (0.5)	1.3	(0.5, 2.9)	0	0.0	(0.0, 0.8)
INVESTIGATIONS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
SARS-CoV-2 antibody test positive	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	4 (0.4)	0.9	(0.2, 2.2)	1 (0.1)	0.2	(0.0, 1.2)
Musculoskeletal chest pain	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Myalgia	3 (0.3)	0.7	(0.1, 1.9)	1 (0.1)	0.2	(0.0, 1.2)
NERVOUS SYSTEM DISORDERS	5 (0.4)	1.1	(0.4, 2.6)	5 (0.4)	1.1	(0.4, 2.6)
Dizziness	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
Headache	3 (0.3)	0.7	(0.1, 1.9)	3 (0.3)	0.7	(0.1, 1.9)

14.32. Incidence Rates of at Least 1 Related Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Migraine	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Presyncope	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
PSYCHIATRIC DISORDERS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Disorientation	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Rhinorrhoea	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	2 (0.2)	0.4	(0.1, 1.6)	7 (0.6)	1.6	(0.6, 3.2)
Rash	1 (0.1)	0.2	(0.0, 1.2)	2 (0.2)	0.4	(0.1, 1.6)
Rash maculo-papular	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Urticaria	1 (0.1)	0.2	(0.0, 1.2)	4 (0.4)	0.9	(0.2, 2.3)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_rel_unb1_ped6

14.33. Incidence Rates of at Least 1 Severe Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	13 (1.1)	2.8	(1.5, 4.9)	5 (0.4)	1.1	(0.4, 2.6)
GASTROINTESTINAL DISORDERS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Abdominal pain	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Constipation	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	2 (0.2)	0.4	(0.1, 1.6)	1 (0.1)	0.2	(0.0, 1.2)
Fatigue	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Pyrexia	2 (0.2)	0.4	(0.1, 1.6)	0	0.0	(0.0, 0.8)
INFECTIONS AND INFESTATIONS	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
Anal abscess	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Appendicitis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	2 (0.2)	0.4	(0.1, 1.6)	2 (0.2)	0.4	(0.1, 1.6)
Femur fracture	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Patella fracture	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Procedural pain	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Upper limb fracture	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Arthralgia	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
NERVOUS SYSTEM DISORDERS	2 (0.2)	0.4	(0.1, 1.6)	1 (0.1)	0.2	(0.0, 1.2)
Headache	1 (0.1)	0.2	(0.0, 1.2)	1 (0.1)	0.2	(0.0, 1.2)
Migraine	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
PSYCHIATRIC DISORDERS	4 (0.4)	0.9	(0.2, 2.2)	0	0.0	(0.0, 0.8)
Anxiety	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Depression	2 (0.2)	0.4	(0.1, 1.6)	0	0.0	(0.0, 0.8)
Suicidal ideation	2 (0.2)	0.4	(0.1, 1.6)	0	0.0	(0.0, 0.8)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Urticaria	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)

14.33. Incidence Rates of at Least 1 Severe Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
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14.34. Incidence Rates of at Least 1 Life-Threatening Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	2 (0.2)	0.4	(0.1, 1.6)	1 (0.1)	0.2	(0.0, 1.2)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Pyrexia	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
INFECTIONS AND INFESTATIONS	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Appendicitis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
Focal peritonitis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.2)
PSYCHIATRIC DISORDERS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Suicidal ideation	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File:
./nda2 unblinded/C4591001 S Peds/adae s131 lif unb1 ped6

14.35. Incidence Rates of at Least 1 Adverse Event From Unblinding Date to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2 – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1107, TE[b]=3.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Any event	18 (1.6)	5.4	(3.2, 8.5)
CARDIAC DISORDERS	1 (0.1)	0.3	(0.0, 1.7)
Tachycardia	1 (0.1)	0.3	(0.0, 1.7)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (0.1)	0.3	(0.0, 1.7)
Syringomyelia	1 (0.1)	0.3	(0.0, 1.7)
GASTROINTESTINAL DISORDERS	3 (0.3)	0.9	(0.2, 2.6)
Abdominal pain upper	2 (0.2)	0.6	(0.1, 2.2)
Aphthous ulcer	1 (0.1)	0.3	(0.0, 1.7)
Nausea	1 (0.1)	0.3	(0.0, 1.7)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	4 (0.4)	1.2	(0.3, 3.1)
Fatigue	2 (0.2)	0.6	(0.1, 2.2)
Injection site pain	3 (0.3)	0.9	(0.2, 2.6)
Pain	1 (0.1)	0.3	(0.0, 1.7)
Pyrexia	2 (0.2)	0.6	(0.1, 2.2)
INFECTIONS AND INFESTATIONS	3 (0.3)	0.9	(0.2, 2.6)
Appendicitis	2 (0.2)	0.6	(0.1, 2.2)
Otitis media	1 (0.1)	0.3	(0.0, 1.7)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	2 (0.2)	0.6	(0.1, 2.2)
Hand fracture	1 (0.1)	0.3	(0.0, 1.7)
Upper limb fracture	1 (0.1)	0.3	(0.0, 1.7)
NERVOUS SYSTEM DISORDERS	6 (0.5)	1.8	(0.7, 3.9)
Dizziness	2 (0.2)	0.6	(0.1, 2.2)
Headache	2 (0.2)	0.6	(0.1, 2.2)
Presyncope	2 (0.2)	0.6	(0.1, 2.2)
Syncope	1 (0.1)	0.3	(0.0, 1.7)
PSYCHIATRIC DISORDERS	1 (0.1)	0.3	(0.0, 1.7)
Anxiety	1 (0.1)	0.3	(0.0, 1.7)

14.35. Incidence Rates of at Least 1 Adverse Event From Unblinding Date to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2 – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N^a=1107, TE^b=3.3)		
System Organ Class Preferred Term	**n^c (%)**	**IR^d**	**(95% CI^e)**

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the unblinding date to data cutoff date. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
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14.36. Incidence Rates of at Least 1 Related Adverse Event From Unblinding Date to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2 – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1107, TE[b]=3.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Any event	4 (0.4)	1.2	(0.3, 3.1)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	4 (0.4)	1.2	(0.3, 3.1)
Fatigue	2 (0.2)	0.6	(0.1, 2.2)
Injection site pain	3 (0.3)	0.9	(0.2, 2.6)
Pain	1 (0.1)	0.3	(0.0, 1.7)
Pyrexia	2 (0.2)	0.6	(0.1, 2.2)
NERVOUS SYSTEM DISORDERS	2 (0.2)	0.6	(0.1, 2.2)
Dizziness	1 (0.1)	0.3	(0.0, 1.7)
Headache	2 (0.2)	0.6	(0.1, 2.2)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the unblinding date to data cutoff date. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:41)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_rel_ubct1_ped6

14.37. Incidence Rates of at Least 1 Severe Adverse Event From Unblinding Date to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2 – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1107, TE[b]=3.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Any event	3 (0.3)	0.9	(0.2, 2.6)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (0.1)	0.3	(0.0, 1.7)
Syringomyelia	1 (0.1)	0.3	(0.0, 1.7)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	2 (0.2)	0.6	(0.1, 2.2)
Pyrexia	2 (0.2)	0.6	(0.1, 2.2)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the unblinding date to data cutoff date. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:41)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File:
./nda2 unblinded/C4591001 S Peds/adae s131 sev ubct1 ped6

14.38. Number (%) of Subjects Reporting at Least 1 Related Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Any event	34 (3.1)	(2.1, 4.2)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	7 (0.6)	(0.3, 1.3)
Lymphadenopathy	7 (0.6)	(0.3, 1.3)
GASTROINTESTINAL DISORDERS	11 (1.0)	(0.5, 1.8)
Nausea	5 (0.4)	(0.1, 1.0)
Abdominal pain	2 (0.2)	(0.0, 0.6)
Diarrhoea	2 (0.2)	(0.0, 0.6)
Lip swelling	1 (0.1)	(0.0, 0.5)
Mouth swelling	1 (0.1)	(0.0, 0.5)
Oral mucosal blistering	1 (0.1)	(0.0, 0.5)
Vomiting	1 (0.1)	(0.0, 0.5)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	15 (1.3)	(0.8, 2.2)
Fatigue	8 (0.7)	(0.3, 1.4)
Injection site pain	8 (0.7)	(0.3, 1.4)
Pyrexia	5 (0.4)	(0.1, 1.0)
Chills	2 (0.2)	(0.0, 0.6)
Injection site swelling	2 (0.2)	(0.0, 0.6)
Peripheral swelling	1 (0.1)	(0.0, 0.5)
INVESTIGATIONS	1 (0.1)	(0.0, 0.5)
SARS-CoV-2 antibody test positive	1 (0.1)	(0.0, 0.5)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	4 (0.4)	(0.1, 0.9)
Myalgia	3 (0.3)	(0.1, 0.8)
Musculoskeletal chest pain	1 (0.1)	(0.0, 0.5)
NERVOUS SYSTEM DISORDERS	5 (0.4)	(0.1, 1.0)
Headache	3 (0.3)	(0.1, 0.8)
Dizziness	1 (0.1)	(0.0, 0.5)
Migraine	1 (0.1)	(0.0, 0.5)
PSYCHIATRIC DISORDERS	1 (0.1)	(0.0, 0.5)
Disorientation	1 (0.1)	(0.0, 0.5)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (0.1)	(0.0, 0.5)
Urticaria	1 (0.1)	(0.0, 0.5)

14.38. Number (%) of Subjects Reporting at Least 1 Related Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects 12 Through 15 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1113)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])

Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_rel_6m1_ped6

14.39. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 3 to 7 Days After Dose 3, by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1010)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Any event	198 (19.6)	(17.2, 22.2)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.1)	(0.0, 0.6)
Lymphadenitis	1 (0.1)	(0.0, 0.6)
EAR AND LABYRINTH DISORDERS	1 (0.1)	(0.0, 0.6)
Motion sickness	1 (0.1)	(0.0, 0.6)
GASTROINTESTINAL DISORDERS	9 (0.9)	(0.4, 1.7)
Nausea	7 (0.7)	(0.3, 1.4)
Vomiting	2 (0.2)	(0.0, 0.7)
Abdominal pain upper	1 (0.1)	(0.0, 0.6)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	178 (17.6)	(15.3, 20.1)
Injection site pain	131 (13.0)	(11.0, 15.2)
Fatigue	68 (6.7)	(5.3, 8.5)
Chills	29 (2.9)	(1.9, 4.1)
Pyrexia	28 (2.8)	(1.8, 4.0)
Pain	17 (1.7)	(1.0, 2.7)
Injection site erythema	3 (0.3)	(0.1, 0.9)
Injection site swelling	3 (0.3)	(0.1, 0.9)
Injection site bruising	2 (0.2)	(0.0, 0.7)
Malaise	2 (0.2)	(0.0, 0.7)
Injection site hypoaesthesia	1 (0.1)	(0.0, 0.6)
Non-cardiac chest pain	1 (0.1)	(0.0, 0.6)
Thirst	1 (0.1)	(0.0, 0.6)
INFECTIONS AND INFESTATIONS	1 (0.1)	(0.0, 0.6)
Paronychia	1 (0.1)	(0.0, 0.6)
Skin candida	1 (0.1)	(0.0, 0.6)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	2 (0.2)	(0.0, 0.7)
Joint injury	1 (0.1)	(0.0, 0.6)
Muscle strain	1 (0.1)	(0.0, 0.6)
INVESTIGATIONS	2 (0.2)	(0.0, 0.7)
Body temperature increased	2 (0.2)	(0.0, 0.7)
METABOLISM AND NUTRITION DISORDERS	1 (0.1)	(0.0, 0.6)
Decreased appetite	1 (0.1)	(0.0, 0.6)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	24 (2.4)	(1.5, 3.5)

14.39. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 3 to 7 Days After Dose 3, by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1010)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Myalgia	18 (1.8)	(1.1, 2.8)
Pain in extremity	5 (0.5)	(0.2, 1.2)
Musculoskeletal stiffness	1 (0.1)	(0.0, 0.6)
NERVOUS SYSTEM DISORDERS	42 (4.2)	(3.0, 5.6)
Headache	40 (4.0)	(2.8, 5.4)
Dizziness	2 (0.2)	(0.0, 0.7)
Syncope	1 (0.1)	(0.0, 0.6)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1 (0.1)	(0.0, 0.6)
Rhinorrhoea	1 (0.1)	(0.0, 0.6)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	2 (0.2)	(0.0, 0.7)
Hyperhidrosis	1 (0.1)	(0.0, 0.6)
Photosensitivity reaction	1 (0.1)	(0.0, 0.6)

Note: Dose 3 = first dose of BNT162b2 (30 µg).
Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
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14.40. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 4 to 7 Days After Dose 4, by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=992)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Any event	138 (13.9)	(11.8, 16.2)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.1)	(0.0, 0.6)
Lymphadenopathy	1 (0.1)	(0.0, 0.6)
CARDIAC DISORDERS	1 (0.1)	(0.0, 0.6)
Myocarditis	1 (0.1)	(0.0, 0.6)
GASTROINTESTINAL DISORDERS	12 (1.2)	(0.6, 2.1)
Nausea	7 (0.7)	(0.3, 1.4)
Vomiting	5 (0.5)	(0.2, 1.2)
Abdominal pain upper	1 (0.1)	(0.0, 0.6)
Diarrhoea	1 (0.1)	(0.0, 0.6)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	120 (12.1)	(10.1, 14.3)
Injection site pain	60 (6.0)	(4.6, 7.7)
Fatigue	56 (5.6)	(4.3, 7.3)
Pyrexia	41 (4.1)	(3.0, 5.6)
Chills	21 (2.1)	(1.3, 3.2)
Pain	21 (2.1)	(1.3, 3.2)
Malaise	5 (0.5)	(0.2, 1.2)
Injection site bruising	2 (0.2)	(0.0, 0.7)
Injection site erythema	2 (0.2)	(0.0, 0.7)
Axillary pain	1 (0.1)	(0.0, 0.6)
Chest discomfort	1 (0.1)	(0.0, 0.6)
Chest pain	1 (0.1)	(0.0, 0.6)
Injection site reaction	1 (0.1)	(0.0, 0.6)
Injection site swelling	1 (0.1)	(0.0, 0.6)
INFECTIONS AND INFESTATIONS	3 (0.3)	(0.1, 0.9)
Appendicitis	1 (0.1)	(0.0, 0.6)
Pharyngitis streptococcal	1 (0.1)	(0.0, 0.6)
Sinusitis	1 (0.1)	(0.0, 0.6)
INVESTIGATIONS	2 (0.2)	(0.0, 0.7)
Body temperature increased	2 (0.2)	(0.0, 0.7)
METABOLISM AND NUTRITION DISORDERS	1 (0.1)	(0.0, 0.6)
Vitamin D deficiency	1 (0.1)	(0.0, 0.6)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	25 (2.5)	(1.6, 3.7)

14.40. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 4 to 7 Days After Dose 4, by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=992)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Myalgia	21 (2.1)	(1.3, 3.2)
Pain in extremity	3 (0.3)	(0.1, 0.9)
Arthralgia	2 (0.2)	(0.0, 0.7)
Musculoskeletal chest pain	1 (0.1)	(0.0, 0.6)
Neck pain	1 (0.1)	(0.0, 0.6)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (0.1)	(0.0, 0.6)
Skin papilloma	1 (0.1)	(0.0, 0.6)
NERVOUS SYSTEM DISORDERS	40 (4.0)	(2.9, 5.5)
Headache	38 (3.8)	(2.7, 5.2)
Dizziness	2 (0.2)	(0.0, 0.7)
Epilepsy	1 (0.1)	(0.0, 0.6)
PSYCHIATRIC DISORDERS	1 (0.1)	(0.0, 0.6)
Major depression	1 (0.1)	(0.0, 0.6)
RENAL AND URINARY DISORDERS	1 (0.1)	(0.0, 0.6)
Dysuria	1 (0.1)	(0.0, 0.6)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1 (0.1)	(0.0, 0.6)
Cough	1 (0.1)	(0.0, 0.6)
Nasal congestion	1 (0.1)	(0.0, 0.6)

Note: Dose 4 = second dose of BNT162b2 (30 µg).
Note: Subjects who did not receive Dose 4 or who received a different vaccine at Dose 3 and Dose 4 were excluded from this table.
Note: MedDRA (v24.0) coding dictionary applied.
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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_7d4_1_ped6

14.41. Incidence Rates of at Least 1 Related Adverse Event From Dose 3 to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1010, TE[b]=2.9)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Any event	242 (24.0)	82.5	(72.4, 93.5)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	2 (0.2)	0.7	(0.1, 2.5)
Lymphadenitis	1 (0.1)	0.3	(0.0, 1.9)
Lymphadenopathy	1 (0.1)	0.3	(0.0, 1.9)
GASTROINTESTINAL DISORDERS	18 (1.8)	6.1	(3.6, 9.7)
Abdominal pain upper	2 (0.2)	0.7	(0.1, 2.5)
Diarrhoea	1 (0.1)	0.3	(0.0, 1.9)
Nausea	12 (1.2)	4.1	(2.1, 7.1)
Vomiting	6 (0.6)	2.0	(0.8, 4.4)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	223 (22.1)	76.0	(66.3, 86.6)
Axillary pain	1 (0.1)	0.3	(0.0, 1.9)
Chills	45 (4.5)	15.3	(11.2, 20.5)
Fatigue	104 (10.3)	35.4	(29.0, 42.9)
Injection site bruising	3 (0.3)	1.0	(0.2, 3.0)
Injection site erythema	5 (0.5)	1.7	(0.6, 4.0)
Injection site hypoaesthesia	1 (0.1)	0.3	(0.0, 1.9)
Injection site pain	157 (15.5)	53.5	(45.5, 62.5)
Injection site reaction	1 (0.1)	0.3	(0.0, 1.9)
Injection site swelling	4 (0.4)	1.4	(0.4, 3.5)
Malaise	7 (0.7)	2.4	(1.0, 4.9)
Non-cardiac chest pain	1 (0.1)	0.3	(0.0, 1.9)
Pain	35 (3.5)	11.9	(8.3, 16.6)
Pyrexia	63 (6.2)	21.5	(16.5, 27.5)
Thirst	1 (0.1)	0.3	(0.0, 1.9)
INFECTIONS AND INFESTATIONS	1 (0.1)	0.3	(0.0, 1.9)
Appendicitis	1 (0.1)	0.3	(0.0, 1.9)
INVESTIGATIONS	3 (0.3)	1.0	(0.2, 3.0)
Body temperature increased	3 (0.3)	1.0	(0.2, 3.0)
METABOLISM AND NUTRITION DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Decreased appetite	1 (0.1)	0.3	(0.0, 1.9)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	46 (4.6)	15.7	(11.5, 20.9)
Arthralgia	2 (0.2)	0.7	(0.1, 2.5)
Musculoskeletal chest pain	1 (0.1)	0.3	(0.0, 1.9)

14.41. Incidence Rates of at Least 1 Related Adverse Event From Dose 3 to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1010, TE[b]=2.9)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Musculoskeletal stiffness	1 (0.1)	0.3	(0.0, 1.9)
Myalgia	37 (3.7)	12.6	(8.9, 17.4)
Pain in extremity	8 (0.8)	2.7	(1.2, 5.4)
NERVOUS SYSTEM DISORDERS	73 (7.2)	24.9	(19.5, 31.3)
Dizziness	4 (0.4)	1.4	(0.4, 3.5)
Headache	70 (6.9)	23.8	(18.6, 30.1)
Syncope	1 (0.1)	0.3	(0.0, 1.9)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Rhinorrhoea	1 (0.1)	0.3	(0.0, 1.9)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Hyperhidrosis	1 (0.1)	0.3	(0.0, 1.9)

Note: Dose 3 = First dose of BNT162b2 (30 µg).
Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 3 to data cutoff date. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_rel_cut1_ped6

14.42. Number (%) of Subjects Reporting at Least 1 Immediate Adverse Event After Vaccination (Dose 3/4), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=1010)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Any event	7 (0.7)	(0.3, 1.4)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	7 (0.7)	(0.3, 1.4)
Injection site pain	6 (0.6)	(0.2, 1.3)
Injection site erythema	1 (0.1)	(0.0, 0.6)

Note: Dose 3 = first dose of BNT162b2 (30 µg), Dose 4 = second dose of BNT162b2 (30 µg).
Note: MedDRA (v24.0) coding dictionary applied.
Note: Immediate AE refers to an AE reported in the 30-minute observation period after vaccination.
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: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s130_imm_cr1_ped6

14.43. Incidence Rates of at Least 1 Severe Adverse Event From Dose 3 to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1010, TE[b]=2.9)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Any event	12 (1.2)	4.1	(2.1, 7.1)
CARDIAC DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Myocarditis	1 (0.1)	0.3	(0.0, 1.9)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	6 (0.6)	2.0	(0.8, 4.4)
Fatigue	2 (0.2)	0.7	(0.1, 2.5)
Malaise	1 (0.1)	0.3	(0.0, 1.9)
Pyrexia	3 (0.3)	1.0	(0.2, 3.0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	3 (0.3)	1.0	(0.2, 3.0)
Concussion	1 (0.1)	0.3	(0.0, 1.9)
Muscle strain	1 (0.1)	0.3	(0.0, 1.9)
Sunburn	1 (0.1)	0.3	(0.0, 1.9)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Musculoskeletal chest pain	1 (0.1)	0.3	(0.0, 1.9)
Myalgia	1 (0.1)	0.3	(0.0, 1.9)
NERVOUS SYSTEM DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Somnolence	1 (0.1)	0.3	(0.0, 1.9)
PSYCHIATRIC DISORDERS	1 (0.1)	0.3	(0.0, 1.9)
Major depression	1 (0.1)	0.3	(0.0, 1.9)

Note: Dose 3 = First dose of BNT162b2 (30 µg).
Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 3 to data cutoff date. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sev_cut1_ped6

14.44. Incidence Rates of at Least 1 Serious Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Baseline SARS-CoV-2 Status – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Baseline SARS-CoV-2 Status: Negative

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1083, TE[b]=4.4)			Placebo (N[a]=1078, TE[b]=4.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	10 (0.9)	2.3	(1.1, 4.2)	2 (0.2)	0.5	(0.1, 1.7)
GASTROINTESTINAL DISORDERS	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Abdominal pain	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Constipation	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
INFECTIONS AND INFESTATIONS	1 (0.1)	0.2	(0.0, 1.3)	2 (0.2)	0.5	(0.1, 1.7)
Anal abscess	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Appendicitis	0	0.0	(0.0, 0.8)	2 (0.2)	0.5	(0.1, 1.7)
Focal peritonitis	0	0.0	(0.0, 0.8)	1 (0.1)	0.2	(0.0, 1.3)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Femur fracture	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
PSYCHIATRIC DISORDERS	8 (0.7)	1.8	(0.8, 3.6)	0	0.0	(0.0, 0.9)
Anxiety	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Conversion disorder	1 (0.1)	0.2	(0.0, 1.3)	0	0.0	(0.0, 0.9)
Depression	3 (0.3)	0.7	(0.1, 2.0)	0	0.0	(0.0, 0.9)
Suicidal ideation	4 (0.4)	0.9	(0.2, 2.3)	0	0.0	(0.0, 0.9)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: MedDRA (v24.0) coding dictionary applied.
Note: Subjects whose baseline SARS-CoV-2 status cannot be determined because of missing N-binding antibody or NAAT at Visit 1 were not included in the analysis.
Note: Positive = positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19. Negative = negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 12NOV2021 (15:38)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sae_base1_ped6

14.45. Incidence Rates of at Least 1 Serious Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Ethnicity – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Ethnicity: Hispanic/Latino

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=132, TE[b]=0.6)			Placebo (N[a]=130, TE[b]=0.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	2 (1.5)	3.6	(0.4, 12.8)	0	0.0	(0.0, 6.9)
GASTROINTESTINAL DISORDERS	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Abdominal pain	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Constipation	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
PSYCHIATRIC DISORDERS	2 (1.5)	3.6	(0.4, 12.8)	0	0.0	(0.0, 6.9)
Conversion disorder	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)
Suicidal ideation	1 (0.8)	1.8	(0.0, 9.9)	0	0.0	(0.0, 6.9)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (16:25)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sae_eth1_ped6

14.46. Incidence Rates of at Least 1 Serious Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Ethnicity – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Ethnicity: Non-Hispanic/Non-Latino

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=997, TE[b]=4.0)			Placebo (N[a]=996, TE[b]=4.0)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	8 (0.8)	2.0	(0.9, 3.9)	2 (0.2)	0.5	(0.1, 1.8)
INFECTIONS AND INFESTATIONS	1 (0.1)	0.2	(0.0, 1.4)	2 (0.2)	0.5	(0.1, 1.8)
Anal abscess	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Appendicitis	0	0.0	(0.0, 0.9)	2 (0.2)	0.5	(0.1, 1.8)
Focal peritonitis	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.4)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Femur fracture	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
PSYCHIATRIC DISORDERS	6 (0.6)	1.5	(0.6, 3.3)	0	0.0	(0.0, 0.9)
Anxiety	1 (0.1)	0.2	(0.0, 1.4)	0	0.0	(0.0, 0.9)
Depression	3 (0.3)	0.7	(0.2, 2.2)	0	0.0	(0.0, 0.9)
Suicidal ideation	3 (0.3)	0.7	(0.2, 2.2)	0	0.0	(0.0, 0.9)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (16:25)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sae_eth1_ped6

14.47. Incidence Rates of at Least 1 Serious Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: White

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=970, TE[b]=3.9)			Placebo (N[a]=962, TE[b]=3.8)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	7 (0.7)	1.8	(0.7, 3.7)	2 (0.2)	0.5	(0.1, 1.9)
GASTROINTESTINAL DISORDERS	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Abdominal pain	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Constipation	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
INFECTIONS AND INFESTATIONS	1 (0.1)	0.3	(0.0, 1.4)	2 (0.2)	0.5	(0.1, 1.9)
Anal abscess	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Appendicitis	0	0.0	(0.0, 0.9)	2 (0.2)	0.5	(0.1, 1.9)
Focal peritonitis	0	0.0	(0.0, 0.9)	1 (0.1)	0.3	(0.0, 1.5)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Femur fracture	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
PSYCHIATRIC DISORDERS	5 (0.5)	1.3	(0.4, 3.0)	0	0.0	(0.0, 1.0)
Conversion disorder	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Depression	1 (0.1)	0.3	(0.0, 1.4)	0	0.0	(0.0, 1.0)
Suicidal ideation	3 (0.3)	0.8	(0.2, 2.3)	0	0.0	(0.0, 1.0)

Note: MedDRA (v24.0) coding dictionary applied.
Note: All Others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (16:25)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sae_race1_ped6

14.48. Incidence Rates of at Least 1 Serious Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: Black or African American

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=52, TE[b]=0.2)			Placebo (N[a]=57, TE[b]=0.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
PSYCHIATRIC DISORDERS	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
Anxiety	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)
Depression	1 (1.9)	4.0	(0.1, 22.5)	0	0.0	(0.0, 14.1)

Note: MedDRA (v24.0) coding dictionary applied.
Note: All Others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (16:25)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sae_race1_ped6

14.49. Incidence Rates of at Least 1 Serious Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Race – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Race: All Others

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=109, TE[b]=0.4)			Placebo (N[a]=110, TE[b]=0.4)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	2 (1.8)	4.6	(0.6, 16.7)	0	0.0	(0.0, 8.6)
PSYCHIATRIC DISORDERS	2 (1.8)	4.6	(0.6, 16.7)	0	0.0	(0.0, 8.6)
Depression	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)
Suicidal ideation	1 (0.9)	2.3	(0.1, 12.8)	0	0.0	(0.0, 8.6)

Note: MedDRA (v24.0) coding dictionary applied.
Note: All Others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (17:29) Source Data: adae Table Generation: 11NOV2021 (16:25)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sae_race1_ped6

14.50. Incidence Rates of at Least 1 Serious Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Sex – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Sex: Male

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=567, TE[b]=2.3)			Placebo (N[a]=585, TE[b]=2.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	3 (0.5)	1.3	(0.3, 3.8)	2 (0.3)	0.9	(0.1, 3.1)
INFECTIONS AND INFESTATIONS	1 (0.2)	0.4	(0.0, 2.4)	2 (0.3)	0.9	(0.1, 3.1)
Anal abscess	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Appendicitis	0	0.0	(0.0, 1.6)	2 (0.3)	0.9	(0.1, 3.1)
Focal peritonitis	0	0.0	(0.0, 1.6)	1 (0.2)	0.4	(0.0, 2.4)
PSYCHIATRIC DISORDERS	2 (0.4)	0.9	(0.1, 3.1)	0	0.0	(0.0, 1.6)
Depression	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)
Suicidal ideation	1 (0.2)	0.4	(0.0, 2.4)	0	0.0	(0.0, 1.6)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sae_sex1_ped6

14.51. Incidence Rates of at Least 1 Serious Adverse Event From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term, by Sex – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population Sex: Female

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=564, TE[b]=2.3)			Placebo (N[a]=544, TE[b]=2.2)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	7 (1.2)	3.1	(1.2, 6.4)	0	0.0	(0.0, 1.7)
GASTROINTESTINAL DISORDERS	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Abdominal pain	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Constipation	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Femur fracture	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
PSYCHIATRIC DISORDERS	6 (1.1)	2.7	(1.0, 5.8)	0	0.0	(0.0, 1.7)
Anxiety	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Conversion disorder	1 (0.2)	0.4	(0.0, 2.5)	0	0.0	(0.0, 1.7)
Depression	2 (0.4)	0.9	(0.1, 3.2)	0	0.0	(0.0, 1.7)
Suicidal ideation	3 (0.5)	1.3	(0.3, 3.9)	0	0.0	(0.0, 1.7)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:21)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sae_sex1_ped6

14.52. Incidence Rates of at Least 1 Serious Adverse Event From Unblinding Date to Data Cutoff Date (02SEP2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2 – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=1107, TE[b]=3.3)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])
Any event	4 (0.4)	1.2	(0.3, 3.1)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (0.1)	0.3	(0.0, 1.7)
Syringomyelia	1 (0.1)	0.3	(0.0, 1.7)
INFECTIONS AND INFESTATIONS	2 (0.2)	0.6	(0.1, 2.2)
Appendicitis	2 (0.2)	0.6	(0.1, 2.2)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.1)	0.3	(0.0, 1.7)
Upper limb fracture	1 (0.1)	0.3	(0.0, 1.7)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the unblinding date to data cutoff date. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:41)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds/adae_s131_sae_ubct1_ped6

14.53. Incidence Rates of Subjects Withdrawn Because of Adverse Events From Dose 1 to Unblinding Date, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=1131, TE[b]=4.6)			Placebo (N[a]=1129, TE[b]=4.5)		
System Organ Class Preferred Term	n[c] (%)	IR[d]	(95% CI[e])	n[c] (%)	IR[d]	(95% CI[e])
Any event	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)
Pyrexia	1 (0.1)	0.2	(0.0, 1.2)	0	0.0	(0.0, 0.8)

Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
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 the blinded follow-up period. This value is the denominator for the incidence rate calculation.
c. 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.
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.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:29) Source Data: adae Table Generation: 03NOV2021 (10:31)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File:
./nda2 unblinded/C4591001 S Peds/adae s131 wd unb1 ped6

SUPPLEMENTAL FIGURES

None

SUBJECT NARRATIVES

Primary Reason for Narrative	Unique Subject ID
Related Serious Adverse Event	PPD (also Appendicitis)
Safety-Related Subject Withdrawal	
Adverse Event of Clinical Interest	
Appendicitis	
COVID-19 Case (Severe and/or Multiple)	

15. REFERENCES

1. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19. [Internet]. Available from: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020. Published: 11 March 2020. Accessed: 01 April 2020.
2. Rauch S, Jasny E, Schmidt KE, et al. New vaccine technologies to combat outbreak situations. Front Immunol. 2018;9:1963.
3. Sahin U, Karikó K, Türeci Ö. mRNA-based therapeutics--developing a new class of drugs. Nat Rev Drug Discov. 2014;13(10):759-80.

Annotated Study Book for Study Design: C4591001

Study Design Version: 19.0

Sponsor: Pfizer

Protocol: C4591001

Sponsor Drug Name: BLINDED THERAPY

C4591001 - COVID19

Generated by Central Designer TM

March 30, 2021 10:56AM

C4591001: ADVERSE EVENT REPORT (AE) - Repeating Form

#	Category	AE Identifier	Adverse Event	Start Date	Is the Adverse Event Still Ongoing	Toxicity Grade	Serious	Is AE a Result of a Medication Error	Relationship to Study Treatment	Action Taken with Study Treatment	Concomitant Medication Given	Non-Drug Treatment Given	Outcome	Caused Study Discontinuation	Serious Adverse Event Number
1															

Adverse Event Report

1.	Category: [Category]	○ ADVERSE EVENT
2.	AE ID: [AE Identifier]	
3.	Adverse Event: (If possible specify diagnosis, not individual symptoms) [Adverse Event]	
4.	Start Date Time: [Start Date]	/ / : *24-hour clock*
5.	Is the adverse event still ongoing? [Is the Adverse Event Still Ongoing]	○ YES ○ NO End Date Time: / / : *24-hour clock*
6.	Toxicity Grade: [Toxicity Grade]	○ 1 ○ 2 ○ 3 ○ 4
7.	Is the adverse event serious? If Yes, NOTIFY PFIZER IMMEDIATELY. Fatal; Life-threatening; Inpatient hospitalization or prolongation of existing hospitalization; Persistent or significant disability/incapacity; Congenital anomaly/birth defect; Important medical event (i.e. may jeopardize subject and may require medical/surgical intervention to prevent above outcomes). [Serious]	○ YES Is this serious event associated with congenital anomaly or birth defect? ○ YES ○ NO Did this serious event result in death? ○ YES ○ NO Did this serious event require or prolong hospitalization? ○ YES ○ NO Did this serious event result in persistent or significant disability/incapacity? ○ YES ○ NO Is this serious event life threatening? ○ YES ○ NO Other medically important serious event ○ YES ○ NO ○ NO
8.	Is this adverse event the result of a study Medication Error? If Yes, record the type of medication error on the Medication Error Log. [Is AE a Result of a Medication Error]	○ YES ○ NO
9.	Is this event related to study treatment: [Relationship to Study Treatment]	○ NOT RELATED If Not Related to study treatment(s), this event is due to: ○ CONCOMITANT DRUG TREATMENT ○ CONCOMITANT NON-DRUG TREATMENT ○ OTHER If Other, specify: ○ RELATED
10.	Latest Action Taken with Study	○ DRUG WITHDRAWN NOT APPLICABLE

	Treatment: [Action Taken with Study Treatment]	○
11.	Was a Concomitant Medication given? [Concomitant Medication Given]	○ YES ○ NO
12.	Was a Non-Drug Treatment given? [Non-Drug Treatment Given]	○ YES ○ NO
13.	What was the outcome of this adverse event?: [Outcome]	○ FATAL ○ NOT RECOVERED/NOT RESOLVED ○ RECOVERED/RESOLVED ○ RECOVERED/RESOLVED WITH SEQUELAE ○ RECOVERING/RESOLVING ○ UNKNOWN
14.	Did the adverse event cause the subject to be discontinued from the study? [Caused Study Discontinuation]	○ YES ○ NO
15.	Serious Adverse Event Number: For Pfizer Use Only [Serious Adverse Event Number]	
16.	Comparison Term *[hidden]* [Comparison Term]	
17.	Lowest Level Term *[hidden]* [Lowest Level Term]	
18.	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
19.	Dictionary-Derived Term *[hidden]* [Dictionary-Derived Term]	
20.	Preferred Term Code *[hidden]* [Preferred Term Code]	
21.	High Level Term *[hidden]* [High Level Term]	
22.	High Level Term Code *[hidden]* [High Level Term Code]	
23.	High Level Group Term *[hidden]* [High Level Group Term]	
24.	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
25.	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
26.	Primary System Organ Class Code *[hidden]* [Primary System Organ Class Code]	

C4591001: INFORMED CONSENT - BOOSTER (BOOST CONS)		
Informed Consent - Booster		
1.	Consent Was: [Consent Was:]	OBTAINED Date Written Consent Obtained / /

C4591001: INCLUSION/EXCLUSION CRITERIA - BOOSTER (BOOST IE)

	Criterion Description
1.	

Inclusion Criteria Not Met Entry

1.1	Description of Inclusion Criterion Not Met [Criterion Description]	

	Criterion Description
2.	

Exclusion Criteria Met Entry

2.1	Description of Exclusion Criterion Met [Criterion Description]	

C4591001: BOOSTER DOSE TRIGGER FORM (BOOST TRIG)

Booster Dose Trigger Form

1.	Select appropriate response - Will the participant return for consent/eligibility assessment for the booster dose visit? [Trigger Response 13]	○ The participant will return for consent/eligibility assessment for the booster dose visit ○ The participant will NOT return for consent/eligibility assessment for the booster dose visit ○ The participant will return for consent/eligibility assessment for the LOW DOSE booster dose visit (Select this option for participant returning for 5 or 10 mcg booster)

C4591001: LABORATORY DATA - HEMATOLOGY (CD4)

Laboratory Data Hematology

1.	Lab Panel: [Category for Lab Test]	○ HEMATOLOGY
2.	Laboratory Name and Address [Vendor Name (DERIVED)]	
3.	Collection Date: [Collection Date:]	/ /
4.	Specimen Type: [Specimen Type]	○ BLOOD

Lab Result

#	Sponsor-Defined Identifier	Test:	Result:	Not Done:	Lab Normal Range
5.a		CD4_PX4722			

Lab Result Entry

5.1	Sponsor ID: [Sponsor-Defined Identifier]	
5.2	Test: [Test:]	○ CD4_PX4722
5.3	Result: [Result:]	
5.4	Not Done: *[hidden]* [Not Done:]	○ NOT DONE
5.5	LNMT [Lab Normal Range]	Low High Unit ○ 10^3/mm3 ○ /uL ○ %

C4591001: COHORT SELECTION (COHORT SEL)

Cohort Selection

DO NOT USE THE OPTIONS STAGE 1 NONSENTINEL and STAGE 2 from this CRF. As per protocol amendment 5, STAGE 3 option is equivalent to PHASE 2/3.

1.	Select appropriate response - Protocol version [Trigger Response 1]	
2.	Select appropriate response - What cohort does the subject belong to? [Trigger Response 10]	○ STAGE 1 SENTINEL COHORTS ○ STAGE 1 NONSENTINEL COHORTS ○ STAGE 2 COHORTS ○ STAGE 3 COHORTS

C4591001: CONCOMITANT MEDICATIONS - BASELINE (CONMED BSL) - Repeating Form

#	Sponsor-Defined Identifier	Category for Medication	Concomitant Medications Pre-specified	Name of Medication	Dose Description	Dose Unit	Dose Frequency	Route	Start Date
1									

Concomitant Medications

1.	What is the medication identifier? [Sponsor-Defined Identifier]	
2.	Category: [Category for Medication]	○ GENERAL CONCOMITANT MEDICATIONS
3.	Concomitant Medications Pre-specified: [Concomitant Medications Pre-specified]	○ NO
4.	Medication: Provide the complete generic drug name (including salt form, where applicable). Where generic name is unknown, enter the full trade or proprietary name. Include clarifying information in the Medication text (e.g., Ingredient(s), route, use, formulation). [Name of Medication]	
5.	Dose: [Dose Description]	
6.	Dose Unit: [Dose Unit]	
7.	Dose Frequency: [Dose Frequency]	
8.	Route: [Route]	
9.	Start Date: [Start Date]	/ /
10.	Comparison Term *[hidden]* [Comparison Term]	
11.	Standardized Medication Name - Dictionary derived. *[hidden]* [Standardized Medication Name]	
12.	Standardized Medication Code - Dictionary derived *[hidden]* [Standardized Medication Code]	

C4591001: CONCOMITANT MEDICATIONS - NON STUDY VACCINATIONS (CONMED VAX) - Repeating Form					
#	Sponsor-Defined Identifier	Category for Medication	Concomitant Medications Pre-specified	Name of Medication	Start Date
1					

Concomitant Medications		
1.	What is the medication identifier? [Sponsor-Defined Identifier]	
2.	Category: [Category for Medication]	○ VACCINATIONS
3.	Concomitant Medications Pre-specified: [Concomitant Medications Pre-specified]	○ NO
4.	Medication: Provide the complete generic drug name (including salt form, where applicable). Where generic name is unknown, enter the full trade or proprietary name. Include clarifying information in the Medication text (e.g., Ingredient(s), route, use, formulation). [Name of Medication]	
5.	Date: [Start Date]	/ /
6.	Comparison Term *[hidden]* [Comparison Term]	
7.	Standardized Medication Name - Dictionary derived. *[hidden]* [Standardized Medication Name]	
8.	Standardized Medication Code - Dictionary derived *[hidden]* [Standardized Medication Code]	

C4591001: MAIN INFORMED CONSENT (CONSENT)		
Informed Consent		
1.	Consent Was: [Consent Was:]	OBTAINED Date Written Consent Obtained / /

C4591001: CONTACT OUTCOME - MONTH 1 (CONTACT 1M)		
Contact Outcome		
1.	Follow-Up Contact Category *[hidden]* [Follow Up Contact Category]	○ CONTACT OUTCOME
2.	Contact Type: [Type of Contact/Visit]	○ CLINIC VISIT ○ TELEHEALTH VISIT
3.	Was contact made? [Was Contact Made]	○ YES Date of Contact: / / ○ NO If No, why?
4.	Comments: [Comments/Findings/Details]	

C4591001: CONTACT OUTCOME - MONTH 6 (CONTACT 6M)		
Contact Outcome		
1.	Follow-Up Contact Category *[hidden]* [Follow Up Contact Category]	○ CONTACT OUTCOME
2.	Contact Type: [Type of Contact/Visit]	○ CLINIC VISIT ○ TELEHEALTH VISIT
3.	Was contact made? [Was Contact Made]	○ YES Date of Contact: / / ○ NO If No, why?
4.	Comments: [Comments/Findings/Details]	

C4591001: CONTACT OUTCOME (CONTACT SV)		
Contact Outcome		
1.	Follow-Up Contact Category *[hidden]* [Follow Up Contact Category]	◯ CONTACT OUTCOME
2.	Contact Type: [Type of Contact/Visit]	◯ TELEPHONE VISIT
3.	Was contact made? [Was Contact Made]	◯ YES Date of Contact: / / ◯ NO If No, why?
4.	Comments: [Comments/Findings/Details]	

C4591001: CONTACT OUTCOME - UNPLANNED (CONTACT UV)

Contact Outcome

1.	Follow-Up Contact Category *[hidden]* [Follow Up Contact Category]	○ CONTACT OUTCOME
2.	Contact Type: [Type of Contact/Visit]	○ TELEPHONE VISIT
3.	Was contact made? [Was Contact Made]	○ YES Date of Contact: / / Contact Outcome: ○ VISIT ARRANGED ○ VISIT ARRANGED, BUT NOT ATTENDED ○ VISIT NOT ARRANGED, REACTION NO LONGER PRESENT ○ VISIT NOT ARRANGED, UNABLE TO ATTEND ○ VISIT NOT REQUIRED, DATA ENTRY ERROR IN E-DIARY ○ VISIT NOT REQUIRED, INVESTIGATOR DECISION ○ NO If No, why?
4.	Comments: [Comments/Findings/Details]	

C4591001: MICROBIOLOGY SPECIMEN (COV19 SITE) - Repeating Form						
#	Date of Collection	Specimen Type	Assay Code and Description	Device Type	Result	Comments:
1						

Microbiology Specimen		
1.	Actual Date of Collection: [Date of Collection]	/ /
2.	Specimen Type: [Specimen Type]	SERUM BLOOD PLASMA
3.	Assay Code and Description: [Assay Code and Description]	SEVERE ACUTE RESP SYNDROME CORONAVIRUS 2
4.	Device Type: [Device Type]	SARS-COV-2 DIAGNOSTIC TEST
5.	Test Result: [Result]	POSITIVE NEGATIVE INDETERMINATE
6.	Comments/Findings/Details: [Comments:]	

C4591001: MICROBIOLOGY SPECIMEN (COVID TEST) - Repeating Form

#	Date of Collection	Specimen Type	Specimen Collection Location	Assay Code and Description	Device Type	Trade Name	Result	Comments:	Trade Name Other, Specify
1									

Microbiology Specimen

1.	Actual Date of Collection: [Date of Collection]	/ /
2.	Specimen Type: [Specimen Type]	SWABBED MATERIAL RESPIRATORY SECRETIONS
3.	Specimen Collection Location: [Specimen Collection Location]	NASOPHARYNX LOWER RESPIRATORY SYSTEM THROAT
4.	Assay Code and Description: [Assay Code and Description]	SEVERE ACUTE RESP SYNDROME CORONAVIRUS 2
5.	Device Type: [Device Type]	SARS-COV-2 DIAGNOSTIC TEST
6.	Trade Name: [Trade Name]	
7.	Test Result: [Result]	POSITIVE NEGATIVE INDETERMINATE
8.	Comments/Findings/Details: [Comments:]	
9.	Trade Name Other, Specify: [Trade Name Other, Specify]	

C4591001: DEATH DETAILS CODED (DEATH DTL)

Death Details

1.	Date of Collection / Notification of Death: [Date of Collection / Notification of Death]	/ /

	Cause of Death Status	Cause of Death
2.		

Cause of Death Entry

2.1	Cause of Death Status: [Cause of Death Status]	○ PRIMARY CAUSE OF DEATH ○ SECONDARY CAUSE OF DEATH
2.2	Cause of Death: [Cause of Death]	
2.3	Comparison Term *[hidden]* [Comparison Term]	
2.4	Lowest Level Term *[hidden]* [Lowest Level Term]	
2.5	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
2.6	Dictionary-Derived Term *[hidden]* [Dictionary-Derived Term]	
2.7	Preferred Term Code *[hidden]* [Preferred Term Code]	
2.8	High Level Term *[hidden]* [High Level Term]	
2.9	High Level Term Code *[hidden]* [High Level Term Code]	
2.10	High Level Group Term *[hidden]* [High Level Group Term]	
2.11	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
2.12	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
2.13	Primary System Organ Class Code *[hidden]* [Primary System Organ Class Code]	

C4591001: DEMOGRAPHY (DEMOG)		
Demography		
1.	Subject ID [Subject ID]	
2.	Birth Date: [Birth Date]	/ /
3.	Sex: [Sex]	FEMALE MALE
4.	Ethnicity: [Ethnicity]	HISPANIC OR LATINO(A) OR OF SPANISH ORIGIN NOT HISPANIC OR LATINO(A) OR OF SPANISH ORIGIN NOT REPORTED
5.	Race: (Check X all that apply): [Race Of Subject]	BLACK OR AFRICAN AMERICAN AMERICAN INDIAN OR ALASKA NATIVE ASIAN NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER WHITE NOT REPORTED
6.	Racial Designation: [Racial Designation]	JAPANESE OTHER

C4591001: DISPOSITION - SCREENING FOR BOOSTER DOSE (DISP BOOST)		
Disposition - Screening for Booster Dose		
1.	Date of Completion/Discontinuation/Death : [Date of Completion/Discontinuation/Death :]	/ /
2.	Phase of Disposition: [Disposition Phase]	REPEAT SCREENING 2
3.	Status: [Status]	
4.	Specify Status: [Specify Status]	

C4591001: DISPOSITION - FOLLOW-UP (DISP FUP)		
Disposition - Follow-Up		
1.	Date of Completion/Discontinuation/Death : [Date of Completion/Discontinuation/Death :]	/ /
2.	Phase of Disposition: [Disposition Phase]	FOLLOW-UP
3.	Status: [Status]	
4.	Specify Status: [Specify Status]	

C4591001: DISPOSITION - SCREENING FOR FURTHER VACCINATION (DISP RESCR)		
Disposition - Screening for Further Vaccination		
1.	Date of Completion/Discontinuation/Death : [Date of Completion/Discontinuation/Death :]	/ /
2.	Phase of Disposition: [Disposition Phase]	REPEAT SCREENING 1
3.	Status: [Status]	
4.	Specify Status: [Specify Status]	

C4591001: DISPOSITION - SCREENING (DISP SCR)		
Disposition - Screening		
1.	Date of Completion/Discontinuation/Death [Date of Completion/Discontinuation/Death]	/ /
2.	Phase of Disposition: [Disposition Phase]	SCREENING
3.	Status: [Status]	
4.	Specify Status: [Specify Status]	

C4591001: DISPOSITION - TREATMENT (DISP TRT)		
Disposition - Treatment		
1.	Date of Completion/Discontinuation/Death : [Date of Completion/Discontinuation/Death :]	/ /
2.	Phase of Disposition: [Disposition Phase]	○ VACCINATION ○ OPEN LABEL TREATMENT ○ SUBSTUDY
3.	Status: [Status]	
4.	Specify Status: [Specify Status]	

C4591001: DATE OF VISIT (DOV)		
Date of Visit		
1.	Date of Visit [Date of Visit]	/ /
2.	Erroneous Visit [Visit Error]	ERRONEOUS VISIT

C4591001: DATE OF VISIT - ILLNESS CONVALESCENT (DOV CONV)		
Date of Visit		
1.	Date of Visit [Date of Visit]	/ /
2.	Erroneous Visit [Visit Error]	ERRONEOUS VISIT
COVID-19 Illness Visit		
3.	COVID-19 Illness Visit: [COVID-19 Illness Visit]	

C4591001: DATE OF VISIT - ILLNESS ONSET (DOV ILL)		
Date of Visit		
1.	Date of Visit [Date of Visit]	/ /
2.	Erroneous Visit [Visit Error]	ERRONEOUS VISIT
COVID-19 Illness Visit		
3.	COVID-19 Illness Visit: [COVID-19 Illness Visit]	

C4591001: DATE OF VISIT - ASYMPTOMATIC SURVEILLANCE (DOV SURV)		
Date of Visit		
1.	Date of Visit [Date of Visit]	/ /
2.	Erroneous Visit [Visit Error]	ERRONEOUS VISIT
COVID-19 Surveillance Visit		
3.	COVID-19 Surveillance Visit: [COVID-19 Surveillance Visit]	

C4591001: DATE OF VISIT - REPEAT SWAB (DOV SWAB)		
Date of Visit		
1.	Date of Visit [Date of Visit]	/ /
2.	Erroneous Visit [Visit Error]	ERRONEOUS VISIT
COVID-19 Repeat Swab		
3.	COVID-19 Repeat Swab: [COVID-19 Repeat Swab]	

C4591001: INFORM ENROLLMENT (ENROLL)		
InForm Enrollment		
1.	Subject ID [Subject ID]	

C4591001: HIV STATUS (HIV)		
HIV Status		
1.	Select appropriate response - What is the subject HIV status? [Trigger Response 2]	◯ The subject is known to be HIV POSITIVE ◯ The subject is NOT known to be HIV POSITIVE

C4591001: LAB CHEMISTRY (HIV RNA)

Lab Chemistry Details

1.	Lab Panel: [Category for Lab Test]	◯ CLINICAL CHEMISTRY
2.	Laboratory Name and Address [Vendor Name]	
3.	Collection Date: [Collection Date:]	/ /
4.	Specimen Type: [Specimen Type]	◯ BLOOD

Lab Result

#	Sponsor-Defined Identifier	Test:	Result:	Not Done:	Lab Normal Range
5.a		HIV RNA (Ultrasensitive)			

Lab Result Entry

5.1	Sponsor ID: [Sponsor-Defined Identifier]	
5.2	Test: [Test:]	◯ HIV RNA (Ultrasensitive)
5.3	Result: [Result:]	
5.4	Not Done: *[hidden]* [Not Done:]	◯ NOT DONE
5.5	LNMT [Lab Normal Range]	Low High Unit ◯ /mL

C4591001: ELECTRONIC SAMPLE TRACKING - HLA (HLA)

Electronic Sample Tracking

1.	Data Origin [Data Origin]	○ SITE
2.	Sample Type [Sample Type]	○ WHOLE_BLOOD
3.	Sample Collected? [Sample Collected]	○ NO ○ YES Date of Collection: / /
4.	If no sample was collected or sample was not collected according to protocol, please provide reason: [Reason sample not collected]	

	Sample ID
5.	

Aliquot Entry

Please enter barcode for each aliquot.

5.1	Sample ID [Sample ID]	

C4591001: HEALTH CARE UTILIZATION (HLTHCARE)

Health Care Utilization

1.	Evaluation Interval: *[hidden]* [Evaluation Interval]	◯ SINCE THE START OF THE RESPIRATORY ILLNESS EPISODE
2.	Disease Name: *[hidden]* [Disease Name]	◯ RESPIRATORY ILLNESS

Health Care Utilization

# ✔	Pre-Specified	Type of Practitioner	Occurrence of Visits or Contacts
3.a	YES	SPECIALIST	
3.b	YES	EMERGENCY ROOM	
3.c	YES	PRIMARY CARE PHYSICIAN	
3.d	YES	URGENT CARE	
3.e	YES	TELEPHONE CONSULTATION	
3.f	YES	OTHER	

Health Care Utilization Entry

3.1	Pre-Specified: *[hidden]* [Pre-Specified]	◯ YES
3.2	Physician or Healthcare Professional: [Type of Practitioner]	◯ SPECIALIST ◯ EMERGENCY ROOM ◯ PRIMARY CARE PHYSICIAN ◯ URGENT CARE ◯ TELEPHONE CONSULTATION ◯ OTHER
3.3	Occurrence of Visits or Contacts: [Occurrence of Visits or Contacts]	◯ YES Number of Visits or Contacts: [ ] ◯ NO

Health Care Utilization Other

4.	Other Type of Practitioner Specify: [Other Type of Practitioner Specify]	[ ]

Health Care Utilization

5.	Has the subject been hospitalized due to potential COVID-19 illness? [Been Hospitalized]	◯ YES Has the subject been in intensive care due to potential COVID-19 illness? ◯ YES ◯ NO ◯ NO

C4591001: HOSPITALIZATION DETAILS (HOSP) - Repeating Form				
#	Hospitalization Category	Hospitalization Term	Admission Date	Ongoing
1				

Hospitalization Details		
1.	Hospitalization Category: [Hospitalization Category]	◯ HOSPITALIZATION STATUS
2.	Hospitalization Term: [Hospitalization Term]	◯ ICU ◯ HOSPITAL
3.	Admission Date: [Admission Date]	/ /
4.	Ongoing? [Ongoing]	◯ YES ◯ NO Discharge Date: / /

C4591001: ILLNESS DETAILS (ILL POTEN)

Illness Details

1.	Category of Clinical Event: [Category of Clinical Event:]	○ POTENTIAL COVID-19 ILLNESS
2.	Was a diagnosis obtained for Potential COVID-19 Illness? [Diagnosis Obtained]	○ YES Respiratory Illness Diagnosis: Date of Diagnosis: / / ○ NO
3.	Toxicity Grade: [Toxicity Grade]	○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5
4.	Comparison Term: *[hidden]* [Comparison Term]	
5.	Lowest Level Term *[hidden]* [Lowest Level Term]	
6.	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
7.	Dictionary Derived Term *[hidden]* [Dictionary Derived Term]	
8.	Preferred Term Code *[hidden]* [Preferred Term Code]	
9.	High Level Term *[hidden]* [High Level Term]	
10.	High Level Term Code *[hidden]* [High Level Term Code]	
11.	High Level Group Term *[hidden]* [High Level Group Term]	
12.	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
13.	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
14.	Primary System Organ Class Code *[hidden]* [Primary System Organ Class Code]	

C4591001: ILLNESS DETAILS - SEVERE (ILL SEVERE)

Illness Details

1.	Category of Clinical Event: [Category of Clinical Event:]	○ SEVERE COVID-19 ILLNESS
2.	Subcategory of Clinical Event: [Subcategory of Clinical Event]	○ SIGNIFICANT ACUTE RENAL DYSFUNCTION ○ SIGNIFICANT ACUTE HEPATIC DYSFUNCTION ○ SIGNIFICANT ACUTE NEUROLOGIC DYSFUNCTION
3.	Was a diagnosis obtained? [Diagnosis Obtained]	○ YES Diagnosis: Start Date: / / Ongoing?: ○ YES ○ NO End Date: / / ○ NO
4.	Toxicity Grade: [Toxicity Grade]	○ 1 ○ 2 ○ 3 ○ 4 ○ 5
5.	Comparison Term: *[hidden]* [Comparison Term]	
6.	Lowest Level Term *[hidden]* [Lowest Level Term]	
7.	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
8.	Dictionary Derived Term *[hidden]* [Dictionary Derived Term]	
9.	Preferred Term Code *[hidden]* [Preferred Term Code]	
10.	High Level Term *[hidden]* [High Level Term]	
11.	High Level Term Code *[hidden]* [High Level Term Code]	
12.	High Level Group Term *[hidden]* [High Level Group Term]	
13.	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
14.	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
15.	Primary System Organ Class Code *[hidden]* [Primary System Organ Class Code]	

C4591001: ILLNESS DETAILS - SEVERE (ILL SEVERE) - Repeating Form

#	Category of Clinical Event:	Subcategory of Clinical Event	Diagnosis Obtained	Toxicity Grade
1				

Illness Details

1.	Category of Clinical Event: [Category of Clinical Event:]	○ SEVERE COVID-19 ILLNESS
2.	Subcategory of Clinical Event: [Subcategory of Clinical Event]	○ SIGNIFICANT ACUTE RENAL DYSFUNCTION ○ SIGNIFICANT ACUTE HEPATIC DYSFUNCTION ○ SIGNIFICANT ACUTE NEUROLOGIC DYSFUNCTION
3.	Was a diagnosis obtained? [Diagnosis Obtained]	○ YES Diagnosis: Start Date: / / Ongoing?: ○ YES ○ NO End Date: / / ○ NO
4.	Toxicity Grade: [Toxicity Grade]	○ 1 ○ 2 ○ 3 ○ 4 ○ 5
5.	Comparison Term: *[hidden]* [Comparison Term]	
6.	Lowest Level Term *[hidden]* [Lowest Level Term]	
7.	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
8.	Dictionary Derived Term *[hidden]* [Dictionary Derived Term]	
9.	Preferred Term Code *[hidden]* [Preferred Term Code]	
10.	High Level Term *[hidden]* [High Level Term]	
11.	High Level Term Code *[hidden]* [High Level Term Code]	
12.	High Level Group Term *[hidden]* [High Level Group Term]	
13.	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
14.	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
15.	Primary System Organ Class Code *[hidden]* [Primary System Organ Class Code]	

C4591001: IMAGING (IMAGING) - Repeating Form

#	Date of Assessment	Location of Assessment	Imaging Method	Overall Assessment
1				

Imaging

1.	Date of Assessment: [Date of Assessment]	/ /
2.	Location of Assessment: [Location of Assessment]	○ CHEST ○ HEAD ○ OTHER If other, specify:
3.	Type of Imaging Exam: [Imaging Method]	○ CT SCAN ○ X-RAY ○ ULTRASOUND ○ MRI ○ OTHER If other, specify:
4.	Assessment: [Overall Assessment]	○ ABNORMAL If abnormal, specify findings: ○ INDETERMINATE ○ NORMAL ○ UNKNOWN ○ NOT EVALUABLE

C4591001: INCLUSION/EXCLUSION CRITERIA (IN EX STG3)

Study eligibility requires subjects to meet all inclusion criteria (YES) and Not meet exclusion criteria (NO).

Inclusion Criteria

#	Inclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
1.a	1	Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study stage)		IN01A00
1.b	2	Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures		IN02A00
1.c	3	Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study		IN03A00
1.d	4	Capable of giving personal signed informed consent, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol		IN04A00

Inclusion Criteria Entry

1.1	Inclusion Number: [Inclusion Number]	○ 1 ○ 2 ○ 3 ○ 4
1.2	Criterion Description: [Criterion Description]	
1.3	Criterion met? [Criterion met?]	○ YES ○ NO Describe details if relevant
1.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	○ IN01A00 ○ IN02A00 ○ IN03A00 ○ IN04A00

Exclusion Criteria

#	Exclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
2.a	1	Other medical or psychiatric condition incl. recent (within past year) or active suicidal ideation/behavior/lab abnormality that may increase the risk of study participation		EX01A00
2.b	2	Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV)		EX02A00
2.c	3	History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s)		EX03A00
2.d	4	Receipt of medications intended to prevent COVID-19		EX04A00
2.e	8	Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination		EX08A00
2.f	9	Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention		EX09A00
2.g	10	Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection		EX10A00
2.h	11	Women who are pregnant or breastfeeding		EX11A00
2.i	12	Previous vaccination with any coronavirus vaccine		EX12A00
2.j	13	Subjects who receive immunosuppressive therapy, such as cytotoxic agents or systemic corticosteroids		EX13A01
2.k	15	Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study		EX14A01
2.l	16	Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation		EX15A01
2.m	17	Previous participation in other studies involving study intervention containing lipid nanoparticles		EX16A01
2.n	22	Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members		EX21A01

Exclusion Criteria Entry

2.1	Exclusion Number: [Exclusion Number]	
2.2	Criterion Description: [Criterion Description]	
2.3	Criterion met? [Criterion met?]	○ YES Describe details if relevant

		○ NO
2.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	

C4591001: INCLUSION/EXCLUSION CRITERIA (IN EX STG3)

Study eligibility requires subjects to meet all inclusion criteria (YES) and Not meet exclusion criteria (NO).

Inclusion Criteria

#	Inclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
1.a	1	Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study stage)		IN01A00
1.b	2	Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures		IN02A00
1.c	3	Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study		IN03A00
1.d	4	Capable of giving personal signed informed consent, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol		IN04A00

Inclusion Criteria Entry

1.1	Inclusion Number: [Inclusion Number]	○ 1 ○ 2 ○ 3 ○ 4
1.2	Criterion Description: [Criterion Description]	
1.3	Criterion met? [Criterion met?]	○ YES ○ NO Describe details if relevant
1.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	○ IN01A00 ○ IN02A00 ○ IN03A00 ○ IN04A00

Exclusion Criteria

#	Exclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
2.a	1	Other medical or psychiatric condition incl. recent (within past year) or active suicidal ideation/behavior/lab abnormality that may increase the risk of study participation		EX01A00
2.b	2	Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV)		EX02A00
2.c	3	History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s)		EX03A00
2.d	4	Receipt of medications intended to prevent COVID-19		EX04A00
2.e	8	Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination		EX08A00
2.f	10	Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection		EX10A00
2.g	11	Women who are pregnant or breastfeeding		EX11A00
2.h	12	Previous vaccination with any coronavirus vaccine		EX12A00
2.i	13	Subjects who receive immunosuppressive therapy, such as cytotoxic agents or systemic corticosteroids		EX13A01
2.j	15	Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study		EX14A01
2.k	16	Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation		EX15A01
2.l	17	Previous participation in other studies involving study intervention containing lipid nanoparticles		EX16A01
2.m	22	Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members		EX21A01

Exclusion Criteria Entry

2.1	Exclusion Number: [Exclusion Number]	
2.2	Criterion Description: [Criterion Description]	
2.3	Criterion met? [Criterion met?]	○ YES Describe details if relevant ○ NO
2.4	Criterion ID: (For Pfizer use	

	only) [Criterion ID: (For Pfizer use only)]	

C4591001: INCLUSION/EXCLUSION CRITERIA (IN EX STG3)

Study eligibility requires subjects to meet all inclusion criteria (YES) and Not meet exclusion criteria (NO).

Inclusion Criteria

#	Inclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
1.a	1	Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study stage)		IN01A00
1.b	2	Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures		IN02A00
1.c	3	Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study		IN03A00
1.d	4	Capable of giving personal signed informed consent, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol		IN04A00

Inclusion Criteria Entry

1.1	Inclusion Number: [Inclusion Number]	○ 1 ○ 2 ○ 3 ○ 4
1.2	Criterion Description: [Criterion Description]	
1.3	Criterion met? [Criterion met?]	○ YES ○ NO Describe details if relevant
1.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	○ IN01A00 ○ IN02A00 ○ IN03A00 ○ IN04A00

Exclusion Criteria

#	Exclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
2.a	1	Other medical or psychiatric condition incl. recent (within past year) or active suicidal ideation/behavior/lab abnormality that may increase the risk of study participation		EX01A00
2.b	2	Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV)		EX02A00
2.c	3	History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s)		EX03A00
2.d	4	Receipt of medications intended to prevent COVID-19		EX04A00
2.e	8	Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination		EX08A00
2.f	9	Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention		EX09A00
2.g	10	Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection		EX10A00
2.h	11	Women who are pregnant or breastfeeding		EX11A00
2.i	12	Previous vaccination with any coronavirus vaccine		EX12A00
2.j	13	Individuals who receive immunosuppressive therapy, such as cytotoxic agents or systemic corticosteroids. Inhaled/nebulized, Intra-articular, intrabursal, or topical corticosteroids are permitted		EX13A00
2.k	14	Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study		EX14A00
2.l	15	Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation		EX15A00
2.m	16	Previous participation in other studies involving study intervention containing lipid nanoparticles		EX16A00
2.n	21	Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members		EX21A00

Exclusion Criteria Entry

2.1	Exclusion Number: [Exclusion Number]	
2.2	Criterion Description: [Criterion Description]	
2.3	Criterion met? [Criterion met?]	○ YES Describe details if relevant

		NO
2.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	

C4591001: INCLUSION/EXCLUSION CRITERIA (INC EXC)

	Criterion Description
1.	

Inclusion Criteria Not Met Entry

1.1	Description of Inclusion Criterion Not Met [Criterion Description]	

	Criterion Description
2.	

Exclusion Criteria Met Entry

2.1	Description of Exclusion Criterion Met [Criterion Description]	

C4591001: INCLUSION/EXCLUSION CRITERIA (INC EXC NS)

Study eligibility requires subjects to meet all inclusion criteria (YES) and Not meet exclusion criteria (NO).

Inclusion Criteria

#	Inclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
1.a	1	Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study stage)		IN01A00
1.b	2	Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures		IN02A00
1.c	3	Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study		IN03A00
1.d	4	Capable of giving personal signed informed consent, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol		IN04A00

Inclusion Criteria Entry

1.1	Inclusion Number: [Inclusion Number]	○ 1 ○ 2 ○ 3 ○ 4
1.2	Criterion Description: [Criterion Description]	
1.3	Criterion met? [Criterion met?]	○ YES ○ NO Describe details if relevant
1.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	○ IN01A00 ○ IN02A00 ○ IN03A00 ○ IN04A00

Exclusion Criteria

#	Exclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
2.a	1	Other medical or psychiatric condition incl. recent (within past year) or active suicidal ideation/behavior/lab abnormality that may increase the risk of study participation		EX01A00
2.b	2	Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV)		EX02A00
2.c	3	History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s)		EX03A00
2.d	4	Receipt of medications intended to prevent COVID-19		EX04A00
2.e	5	Stages 1 and 2 only: Previous clinical or microbiological diagnosis of COVID-19		EX05A00
2.f	8	Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination		EX08A00
2.g	10	Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection		EX10A00
2.h	11	Women who are pregnant or breastfeeding		EX11A00
2.i	12	Previous vaccination with any coronavirus vaccine		EX12A00
2.j	13	Subjects who receive immunosuppressive therapy, such as cytotoxic agents or systemic corticosteroids		EX13A01
2.k	15	Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study		EX14A01
2.l	16	Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation		EX15A01
2.m	17	Previous participation in other studies involving study intervention containing lipid nanoparticles		EX16A01
2.n	22	Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members		EX21A01

Exclusion Criteria Entry

2.1	Exclusion Number: [Exclusion Number]	
2.2	Criterion Description: [Criterion Description]	
2.3	Criterion met? [Criterion met?]	○ YES Describe details if relevant ○ NO

2.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	

C4591001: INCLUSION/EXCLUSION CRITERIA (INC EXC NS)

Study eligibility requires subjects to meet all inclusion criteria (YES) and Not meet exclusion criteria (NO).

Inclusion Criteria

#	Inclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
1.a	1	Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study stage)		IN01A00
1.b	2	Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures		IN02A00
1.c	3	Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study		IN03A00
1.d	4	Capable of giving personal signed informed consent, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol		IN04A00

Inclusion Criteria Entry

1.1	Inclusion Number: [Inclusion Number]	○ 1 ○ 2 ○ 3 ○ 4
1.2	Criterion Description: [Criterion Description]	
1.3	Criterion met? [Criterion met?]	○ YES ○ NO Describe details if relevant
1.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	○ IN01A00 ○ IN02A00 ○ IN03A00 ○ IN04A00

Exclusion Criteria

#	Exclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
2.a	1	Other medical or psychiatric condition incl. recent (within past year) or active suicidal ideation/behavior/lab abnormality that may increase the risk of study participation		EX01A00
2.b	2	Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV)		EX02A00
2.c	3	History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s)		EX03A00
2.d	4	Receipt of medications intended to prevent COVID-19		EX04A00
2.e	5	Stages 1 and 2 only: Previous clinical or microbiological diagnosis of COVID-19		EX05A00
2.f	8	Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination		EX08A00
2.g	9	Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention		EX09A00
2.h	10	Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection		EX10A00
2.i	11	Women who are pregnant or breastfeeding		EX11A00
2.j	12	Previous vaccination with any coronavirus vaccine		EX12A00
2.k	13	Subjects who receive immunosuppressive therapy, such as cytotoxic agents or systemic corticosteroids		EX13A01
2.l	15	Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study		EX14A01
2.m	16	Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation		EX15A01
2.n	17	Previous participation in other studies involving study intervention containing lipid nanoparticles		EX16A01
2.o	22	Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members		EX21A01

Exclusion Criteria Entry

2.1	Exclusion Number: [Exclusion Number]	
2.2	Criterion Description: [Criterion Description]	
2.3	Criterion met? [Criterion met?]	○ YES Describe details if relevant

		○ NO
2.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	

C4591001: INCLUSION/EXCLUSION CRITERIA (INC EXC NS)

Study eligibility requires subjects to meet all inclusion criteria (YES) and Not meet exclusion criteria (NO).

Inclusion Criteria

#	Inclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
1.a	1	Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study stage)		IN01A00
1.b	2	Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures		IN02A00
1.c	3	Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study		IN03A00
1.d	4	Capable of giving personal signed informed consent, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol		IN04A00

Inclusion Criteria Entry

1.1	Inclusion Number: [Inclusion Number]	○ 1 ○ 2 ○ 3 ○ 4
1.2	Criterion Description: [Criterion Description]	
1.3	Criterion met? [Criterion met?]	○ YES ○ NO Describe details if relevant
1.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	○ IN01A00 ○ IN02A00 ○ IN03A00 ○ IN04A00

Exclusion Criteria

#	Exclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
2.a	1	Other medical or psychiatric condition incl. recent (within past year) or active suicidal ideation/behavior/lab abnormality that may increase the risk of study participation		EX01A00
2.b	2	Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV)		EX02A00
2.c	3	History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s)		EX03A00
2.d	4	Receipt of medications intended to prevent COVID-19		EX04A00
2.e	5	Stages 1 and 2 only: Previous clinical or microbiological diagnosis of COVID-19		EX05A00
2.f	8	Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination		EX08A00
2.g	9	Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention		EX09A00
2.h	10	Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection		EX10A00
2.i	11	Women who are pregnant or breastfeeding		EX11A00
2.j	12	Previous vaccination with any coronavirus vaccine		EX12A00
2.k	13	Individuals who receive immunosuppressive therapy, such as cytotoxic agents or systemic corticosteroids. Inhaled/nebulized, Intra-articular, intrabursal, or topical corticosteroids are permitted		EX13A00
2.l	14	Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study		EX14A00
2.m	15	Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation		EX15A00
2.n	16	Previous participation in other studies involving study intervention containing lipid nanoparticles		EX16A00
2.o	21	Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members		EX21A00

Exclusion Criteria Entry

2.1	Exclusion Number: [Exclusion Number]	
2.2	Criterion Description: [Criterion Description]	
2.3	Criterion met? [Criterion met?]	○ YES Describe details if relevant

		NO
2.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	

C4591001: INCLUSION/EXCLUSION CRITERIA (INC EXC S)

Study eligibility requires subjects to meet all inclusion criteria (YES) and Not meet exclusion criteria (NO).

Inclusion Criteria

#	Inclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
1.a	1	Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study stage)		IN01A00
1.b	2	Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures		IN02A00
1.c	3	Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study		IN03A00
1.d	4	Capable of giving personal signed informed consent, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol		IN04A00

Inclusion Criteria Entry

1.1	Inclusion Number: [Inclusion Number]	○ 1 ○ 2 ○ 3 ○ 4
1.2	Criterion Description: [Criterion Description]	
1.3	Criterion met? [Criterion met?]	○ YES ○ NO Describe details if relevant
1.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	○ IN01A00 ○ IN02A00 ○ IN03A00 ○ IN04A00

Exclusion Criteria

#	Exclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
2.a	1	Other medical or psychiatric condition incl. recent (within past year) or active suicidal ideation/behavior/lab abnormality that may increase the risk of study participation		EX01A00
2.b	2	Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV)		EX02A00
2.c	3	History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s)		EX03A00
2.d	4	Receipt of medications intended to prevent COVID-19		EX04A00
2.e	5	Stages 1 and 2 only: Previous clinical or microbiological diagnosis of COVID-19		EX05A00
2.f	6	Sentinel participants in Stage 1 only: Individuals at high risk for severe COVID-19 (full details in protocol)		EX06A01
2.g	7	Sentinel participants in Stage 1 only: Individuals currently working in occupations with high risk of exposure to SARS-CoV-2 (eg, healthcare worker, emergency response personnel)		EX07A00
2.h	8	Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination		EX08A00
2.i	9	Sentinel participants in Stage 1 only: Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention		EX09A04
2.j	10	Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection		EX10A00
2.k	11	Women who are pregnant or breastfeeding		EX11A00
2.l	12	Previous vaccination with any coronavirus vaccine		EX12A00
2.m	13	Subjects who receive immunosuppressive therapy, such as cytotoxic agents or systemic corticosteroids		EX13A01
2.n	14	Sentinel participants in Stage 1 only: Regular receipt of inhaled/nebulized corticosteroids		EX22A01
2.o	15	Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study		EX14A01
2.p	16	Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation		EX15A01
2.q	17	Previous participation in other studies involving study intervention containing lipid nanoparticles		EX16A01
2.r	18	Sentinel participants in Stage 1 only: Positive serological test for SARS-CoV-2 IgM and/or IgG antibodies at the screening visit		EX17A01
2.s	19	Sentinel participants in Stage 1 only: Screening hematology/blood chemistry lab >=Grade 1 abnormality. Except Bilirubin, other stable Grade1 abnormalities may be considered eligible by Investigator		EX18A01
2.t	20	Sentinel participants in Stage 1 only: Positive test for HIV, hepatitis B surface antigen		EX19A01

		(HBsAg), hepatitis B core antibodies (HBc Abs), or hepatitis C virus antibodies (HCV Abs) at screening visit		
2.u	21	Sentinel participants in Stage 1 only: SARS-CoV-2 NAAT-positive nasal swab within 24 hours before receipt of study intervention		EX20A01
2.v	22	Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members		EX21A01

Exclusion Criteria Entry

2.1	Exclusion Number: [Exclusion Number]	
2.2	Criterion Description: [Criterion Description]	
2.3	Criterion met? [Criterion met?]	YES Describe details if relevant NO
2.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	

C4591001: INCLUSION/EXCLUSION CRITERIA (INC EXC S)

Study eligibility requires subjects to meet all inclusion criteria (YES) and Not meet exclusion criteria (NO).

Inclusion Criteria

#	Inclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
1.a	1	Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study stage)		IN01A00
1.b	2	Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures		IN02A00
1.c	3	Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study		IN03A00
1.d	4	Capable of giving personal signed informed consent, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol		IN04A00

Inclusion Criteria Entry

1.1	Inclusion Number: [Inclusion Number]	○ 1 ○ 2 ○ 3 ○ 4
1.2	Criterion Description: [Criterion Description]	
1.3	Criterion met? [Criterion met?]	○ YES ○ NO Describe details if relevant
1.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	○ IN01A00 ○ IN02A00 ○ IN03A00 ○ IN04A00

Exclusion Criteria

#	Exclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
2.a	1	Other medical or psychiatric condition incl. recent (within past year) or active suicidal ideation/behavior/lab abnormality that may increase the risk of study participation		EX01A00
2.b	2	Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV)		EX02A00
2.c	3	History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s)		EX03A00
2.d	4	Receipt of medications intended to prevent COVID-19		EX04A00
2.e	5	Stages 1 and 2 only: Previous clinical or microbiological diagnosis of COVID-19		EX05A00
2.f	6	Sentinel participants in Stage 1 only: Individuals at high risk for severe COVID-19		EX06A00
2.g	7	Sentinel participants in Stage 1 only: Individuals currently working in occupations with high risk of exposure to SARS-CoV-2 (eg, healthcare worker, emergency response personnel)		EX07A00
2.h	8	Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination		EX08A00
2.i	9	Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention		EX09A00
2.j	10	Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection		EX10A00
2.k	11	Women who are pregnant or breastfeeding		EX11A00
2.l	12	Previous vaccination with any coronavirus vaccine		EX12A00
2.m	13	Individuals who receive immunosuppressive therapy, such as cytotoxic agents or systemic corticosteroids. Inhaled/nebulized, Intra-articular, intrabursal, or topical corticosteroids are permitted		EX13A00
2.n	14	Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study		EX14A00
2.o	15	Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation		EX15A00
2.p	16	Previous participation in other studies involving study intervention containing lipid nanoparticles		EX16A00
2.q	17	Sentinel participants in Stage 1 only: Positive serological test for SARS-CoV-2 IgM and/or IgG antibodies at the screening visit		EX17A00
2.r	18	Sentinel participants in Stage 1 only: Screening hematology/blood chemistry lab >=Grade 1 abnormality. Except Bilirubin, other stable Grade1 abnormalities may be considered eligible by Investigator		EX18A00
2.s	19	Sentinel participants in Stage 1 only: Positive test for HIV, hepatitis B surface antigen (HBsAg), hepatitis B core antibodies (HBc Abs), or hepatitis C virus antibodies (HCV Abs) at screening visit		EX19A00

2.t	20	Sentinel participants in Stage 1 only: SARS-CoV-2 NAAT-positive nasal swab within 24 hours before receipt of study intervention		EX20A00
2.u	21	Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members		EX21A00

Exclusion Criteria Entry		
2.1	Exclusion Number: [Exclusion Number]	
2.2	Criterion Description: [Criterion Description]	
2.3	Criterion met? [Criterion met?]	YES Describe details if relevant NO
2.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	

C4591001: INCLUSION/EXCLUSION CRITERIA (INC EXC S)

Study eligibility requires subjects to meet all inclusion criteria (YES) and Not meet exclusion criteria (NO).

Inclusion Criteria

#	Inclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
1.a	1	Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study stage)		IN01A00
1.b	2	Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures		IN02A00
1.c	3	Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study		IN03A00
1.d	4	Capable of giving personal signed informed consent, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol		IN04A00

Inclusion Criteria Entry

1.1	Inclusion Number: [Inclusion Number]	○ 1 ○ 2 ○ 3 ○ 4
1.2	Criterion Description: [Criterion Description]	
1.3	Criterion met? [Criterion met?]	○ YES ○ NO Describe details if relevant
1.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	○ IN01A00 ○ IN02A00 ○ IN03A00 ○ IN04A00

Exclusion Criteria

#	Exclusion Number	Criterion Description	Criterion met?	Criterion ID: (For Pfizer use only)
2.a	1	Other medical or psychiatric condition incl. recent (within past year) or active suicidal ideation/behavior/lab abnormality that may increase the risk of study participation		EX01A00
2.b	2	Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV)		EX02A00
2.c	3	History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s)		EX03A00
2.d	4	Receipt of medications intended to prevent COVID-19		EX04A00
2.e	5	Stages 1 and 2 only: Previous clinical or microbiological diagnosis of COVID-19		EX05A00
2.f	6	Sentinel participants in Stage 1 only: Individuals at high risk for severe COVID-19 (full details in protocol)		EX06A01
2.g	7	Sentinel participants in Stage 1 only: Individuals currently working in occupations with high risk of exposure to SARS-CoV-2 (eg, healthcare worker, emergency response personnel)		EX07A00
2.h	8	Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination		EX08A00
2.i	9	Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention		EX09A00
2.j	10	Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection		EX10A00
2.k	11	Women who are pregnant or breastfeeding		EX11A00
2.l	12	Previous vaccination with any coronavirus vaccine		EX12A00
2.m	13	Subjects who receive immunosuppressive therapy, such as cytotoxic agents or systemic corticosteroids		EX13A01
2.n	14	Sentinel participants in Stage 1 only: Regular receipt of inhaled/nebulized corticosteroids		EX22A01
2.o	15	Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study		EX14A01
2.p	16	Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation		EX15A01
2.q	17	Previous participation in other studies involving study intervention containing lipid nanoparticles		EX16A01
2.r	18	Sentinel participants in Stage 1 only: Positive serological test for SARS-CoV-2 IgM and/or IgG antibodies at the screening visit		EX17A01
2.s	19	Sentinel participants in Stage 1 only: Screening hematology/blood chemistry lab >=Grade 1 abnormality. Except Bilirubin, other stable Grade1 abnormalities may be considered eligible by Investigator		EX18A01
2.t	20	Sentinel participants in Stage 1 only: Positive test for HIV, hepatitis B surface antigen		EX19A01

		(HBsAg), hepatitis B core antibodies (HBc Abs), or hepatitis C virus antibodies (HCV Abs) at screening visit		
2.u	21	Sentinel participants in Stage 1 only: SARS-CoV-2 NAAT-positive nasal swab within 24 hours before receipt of study intervention		EX20A01
2.v	22	Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members		EX21A01

Exclusion Criteria Entry		
2.1	Exclusion Number: [Exclusion Number]	
2.2	Criterion Description: [Criterion Description]	
2.3	Criterion met? [Criterion met?]	YES Describe details if relevant NO
2.4	Criterion ID: (For Pfizer use only) [Criterion ID: (For Pfizer use only)]	

C4591001: CASEBOOK SIGNATURE FORM (INVSIG)		
Casebook Signature Form		
1.	Casebook Signature [Casebook Signature]	Click Here to Enable

C4591001: CENTRAL LAB SAMPLE COLLECTION (LAB)

Central Lab Sample Collection

1.	Collection Date: [Collection Date:]	/ /
2.	Specimen Type: [Specimen Type]	○ BLOOD

Lab Test

#	Category for Lab Test	Subcategory for Lab Test	Lab Sub-Panel Collected
3.a	CLINICAL CHEMISTRY	BLOOD CHEMISTRY	
3.b	HEMATOLOGY	DIFFERENTIAL	

Lab Test Entry

3.1	Lab Panel: [Category for Lab Test]	○ HEMATOLOGY ○ CLINICAL CHEMISTRY
3.2	Lab Sub-Panel: [Subcategory for Lab Test]	○ DIFFERENTIAL ○ BLOOD CHEMISTRY
3.3	Was the lab sub-panel collected?: [Lab Sub-Panel Collected]	○ YES ○ NO

C4591001: CENTRAL LAB SAMPLE COLLECTION - BASELINE (LAB BSL)

Central Lab Sample Collection

1.	Collection Date: [Collection Date:]	/ /
2.	Specimen Type: [Specimen Type]	○ BLOOD

Lab Test

#	Category for Lab Test	Subcategory for Lab Test	Lab Sub-Panel Collected
3.a	CLINICAL CHEMISTRY	BLOOD CHEMISTRY	
3.b	CLINICAL CHEMISTRY	VIROLOGY	
3.c	HEMATOLOGY	DIFFERENTIAL	

Lab Test Entry

3.1	Lab Panel: [Category for Lab Test]	○ HEMATOLOGY ○ CLINICAL CHEMISTRY
3.2	Lab Sub-Panel: [Subcategory for Lab Test]	○ DIFFERENTIAL ○ BLOOD CHEMISTRY ○ VIROLOGY
3.3	Was the lab sub-panel collected?: [Lab Sub-Panel Collected]	○ YES ○ NO

C4591001: LOCAL LABORATORY DATA - REPEATING CHEMISTRY (LAB CHEM) - Repeating Form

#	Category for Lab Test	Vendor Name	Collection Date:	Specimen Type	Lab Result
1					

Lab Chemistry Details

1.	Lab Panel: [Category for Lab Test]	○ CLINICAL CHEMISTRY
2.	Laboratory Name and Address [Vendor Name]	
3.	Collection Date: [Collection Date:]	/ /
4.	Specimen Type: [Specimen Type]	○ BLOOD

Lab Result

# ✔	Sponsor-Defined Identifier	Test:	Result:	Not Done:	Lab Normal Range
5.a		C Reactive Protein_PX329			

Lab Result Entry

5.1	Sponsor ID: [Sponsor-Defined Identifier]	
5.2	Test: [Test:]	○ C Reactive Protein_PX329
5.3	Result: [Result:]	
5.4	Not Done: *[hidden]* [Not Done:]	○ NOT DONE
5.5	LNMT [Lab Normal Range]	Low High Unit

C4591001: LOCAL LABORATORY DATA - REPEATING CHEMISTRY (LAB CHEM) - Repeating Form

#	Category for Lab Test	Vendor Name	Collection Date:	Specimen Type	Lab Result
1					

Lab Chemistry Details

1.	Lab Panel: [Category for Lab Test]	○CLINICAL CHEMISTRY
2.	Laboratory Name and Address [Vendor Name]	
3.	Collection Date: [Collection Date:]	/ /
4.	Specimen Type: [Specimen Type]	○BLOOD

Lab Result

# ✔	Sponsor-Defined Identifier	Test:	Result:	Not Done:	Lab Normal Range
5.a		C Reactive Protein_PX329			
5.b		Alanine Aminotransferase_PX30			
5.c		Aspartate Aminotransferase_PX28			
5.d		Alkaline Phosphatase_PX35			
5.e		Bilirubin_PX21			
5.f		Blood Urea Nitrogen_PX47			
5.g		Creatinine_PX48			

Lab Result Entry

5.1	Sponsor ID: [Sponsor-Defined Identifier]	
5.2	Test: [Test:]	
5.3	Result: [Result:]	
5.4	Not Done: [Not Done:]	○NOT DONE
5.5	LNMT [Lab Normal Range]	Low High Unit

C4591001: LOCAL LABORATORY DATA - REPEATING Hematology (LAB HEM) - Repeating Form

#	Category for Lab Test	Vendor Name (DERIVED)	Collection Date:	Specimen Type	Lab Result
1					

Laboratory Data Hematology

1.	Lab Panel: [Category for Lab Test]	○ HEMATOLOGY
2.	Laboratory Name and Address [Vendor Name (DERIVED)]	
3.	Collection Date: [Collection Date:]	/ /
4.	Specimen Type: [Specimen Type]	○ BLOOD

Lab Result

# ✔	Sponsor-Defined Identifier	Test:	Result:	Not Done:	Lab Normal Range
5.a		Hemoglobin_PX1			
5.b		Hematocrit_PX2			
5.c		Erythrocytes_PX3			
5.d		Platelets_PX5			
5.e		Leukocytes_PX7			
5.f		Neutrophils_PX608			
5.g		Eosinophils_PX609			
5.h		Monocytes_PX612			
5.i		Basophils_PX610			
5.j		Lymphocytes_PX611			

Lab Result Entry

5.1	Sponsor ID: [Sponsor-Defined Identifier]	
5.2	Test: [Test:]	
5.3	Result: [Result:]	
5.4	Not Done: [Not Done:]	○ NOT DONE
5.5	LNMT [Lab Normal Range]	Low High Unit

C4591001: CENTRAL LAB SAMPLE COLLECTION - HLA (LAB HLA)

Central Lab Sample Collection

1.	Collection Date: [Collection Date:]	/ /
2.	Specimen Type: [Specimen Type]	○ BLOOD

Lab Test

#	Category for Lab Test	Subcategory for Lab Test	Lab Sub-Panel Collected
3.a	HEMATOLOGY	IMMUNOLOGY	

Lab Test Entry

3.1	Lab Panel: [Category for Lab Test]	○ HEMATOLOGY
3.2	Lab Sub-Panel: [Subcategory for Lab Test]	○ IMMUNOLOGY
3.3	Was the lab sub-panel collected?: [Lab Sub-Panel Collected]	○ YES ○ NO

C4591001: CENTRAL LAB SAMPLE COLLECTION - PBMC (LAB PBMC)

Central Lab Sample Collection

1.	Collection Date: [Collection Date:]	/ /
2.	Specimen Type: [Specimen Type]	○ BLOOD

Lab Test

#	Category for Lab Test	Subcategory for Lab Test	Lab Sub-Panel Collected
3.a	HEMATOLOGY	IMMUNOLOGY	

Lab Test Entry

3.1	Lab Panel: [Category for Lab Test]	○ HEMATOLOGY
3.2	Lab Sub-Panel: [Subcategory for Lab Test]	○ IMMUNOLOGY
3.3	Was the lab sub-panel collected?: [Lab Sub-Panel Collected]	○ YES ○ NO

C4591001: LAB URINALYSIS - PREGNANCY TEST (LAB PREG)

Lab Urinalysis

1.	Lab Panel: [Category for Lab Test]	◯ URINALYSIS
2.	Lab Sub-Panel: [Subcategory for Lab Test]	◯ PREGNANCY
3.	Collection Date: [Collection Date:]	/ /
4.	Laboratory Name and Address (Derived) [Vendor Name (DERIVED)]	
5.	Specimen Type: [Specimen Type]	◯ URINE

Lab Result

#	Sponsor-Defined Identifier	Test:	Result:	Not Done:
6.a		Choriogonadotropin Beta_PX113		

Lab Result Entry

6.1	Sponsor ID: [Sponsor-Defined Identifier]	
6.2	Test: [Test:]	◯ Choriogonadotropin Beta_PX113
6.3	Result: [Result:]	◯ NEGATIVE ◯ POSITIVE
6.4	Not Done: [Not Done:]	◯ NOT DONE

C4591001: MEDICATION ERROR (MED ERROR) - Repeating Form

#	Category	Medication Error	Start Date	Is the medication error Still Ongoing	Study Medication Errors Action	Concomitant Medication Given	Non-Drug Treatment Given	Caused Study Discontinuation	Medication Error Associated With AE	Serious Adverse Event Number
1										

Medication Error

1.	Category: [Category]	◯ MEDICATION ERROR
2.	Medication Error (Type of Medication Error): [Medication Error]	
3.	If this is a dispensing error, record the incorrect container number that was dispensed/administered to the subject: *[hidden]* [Incorrect package ID]	
4.	Start Date: [Start Date]	/ /
5.	Is the medication error still ongoing? [Is the medication error Still Ongoing]	◯ YES ◯ NO End Date: / /
6.	Latest Action Taken with Study Treatment: [Study Medication Errors Action]	◯ NO ACTION TAKEN ◯ PERMANENTLY DISCONTINUED
7.	Was a Concomitant Medication given? [Concomitant Medication Given]	◯ YES ◯ NO
8.	Was a Non-Drug Treatment given? [Non-Drug Treatment Given]	◯ YES ◯ NO
9.	Did the Medication Error cause the subject to be discontinued from the study? [Caused Study Discontinuation]	◯ YES ◯ NO
10.	Was this medication error associated with any adverse events? [Medication Error Associated With AE]	◯ YES AE ID: AE ID: AE ID: AE ID: AE ID: ◯ NO
11.	Serious Adverse Event Number: For Pfizer Use Only [Serious Adverse Event Number]	
12.	Comparison Term *[hidden]* [Comparison Term]	
13.	Lowest Level Term *[hidden]* [Lowest Level Term]	
14.	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
15.	Dictionary-Derived Term *[hidden]* [Dictionary-Derived Term]	

16.	Preferred Term Code *[hidden]* [Preferred Term Code]	
17.	High Level Term *[hidden]* [High Level Term]	
18.	High Level Term Code *[hidden]* [High Level Term Code]	
19.	High Level Group Term *[hidden]* [High Level Group Term]	
20.	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
21.	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
22.	Primary System Organ Class Code *[hidden]* [Primary System Organ Class Code]	

C4591001: GENERAL MEDICAL HISTORY (MEDHX)

	Line/MH Number	Medical History Term	Start Date	Ongoing
1.				

Medical History Details Entry

1.1	Line/MH Number: [Line/MH Number]	
1.2	Disease/Syndrome/Surgery/Non-Drug Allergies/Drug Allergies: [Medical History Term]	
1.3	Start Date: [Start Date]	/ /
1.4	Ongoing: [Ongoing]	YES NO End Date: / /
1.5	Comparison Term *[hidden]* [Comparison Term]	
1.6	Lowest Level Term *[hidden]* [Lowest Level Term]	
1.7	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
1.8	Dictionary Derived Term *[hidden]* [Dictionary Derived Term]	
1.9	Preferred Term Code *[hidden]* [Preferred Term Code]	
1.10	High Level Term *[hidden]* [High Level Term]	
1.11	High Level Term Code *[hidden]* [High Level Term Code]	
1.12	High Level Group Term *[hidden]* [High Level Group Term]	
1.13	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
1.14	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
1.15	Primary System Organ Class Code *[hidden]* [Primary System Organ Class Code]	

C4591001: OXYGENATION PARAMETERS (OXYGEN) - Repeating Form			
#	Date Time of Assessment	Arterial Blood Gases PaO2	FiO2 (Fraction of Inhaled Oxygen)
1			

Oxygenation Parameters		
1.	Date Time of Assessment: [Date Time of Assessment]	/ / : *24-hour clock*
2.	Arterial Blood Gases PaO2 (mmHg): [Arterial Blood Gases PaO2]	
3.	FiO2 (Fraction of Inhaled Oxygen): [FiO2 (Fraction of Inhaled Oxygen)]	

C4591001: PBMC/HLA BLOOD SAMPLE TRIGGER FORM (PBMC TRIG)

PBMC/HLA Blood Sample Trigger Form

1.	Select appropriate response - Is the participant part of the group collecting blood samples for PBMC isolation and HLA typing (select sites only)? [Trigger Response 15]	◯ Yes, the participant is part of the group collecting blood samples for PBMC isolation and HLA typing ◯ No, the participant is NOT part of the group collecting blood samples for PBMC isolation and HLA typing

C4591001: PHYSICAL EXAMINATION (PHYS EXAM)

Physical Examination

1.	Exam Date: [Exam Date]	/ /

Physical Examination Result

#	Body System Examined	Result
2.a	GENERAL APPEARANCE	
2.b	SKIN	
2.c	HEAD	
2.d	EYES	
2.e	EARS	
2.f	NOSE	
2.g	THROAT	
2.h	HEART	
2.i	LUNGS	
2.j	ABDOMEN	
2.k	MUSCULOSKELETAL	
2.l	EXTREMITIES	
2.m	NEUROLOGICAL	
2.n	LYMPH NODES	

Physical Examination Result Entry

2.1	Body System Examined: [Body System Examined]	
2.2	Result: [Result]	◯ NORMAL ◯ ABNORMAL If abnormal findings, specify: (If clinically significant, record on the Medical History or Adverse Event CRF as appropriate). Are there clinically significant findings? ◯ YES ◯ NO ◯ NOT DONE

C4591001: ELECTRONIC SAMPLE TRACKING - PRIOR COVID-19 INFECTION (PRIORCOV19)

Electronic Sample Tracking

1.	Data Origin [Data Origin]	○ SITE
2.	Sample Type [Sample Type]	○ SERUM
3.	Sample Collected? [Sample Collected]	○ NO ○ YES Date of Collection: / /
4.	If no sample was collected or sample was not collected according to protocol, please provide reason: [Reason sample not collected]	

	Sample ID
5.	

Aliquot Entry

Please enter barcode for each aliquot.

5.1	Sample ID [Sample ID]	

C4591001: CONCOMITANT MEDICATIONS - PROHIBITED (PROHIB CM) - Repeating Form

#	Sponsor-Defined Identifier	Category for Medication	Concomitant Medications Pre-specified	Name of Medication	Dose Description	Dose Unit	Dose Frequency	Route	Start Date	Ongoing
1										

Concomitant Medications

1.	What is the medication identifier? [Sponsor-Defined Identifier]	
2.	Category: [Category for Medication]	◯ CONCOMITANT IMMUNOSUPPRESSIVE THERAPY ◯ CORTICOSTEROIDS ◯ IMMUNOGLOBULINS
3.	Concomitant Medications Pre-specified: [Concomitant Medications Pre-specified]	◯ NO
4.	Medication: Provide the complete generic drug name (including salt form, where applicable). Where generic name is unknown, enter the full trade or proprietary name. Include clarifying information in the Medication text (e.g., Ingredient(s), route, use, formulation). [Name of Medication]	
5.	Dose: [Dose Description]	
6.	Dose Unit: [Dose Unit]	
7.	Dose Frequency: [Dose Frequency]	
8.	Route: [Route]	
9.	Start Date: [Start Date]	/ /
10.	Ongoing? [Ongoing]	◯ YES ◯ NO End Date: / /
11.	Comparison Term *[hidden]* [Comparison Term]	
12.	Standardized Medication Name - Dictionary derived. *[hidden]* [Standardized Medication Name]	
13.	Standardized Medication Code - Dictionary derived *[hidden]* [Standardized Medication Code]	

C4591001: RADIATION TREATMENT (PROHIB ND) - Repeating Form

#	Category	Treatment Identifier	Con Non-Drug Treatments Pre-specified	Treatment	Start Date	Ongoing?
1						

Radiation Treatment

1.	Category: [Category]	◯ RADIATION THERAPY
2.	What is the treatment Identifier? [Treatment Identifier]	
3.	Concomitant Non-drug Treatment Pre-specified: [Con Non-Drug Treatments Pre-specified]	◯ YES
4.	Treatment: [Treatment]	
5.	Start Date: [Start Date]	/ /
6.	Ongoing? [Ongoing?]	◯ YES ◯ NO End Date: / /
7.	Comparison Term *[hidden]* [Comparison Term]	
8.	Lowest Level Term *[hidden]* [Lowest Level Term]	
9.	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
10.	Dictionary Derived Term *[hidden]* [Dictionary Derived Term]	
11.	Preferred Term Code *[hidden]* [Preferred Term Code]	
12.	High Level Term *[hidden]* [High Level Term]	
13.	High Level Term Code *[hidden]* [High Level Term Code]	
14.	High Level Group Term *[hidden]* [High Level Group Term]	
15.	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
16.	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
17.	Primary System Organ Class Code *[hidden]* [Primary System Organ Class Code]	

C4591001: VITAL SIGNS - PULSE OX ROOM AIR (PULSE OX) - Repeating Form		
#	Date:	Vital Signs Details
1		

Vital Signs		
1.	Date: [Date:]	/ /

Vital Signs Details		
# ✔	Record Identifier:	Oxygen Saturation
2.a	1	

Vital Signs Details Entry		
2.1	Record Identifier: [Record Identifier:]	1
2.2	SPO2 Pulse Oximetry % [Oxygen Saturation]	

C4591001: RANDOMIZATION (RAND)		
Disposition		
1.	Randomization Date : [Randomization Date :]	/ /
2.	Randomization Number: [Randomization Number]	
3.	Randomization Group: [Randomization Group]	

C4591001: RANDOMIZATION - BOOSTER (RAND BOOST)		
Disposition		
1.	Randomization Date : [Randomization Date :]	/ /
2.	Randomization Number: [Randomization Number]	
3.	Rerandomization SSID: [Rerandomization SSID]	

C4591001: REACTOGENICITY DIARY (REAC DIARY)		
Reactogenicity Diary		
1.	Select appropriate response - Reactogenicity diary collection [Trigger Response 9]	◯ YES - REACTOGENICITY E-DIARY COLLECTED FOR THIS SUBJECT ◯ NO - REACTOGENICITY E-DIARY NOT COLLECTED FOR THIS SUBJECT

C4591001: UNPLANNED ASSESSMENT OF LOCAL REACTION - SYSTEMIC EVENT (REACTION)

Unplanned Assessment Of Local Reaction

1.	CISR Category *[hidden]* [CISR Category]	○ UNPLANNED ASSESSMENT OF LOCAL REACTION/SYSTEMIC EVENT
2.	Date of Assessment: [Date of Assessment]	/ /
3.	Injection Site Location [Injection Site Location]	○ DELTOID MUSCLE
4.	Injection Site Body Side: [Injection Site Body Side]	○ LEFT ○ RIGHT

Reaction

#	Reaction:	Reaction Present:
5.a	REDNESS	
5.b	SWELLING	

Reaction Entry

5.1	Reaction: [Reaction:]	○ REDNESS ○ SWELLING
5.2	Reaction Present: [Reaction Present:]	○ YES Maximum Diameter (cm): Minimum Diameter (cm): Meets Grade 4 Reaction Criteria: ○ YES ○ NO ○ NO

Symptom

#	Symptom:	Symptom Present:
6.a	PAIN AT INJECTION SITE	
6.b	FATIGUE/TIREDNESS	
6.c	HEADACHE	
6.d	VOMITING	
6.e	DIARRHEA	
6.f	NEW OR WORSENED MUSCLE PAIN	
6.g	NEW OR WORSENED JOINT PAIN	
6.h	CHILLS	

Symptom Entry

6.1	Symptom: [Symptom:]	
6.2	Symptom Present: [Symptom Present:]	○ YES Symptom Grade: ○ 1 ○ 2 ○ 3 ○ 4 Event related to Study Treament? ○ YES ○ NO ○ NO

C4591001: RESPIRATORY TREATMENT (RESP TX) - Repeating Form

#	Treatment Identifier	Con Non-Drug Treatments Pre-specified	Treatment	Treatment	Start Date	Ongoing?
1						

Respiratory Treatment

1.	What is the treatment Identifier? [Treatment Identifier]	
2.	Concomitant Non-drug Treatment Pre-specified: [Con Non-Drug Treatments Pre-specified]	○ YES
3.	Treatment: [Treatment]	○ INTUBATION ○ NON-INVASIVE POSITIVE PRESSURE VENTILATION ○ CPAP ○ OXYGEN THERAPY
4.	Treatment: [Treatment]	
5.	Start Date: [Start Date]	/ /
6.	Ongoing? [Ongoing?]	○ YES ○ NO End Date: / /
7.	Comparison Term *[hidden]* [Comparison Term]	
8.	Lowest Level Term *[hidden]* [Lowest Level Term]	
9.	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
10.	Dictionary Derived Term *[hidden]* [Dictionary Derived Term]	
11.	Preferred Term Code *[hidden]* [Preferred Term Code]	
12.	High Level Term *[hidden]* [High Level Term]	
13.	High Level Term Code *[hidden]* [High Level Term Code]	
14.	High Level Group Term *[hidden]* [High Level Group Term]	
15.	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
16.	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
17.	Primary System Organ Class Code *[hidden]* [Primary System Organ Class Code]	

C4591001: RESPIRATORY TREATMENT (RESP TX) - Repeating Form

#	Treatment Identifier	Con Non-Drug Treatments Pre-specified	Treatment	Treatment	Start Date	Ongoing?
1						

Respiratory Treatment

1.	What is the treatment Identifier? [Treatment Identifier]	
2.	Concomitant Non-drug Treatment Pre-specified: [Con Non-Drug Treatments Pre-specified]	○ YES
3.	Treatment: [Treatment]	○ NON-INVASIVE POSITIVE PRESSURE VENTILATION ○ CPAP ○ MECHANICAL VENTILATION ○ EXTRACORPOREAL MEMBRANE OXYGENATION ○ HIGH FLOW OXYGEN THERAPY
4.	Treatment: [Treatment]	
5.	Start Date: [Start Date]	/ /
6.	Ongoing? [Ongoing?]	○ YES ○ NO End Date: / /
7.	Comparison Term *[hidden]* [Comparison Term]	
8.	Lowest Level Term *[hidden]* [Lowest Level Term]	
9.	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
10.	Dictionary Derived Term *[hidden]* [Dictionary Derived Term]	
11.	Preferred Term Code *[hidden]* [Preferred Term Code]	
12.	High Level Term *[hidden]* [High Level Term]	
13.	High Level Term Code *[hidden]* [High Level Term Code]	
14.	High Level Group Term *[hidden]* [High Level Group Term]	
15.	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
16.	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
17.	Primary System Organ Class Code *[hidden]* [Primary System Organ Class Code]	

C4591001: FURTHER VACCINATION CONFIRMATION (REVAX CONF)		
Further Vaccination Confirmation		
1.	Select appropriate response - Is participant willing to return for Vaccination 3? [Trigger Response 1]	○ Participant is willing to return for Vaccination 3 Participant is: ○ eligible per local/national recommendations and confirmed to have received only placebo at Vaccination 1/2 ○ eligible per other protocol allowance(s) and confirmed to have received only placebo at Vaccination 1/2 ○ eligible and NOT confirmed to have received only placebo at Vaccination 1/2 ○ Participant is NOT willing to return for Vaccination 3 OR otherwise not eligible

C4591001: INFORMED CONSENT - FURTHER VACCINATION (REVAX CONS)		
Informed Consent - Further Vaccination		
1.	Consent Was: [Consent Was:]	OBTAINED Date Written Consent Obtained / /

C4591001: INCLUSION/EXCLUSION CRITERIA - FURTHER VACCINATION (REVAX IE)		
	Criterion Description	
1.		
Inclusion Criteria Not Met Entry		
1.1	Description of Inclusion Criterion Not Met [Criterion Description]	
	Criterion Description	
2.		
Exclusion Criteria Met Entry		
2.1	Description of Exclusion Criterion Met [Criterion Description]	

C4591001: ELECTRONIC SAMPLE TRACKING - REPEAT SWAB (RSWAB)		
Electronic Sample Tracking		
1.	Data Origin [Data Origin]	○ SITE
2.	Sample Type [Sample Type]	○ NASAL_SWAB ○ NASAL_SWAB_SELF
3.	Sample Collected? [Sample Collected]	○ NO ○ YES Date of Collection: / /
4.	If no sample was collected or sample was not collected according to protocol, please provide reason: [Reason sample not collected]	
	Sample ID	
5.		
Aliquot Entry		
Please enter barcode for each aliquot.		
5.1	Sample ID [Sample ID]	

C4591001: ELECTRONIC SAMPLE TRACKING - IMMUNOGENICITY (SAMP TRK)

Electronic Sample Tracking

1.	Data Origin [Data Origin]	○ SITE
2.	Sample Type [Sample Type]	○ SERUM
3.	Sample Collected? [Sample Collected]	○ NO ○ YES Date of Collection: / /
4.	If no sample was collected or sample was not collected according to protocol, please provide reason: [Reason sample not collected]	

	Sample ID
5.	

Aliquot Entry

Please enter barcode for each aliquot.

5.1	Sample ID [Sample ID]	

C4591001: INFORM SCREENING (SCREEN)		
InForm Screening		
1.	InForm Initials *[hidden]* [InForm Initials]	
2.	Birth Date: [Birth Year]	/ /

C4591001: ELECTRONIC SAMPLE TRACKING - NASAL SWAB SELF (SELF SWAB)

Electronic Sample Tracking

1.	Data Origin [Data Origin]	○ SITE
2.	Sample Type [Sample Type]	○ NASAL_SWAB_SELF
3.	Sample Collected? [Sample Collected]	○ NO ○ YES Date of Collection: / /
4.	If no sample was collected or sample was not collected according to protocol, please provide reason: [Reason sample not collected]	

	Sample ID
5.	

Aliquot Entry

Please enter barcode for each aliquot.

5.1	Sample ID [Sample ID]	

C4591001: SIGNS AND SYMPTOMS OF POTENTIAL COVID-19 (SOD)

Signs and Symptoms

1.	Date of Assessment: [Date of assessment]	/ /
2.	Date of First Symptom Started: [First Symptom Started Date]	/ /
3.	Symptoms Ongoing? [Symptoms Ongoing]	YES NO Date of Last Symptom Resolved: / /

Symptoms

# ✔	Event Pre-specified	Symptoms	Symptom Present
4.a	YES	FEVER	
4.b	YES	LOSS OF TASTE/SMELL	
4.c	YES	NEW OR INCREASED COUGH	
4.d	YES	NEW OR INCREASED NASAL CONGESTION	
4.e	YES	NEW OR INCREASED NASAL DISCHARGE	
4.f	YES	NEW OR INCREASED SHORTNESS OF BREATH	
4.g	YES	NEW OR INCREASED SORE THROAT	
4.h	YES	NEW OR INCREASED SPUTUM PRODUCTION	
4.i	YES	NEW OR INCREASED WHEEZING	

Symptoms Entry

4.1	Event Pre-specified: *[hidden]* [Event Pre-specified]	YES
4.2	Symptoms: [Symptoms]	
4.3	Was symptom present? [Symptom Present]	YES NO

	Symptoms - Other
5. ✔	

Symptoms - Other Entry

5.1	Symptoms - Other Text: [Symptoms - Other]	
5.2	Comparison Term: *[hidden]* [Comparison Term]	
5.3	Lowest Level Term *[hidden]* [Lowest Level Term]	
5.4	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
5.5	Dictionary Derived Term *[hidden]* [Dictionary Derived Term]	
5.6	Preferred Term Code *[hidden]* [Preferred Term Code]	
5.7	High Level Term *[hidden]* [High Level Term]	
5.8	High Level Term Code *[hidden]* [High Level Term Code]	
5.9	High Level Group Term *[hidden]* [High Level Group Term]	
5.10	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
5.11	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
5.12	Primary System Organ Class Code *[hidden]* [Primary System Organ Class	

	Code]	

C4591001: SIGNS AND SYMPTOMS OF POTENTIAL COVID-19 (SOD)

Signs and Symptoms

1.	Date of Assessment: [Date of assessment]	/ /
2.	Date of First Symptom Started: [First Symptom Started Date]	/ /
3.	Symptoms Ongoing? [Symptoms Ongoing]	YES NO Date of Last Symptom Resolved: / /

Symptoms

# ✔	Event Pre-specified	Symptoms	Symptom Present
4.a	YES	FEVER	
4.b	YES	NEW OR INCREASED COUGH	
4.c	YES	NEW OR INCREASED SHORTNESS OF BREATH	
4.d	YES	CHILLS	
4.e	YES	NEW OR INCREASED MUSCLE PAIN	
4.f	YES	NEW LOSS OF TASTE OR SMELL	
4.g	YES	NEW OR INCREASED SORE THROAT	
4.h	YES	DIARRHEA	
4.i	YES	VOMITING	

Symptoms Entry

4.1	Event Pre-specified: *[hidden]* [Event Pre-specified]	YES
4.2	Symptoms: [Symptoms]	
4.3	Was symptom present? [Symptom Present]	YES NO

	Symptoms - Other
5. ✔	

Symptoms - Other Entry

5.1	Symptoms - Other Text: [Symptoms - Other]	
5.2	Comparison Term: *[hidden]* [Comparison Term]	
5.3	Lowest Level Term *[hidden]* [Lowest Level Term]	
5.4	Lowest Level Term Code *[hidden]* [Lowest Level Term Code]	
5.5	Dictionary Derived Term *[hidden]* [Dictionary Derived Term]	
5.6	Preferred Term Code *[hidden]* [Preferred Term Code]	
5.7	High Level Term *[hidden]* [High Level Term]	
5.8	High Level Term Code *[hidden]* [High Level Term Code]	
5.9	High Level Group Term *[hidden]* [High Level Group Term]	
5.10	High Level Group Term Code *[hidden]* [High Level Group Term Code]	
5.11	Primary System Organ Class *[hidden]* [Primary System Organ Class]	
5.12	Primary System Organ Class Code *[hidden]* [Primary System Organ Class	

	Code]	

C4591001: STRATIFICATION (STRAT)		
Stratification		
1.	Select appropriate response - Randomization Stage [Trigger Response 3]	◯ Non-Sentinel Stage 1
2.	Select appropriate response - Randomization Age Group [Trigger Response 4]	◯ Age 18 to 55 ◯ Age 65 to 85
3.	Select appropriate response - Randomization Dose [Trigger Response 5]	◯ 10 mcg ◯ 20 mcg ◯ 30 mcg
4.	Select appropriate response - Randomization Dose Group [Trigger Response 8]	◯ 21 Day ◯ 60 Day
5.	Select appropriate response - BNT Number [Trigger Response 7]	◯ (BNT162b1 or PBO) ◯ (BNT162b2 or PBO) ◯ (BNT162b3 or PBO)

C4591001: STRATIFICATION (STRAT)		
Stratification		
1.	Select appropriate response - Randomization Stage [Trigger Response 3]	◯ Stage 1 ◯ Stage 2
2.	Select appropriate response - Randomization Age Group [Trigger Response 4]	◯ Age 18 to 55 ◯ Age 56 to 85 ◯ Age 65 to 85
3.	Select appropriate response - Randomization Dose [Trigger Response 5]	◯ Low dose level (3mcg) ◯ Medium dose level (10mcg) ◯ High dose level (30mcg) ◯ Low dose level (10mcg) ◯ Medium dose level (30mcg) ◯ High dose level (100mcg) ◯ Low dose level (0.1mcg) ◯ Medium dose level (0.3mcg) ◯ High dose level (1mcg) ◯ Mid-High dose level (50mcg) ◯ Low-Mid dose level (20mcg)
4.	Select appropriate response - Randomization Dose Group *[hidden]* [Trigger Response 6]	◯ 21 Day 2-dose group ◯ 60 Day 2-dose group ◯ 1-dose group
5.	Select appropriate response - Randomization Dose Group [Trigger Response 8]	◯ 21 Day ◯ 60 Day
6.	Select appropriate response - BNT Number [Trigger Response 7]	◯ (BNT162a1 or PBO) ◯ (BNT162b1 or PBO) ◯ (BNT162b2 or PBO) ◯ (BNT162c2 or PBO) ◯ (BNT162b3 or PBO)

C4591001: STRATIFICATION (STRAT)		
Stratification		
1.	Select appropriate response - Randomization Stage [Trigger Response 3]	◯ Stage 2
2.	Select appropriate response - Randomization Age Group [Trigger Response 4]	◯ Age 18 to 55 ◯ Age 56 to 85
3.	Select appropriate response - Randomization Dose [Trigger Response 5]	◯ 10 mcg ◯ 20 mcg ◯ 30 mcg
4.	Select appropriate response - BNT Number [Trigger Response 7]	◯ (BNT162b1 or PBO) ◯ (BNT162b2 or PBO) ◯ (BNT162b3 or PBO)

C4591001: SUBJECT STATUS (SUB STATU)		
Subject Status		
1.	Subject Status [Subject Status]	
2.	Subject Status Date [Status Date]	/ /

C4591001: INFORMED CONSENT - ASYMPTOMATIC SURVEILLANCE (SURV CONS)		
Informed Consent - Asymptomatic Surveillance		
1.	Consent Was: [Consent Was:]	○ OBTAINED Date Written Consent Obtained / /

C4591001: ELECTRONIC SAMPLE TRACKING - NASAL SWAB (SWAB PFE)		
Electronic Sample Tracking		
1.	Data Origin [Data Origin]	○ SITE
2.	Sample Type [Sample Type]	○ NASAL_SWAB
3.	Sample Collected? [Sample Collected]	○ NO ○ YES Date of Collection: / /
4.	If no sample was collected or sample was not collected according to protocol, please provide reason: [Reason sample not collected]	

	Sample ID
5.	

Aliquot Entry		
Please enter barcode for each aliquot.		
5.1	Sample ID [Sample ID]	

C4591001: MICROBIOLOGY SPECIMEN (SWAB SITE) - Repeating Form

#	Date of Collection	Specimen Type	Specimen Collection Location	Assay Code and Description	Device Type	Trade Name	Result	Comments:
1								

Microbiology Specimen

1.	Actual Date of Collection: [Date of Collection]	/ /
2.	Specimen Type: [Specimen Type]	○ SWABBED MATERIAL
3.	Specimen Collection Location: [Specimen Collection Location]	○ NASAL CAVITY
4.	Assay Code and Description: [Assay Code and Description]	○ SEVERE ACUTE RESP SYNDROME CORONAVIRUS 2
5.	Device Type: [Device Type]	○ SARS-COV-2 DIAGNOSTIC TEST
6.	Trade Name: [Trade Name]	○ CEPHEID XPERT XPRESS SARS-COV-2 TEST
7.	Test Result: [Result]	○ POSITIVE ○ NEGATIVE ○ INDETERMINATE
8.	Comments/Findings/Details: [Comments:]	

C4591001: VACCINATION SYMPTOMS DIARY - SYMPTOM RESOLVED DATES (SYMPRDATE)

Vaccination Symptoms Diary - Symptom Resolved Dates

1.	Were medications to treat fever/pain given on the last day the Subject Diary was completed? [Fever/Pain Medication on Last Diary Day]	◯ YES Ongoing? ◯ YES ◯ NO Stop Date: [ ] / [ ] / [ ] ◯ NO

#	Symptom:	Were fever or systemic symptoms present on the last day the Subject Diary was completed?
2.a	FEVER	
2.b	FATIGUE	
2.c	HEADACHE	
2.d	CHILLS	
2.e	VOMITING	
2.f	DIARRHEA	
2.g	NEW OR WORSENED MUSCLE PAIN	
2.h	NEW OR WORSENED JOINT PAIN	

2.1	Symptom: [Symptom:]	[ ]
2.2	Were fever or systemic symptoms present on the last day the Subject Diary was completed? [Were fever or systemic symptoms present on the last day the Subject Diary was completed?]	◯ YES Ongoing? ◯ YES ◯ NO Stop Date: [ ] / [ ] / [ ] ◯ NO
3.	Injection Site Location: [Injection Site Location:]	◯ DELTOID MUSCLE
4.	Injection Site Body Side: [Injection Site Body Side:]	◯ LEFT ◯ RIGHT

#	Injection Site Reaction:	Were injection site reactions present on the last day the Subject Diary was completed?
5.a	REDNESS	
5.b	SWELLING	
5.c	PAIN AT INJECTION SITE	

5.1	Injection Site Reaction: [Injection Site Reaction:]	◯ REDNESS ◯ SWELLING ◯ PAIN AT INJECTION SITE
5.2	Were injection site reactions present on the last day the Subject Diary was completed? [Were injection site reactions present on the last day the Subject Diary was completed?]	◯ YES Ongoing? ◯ YES ◯ NO Stop Date: [ ] / [ ] / [ ] ◯ NO

C4591001: TRANSFUSIONS (TRANSFUSE) - Repeating Form		
#	Transfusion Type	Date of Transfusion
1		

1.	Transfusion Type: [Transfusion Type]	◯ PACKED RBC ◯ PLATELETS ◯ WHOLE BLOOD ◯ PLASMA ◯ OTHER Specify:
2.	Date of Transfusion: [Date of Transfusion]	/ /

C4591001: TREATMENT UNBLINDED (TRN UNBLN)		
Treatment Unblinded		
1.	Date Treatment Unblinded : [Date Treatment Unblinded :]	/ /
2.	Primary Reason for Unblinding: [Primary Reason for Unblinding]	○ SUBJECT SAFETY CONCERN ○ OTHER If other, specify: ○ ASSESS ELIGIBILITY FOR ADDITIONAL VACCINATION

C4591001: TREATMENT UNBLINDED - BOOSTER (TRN UNBLNB)		
Treatment Unblinded - Booster		
1.	Date Treatment Unblinded : [Date Treatment Unblinded :]	/ /
2.	Primary Reason for Unblinding: [Primary Reason for Unblinding]	○ SUBJECT SAFETY CONCERN ○ OTHER If other, specify:

C4591001: UNPLANNED VISIT (UNPL)		
Unplanned Assessments		
1.	Assessments [Assessments]	☐ CONTACT OUTCOME

C4591001: VACCINATION (VACIN TRT)

Vaccination

1.	Was there a temporary delay of vaccination? [Temporary Delay of Vaccination]	○ YES Date of First Delay: / / / Reason(s) for Temporary Delay of Vaccination ☐ FEVER OR ACUTE ILLNESS ☐ RECENT SYSTEMIC CORTICOSTEROID TREATMENT ☐ RECENT NON-STUDY VACCINATION ☐ ANTICIPATED NON-STUDY VACCINATION ○ NO
2.	Treatment Name [Treatment Name]	
3.	Formulation: [Formulation:]	○ INJECTION
4.	Dose Date Time: [Dose Date Time:]	/ / : *24-hour clock*
5.	Anatomical Location: [Anatomical Location:]	○ DELTOID MUSCLE
6.	Body Side: [Body Side:]	○ LEFT ○ RIGHT
7.	Route: [Route:]	○ INTRAMUSCULAR
8.	Planned Dose: [Planned Dose]	
9.	Planned Dose Unit: [Planned Dose Unit]	○ ug
10.	Actual Dose: [Actual Dose:]	
11.	Unit: [Unit:]	○ ug
12.	Was the Actual Dose adjusted from planned? [Dose Adjusted From Planned]	○ YES What was the reason the dose was adjusted? ○ ADVERSE EVENT(S) ○ INSUFFICIENT CLINICAL RESPONSE ○ OTHER SPECIFY If other, specify: ○ NO
13.	Timeframe Subject Was Observed [Timeframe Subject Was Observed]	○ THE PROTOCOL SPECIFIED OBSERVATION PERIOD
14.	Was the subject observed for at least the protocol specified observation period after investigational product administration? [Observed Post Dose For Specified Time]	○ YES ○ NO If No, specify reason:
15.	Comparison Term *[hidden]* [Comparison Term]	
16.	Standardized Medication Name -	

	Dictionary Derived. *[hidden]* [Standardized Medication Name]	
17.	Standardized Medication Code - Dictionary Derived *[hidden]* [Standardized Medication Code]	

C4591001: VACCINATION (VACIN TRT)

Vaccination

1.	Was there a temporary delay of vaccination? [Temporary Delay of Vaccination]	○ YES Date of First Delay: / / Reason(s) for Temporary Delay of Vaccination ☐ FEVER OR ACUTE ILLNESS ☐ RECENT SYSTEMIC CORTICOSTEROID TREATMENT ☐ RECENT NON-STUDY VACCINATION ☐ ANTICIPATED NON-STUDY VACCINATION ○ NO
2.	Treatment Name [Treatment Name]	
3.	Formulation: [Formulation:]	○ INJECTION
4.	Dose Date Time: [Dose Date Time:]	/ / : *24-hour clock*
5.	Anatomical Location: [Anatomical Location:]	○ DELTOID MUSCLE
6.	Body Side: [Body Side:]	○ LEFT ○ RIGHT
7.	Route: [Route:]	○ INTRAMUSCULAR
8.	Container Number: *[hidden]* [PAC / Kit Number:]	
9.	Actual Dose: [Actual Dose:]	
10.	Unit: [Unit:]	○ mL ○ ug
11.	Timeframe Subject Was Observed [Timeframe Subject Was Observed]	○ THE PROTOCOL SPECIFIED OBSERVATION PERIOD ○ 30 MINUTES
12.	Was the subject observed for at least the protocol specified observation period after investigational product administration? [Observed Post Dose For Specified Time]	○ YES ○ NO If No, specify reason:
13.	Comparison Term *[hidden]* [Comparison Term]	
14.	Standardized Medication Name - Dictionary Derived. *[hidden]* [Standardized Medication Name]	
15.	Standardized Medication Code - Dictionary Derived *[hidden]*	

	[Standardized Medication Code]	

C4591001: CONCOMITANT MEDICATIONS - VASOPRESSORS (VASOPRESS) - Repeating Form

#	Sponsor-Defined Identifier	Category for Medication	Concomitant Medications Pre-specified	Name of Medication	Start Date	Ongoing
1						

Concomitant Medications

1.	What is the medication identifier? [Sponsor-Defined Identifier]	
2.	Category: [Category for Medication]	○ GENERAL CONCOMITANT MEDICATIONS
3.	Concomitant Medications Pre-specified: [Concomitant Medications Pre-specified]	○ NO
4.	Medication: Provide the complete generic drug name (including salt form, where applicable). Where generic name is unknown, enter the full trade or proprietary name. Include clarifying information in the Medication text (e.g., Ingredient(s), route, use, formulation). [Name of Medication]	
5.	Start Date: [Start Date]	/ /
6.	Ongoing? [Ongoing]	○ YES ○ NO End Date: / /
7.	Comparison Term *[hidden]* [Comparison Term]	
8.	Standardized Medication Name - Dictionary derived. *[hidden]* [Standardized Medication Name]	
9.	Standardized Medication Code - Dictionary derived *[hidden]* [Standardized Medication Code]	

C4591001: VACCINATION 4 TRIGGER FORM (VAX4 TRIG)		
Vaccination 4 Trigger Form		
1.	Select appropriate response - Has the participant been selected to receive an additional (4th) dose of BNT162b2SA? [Trigger Response 14]	◯ Yes, the participant has been selected to receive an additional (4th) dose of BNT162b2SA ◯ No, the participant has NOT been selected to receive an additional (4th) dose of BNT162b2SA

C4591001: VITAL SIGNS - TEMP (VITAL TEMP)

Vital Signs

1.	Date: [Date:]	/ /

Vital Signs Details

#	Record Identifier:	Temperature	Temperature Unit	Temperature Location:
2.a	1			

Vital Signs Details Entry

2.1	Record Identifier: [Record Identifier:]	○ 1
2.2	Temperature: [Temperature]	
2.3	Unit: [Temperature Unit]	○ F ○ C
2.4	Temperature Location: [Temperature Location:]	○ ORAL CAVITY ○ EAR ○ RECTUM ○ AXILLA ○ FOREHEAD

C4591001: VITAL SIGNS - BASELINE (VITALS BSL)

Vital Signs

1.	Date: [Date:]	/ /
2.	Weight: [Weight]	
3.	Unit: [Weight Unit]	kg LB
4.	Height: [Height]	
5.	Unit: [Height Unit]	cm in
6.	Body Mass Index: [Body Mass Index]	

Vital Signs Details

#	Record Identifier:	Temperature	Temperature Unit	Temperature Location:	Systolic:	Diastolic:	BP Position	Pulse:
7.a	1						SITTING	

Vital Signs Details Entry

7.1	Record Identifier: [Record Identifier:]	1
7.2	Temperature: [Temperature]	
7.3	Unit: [Temperature Unit]	C F
7.4	Temperature Location: [Temperature Location:]	ORAL CAVITY EAR RECTUM AXILLA FOREHEAD
7.5	Systolic: [Systolic:]	
7.6	Diastolic: [Diastolic:]	
7.7	BP Position: [BP Position]	SITTING
7.8	Pulse: [Pulse:]	

C4591001: VITAL SIGNS - BASELINE (VITALS BSL)

Vital Signs

1.	Date: [Date:]	/ /
2.	Weight: [Weight]	
3.	Unit: [Weight Unit]	kg LB
4.	Height: [Height]	
5.	Unit: [Height Unit]	cm in
6.	Body Mass Index: [Body Mass Index]	

Vital Signs Details

#	Record Identifier:	Temperature	Temperature Unit	Temperature Location:
7.a	1			

Vital Signs Details Entry

7.1	Record Identifier: [Record Identifier:]	1
7.2	Temperature: [Temperature]	
7.3	Unit: [Temperature Unit]	C F
7.4	Temperature Location: [Temperature Location:]	ORAL CAVITY EAR RECTUM AXILLA FOREHEAD

C4591001: VITAL SIGNS - COVID (VITALS COV) - Repeating Form

#	Date:	Vital Signs Details
1		

Vital Signs

1.	Date: [Date:]	/ /

Vital Signs Details

# ✔	Record Identifier:	Systolic:	Diastolic:	Respiratory Rate in respirations/minute	Heart Rate in beats/minute
2.a	1				

Vital Signs Details Entry

2.1	Record Identifier: [Record Identifier:]	1
2.2	Systolic: [Systolic:]	
2.3	Diastolic: [Diastolic:]	
2.4	Respiratory Rate in respirations/minute: [Respiratory Rate in respirations/minute]	
2.5	Heart Rate in beats/minute: [Heart Rate in beats/minute]	

C4591001: VITAL SIGNS (VITALS FUP)

Vital Signs

1.	Date: [Date:]	/ /

Vital Signs Details

#	Record Identifier:	Temperature	Temperature Unit	Temperature Location:	Systolic:	Diastolic:	BP Position	Pulse:
2.a	1						SITTING	

Vital Signs Details Entry

2.1	Record Identifier: [Record Identifier:]	○ 1
2.2	Temperature: [Temperature]	
2.3	Unit: [Temperature Unit]	○ F ○ C
2.4	Temperature Location: [Temperature Location:]	○ ORAL CAVITY ○ EAR ○ RECTUM ○ AXILLA ○ FOREHEAD
2.5	Systolic: [Systolic:]	
2.6	Diastolic: [Diastolic:]	
2.7	BP Position: [BP Position]	○ SITTING
2.8	Pulse: [Pulse:]	

C4591001: WITHDRAWAL OF CONSENT (WOC)		
Withdrawal Of Consent		
1.	Withdrawal of Consent Date : [Withdrawal of Consent Date :]	/ /

A-1426-0086 / C4591001-Post-12-July-2020
App Subject Facing Screen Report

Localized texts are displayed in English (US).

Contents

Localized months and days of the week will display throughtout the app.

Month	January	February	March	April	May	June	July	August	September	October	November	December
Abbr.	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec

Days	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Abbr.	Mon	Tue	Wed	Thu	Fri	Sat	Sun

Note: Text below the screens/messages is for information purposes only and gives instruction on when particular wording on a screen/message may display or what a computed value may display

1 Notifications / Subject card

Email notification/Subject card to provisioned device subjects:

Welcome to the C4591001-Post-12-July-2020 study!

Email notification only: [Hello, **]**

The information below will guide you on how to start using the TrialMax App.

On the phone provided to you by the study clinic, open the TrialMax App and type in the following code to activate it:
[Activation Code]

Then log in with your temporary PIN provided by your study clinic personnel. You will be asked to change the PIN to a new personal one.

During your study clinic visit, the study personnel will help you with any questions related to the TrialMax App activation.

You must activate the App with the provided activation code during your study clinic visit. If you need any help with the activation, contact your study clinic or the Helpdesk.

If you contact your study clinic or the Helpdesk, you may need to give the following information:

Subject card only: [Participant number: XXXXXXXX **]**

Subject card only: [Site number: XXXX **]**

Trial ID: C4591001-Post-12-July-2020

Email notification only: [----------
This is an automatic e-mail message sent by Signant Health, an electronic patient diary provider for clinical trials. This email message and its contents are for the sole use of the intended recipient(s) and may contain confidential and privileged information. Any unauthorized review, use, disclosure or distribution is strictly prohibited. Please do not reply to this email; the email address cannot receive messages. If you need any assistance, please contact the Helpdesk. **]**

SMS Body for Provisioned Devices:
Welcome to the C4591001-Post-12-July-2020 Study! Activate the TrialMax App with code:

[Activation Code]

Email notification/Subject card to BYOD subjects:

Welcome to the C4591001-Post-12-July-2020 study!

Email notification only: [Hello, **]**

The information below will guide you on how to install the TrialMax App onto your cell phone and how to start using the TrialMax App after the installation.

Email notification only: [To install the TrialMax App, tap the link below and follow the on-screen instructions. **]**

Subject card only: [To install the TrialMax App, tap the link in the installation text message (SMS) or email you will receive in a few minutes, and follow the on-screen instructions.

If you have not received the text message or email, enter the following internet address into the web browser of your device: **]**
[Link]

After the installation has completed, open the TrialMax App and type in the following code to activate it:
[Activation Code]

Then log in with your temporary PIN provided by your study clinic personnel. You will be asked to change the PIN to a new personal one.

During your study clinic visit, the study clinic personnel will help you with any questions related to the TrialMax App installation.

You must activate the App with the provided activation code during your study clinic visit. If you need any help with the installation, contact your study clinic or the Helpdesk.

If you contact your study clinic or the Helpdesk, you may need to give the following information:

Subject card only: [Participant number: XXXXXXXX **]**

Subject card only: [Site number: XXXX **]**

Trial ID: C4591001-Post-12-July-2020

Email notification only: [----------
This is an automatic e-mail message sent by Signant Health, an electronic patient diary provider for clinical trials. This email message and its contents are for the sole use of the intended recipient(s) and may contain confidential and privileged information. Any unauthorized review,

use, disclosure or distribution is strictly prohibited. Please do not reply to this email; the email address cannot receive messages. If you need any assistance, please contact the Helpdesk. **]**

SMS Body for BYOD subjects:

Welcome to the C4591001-Post-12-July-2020 Study! To install the TrialMax App, select the link:
[Link]
Activate the TrialMax App with code:
[Activation Code]

App notification:

Please fill in your diary!

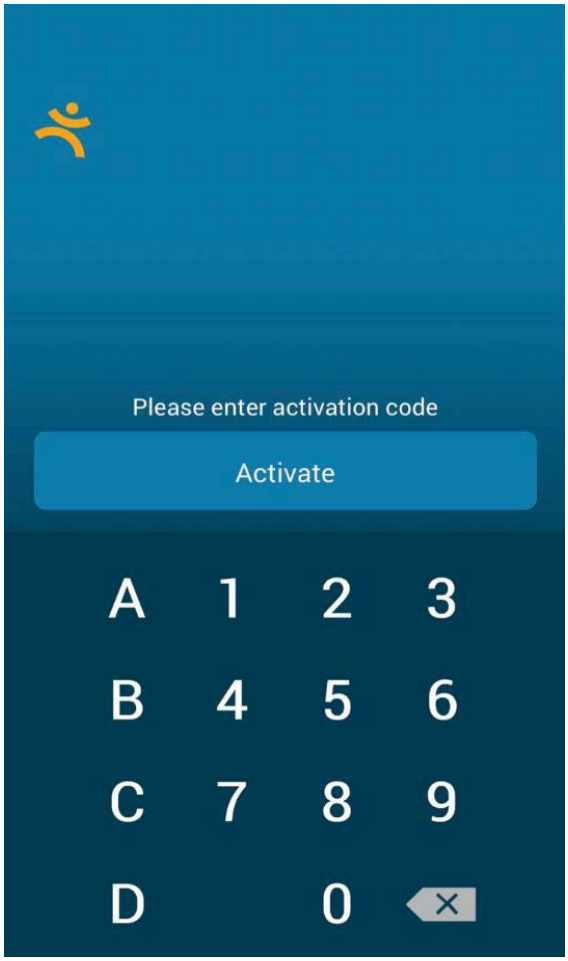
Email notification subject :
COVID-19 Illness Diary Reminder

Email and SMS Body for COVID-19 Illness Diary Reminder:

Please continue to complete the illness diary weekly or if you experience COVID-19 symptoms or have a COVID-19 diagnosis. Contact your study doctor with any suspected COVID-19 symptoms.

Email notification only: [----------
This is an automatic e-mail message sent by Signant Health, an electronic patient diary provider for clinical trials. This email message and its contents are for the sole use of the intended recipient(s) and may contain confidential and privileged information. Any unauthorized review, use, disclosure or distribution is strictly prohibited. Please do not reply to this email; the email address cannot receive messages. If you need any assistance, please contact the Helpdesk. **]**

2 Common



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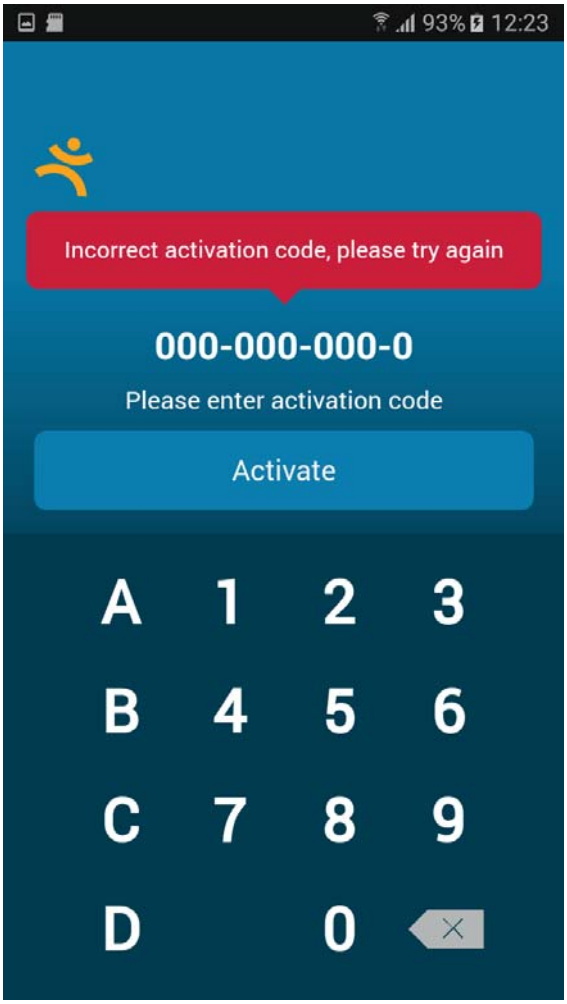

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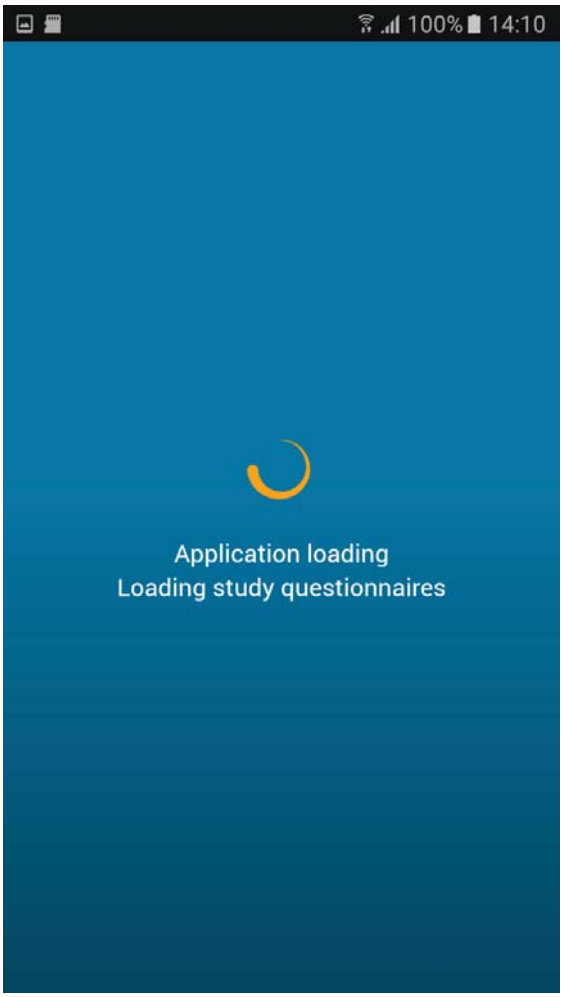

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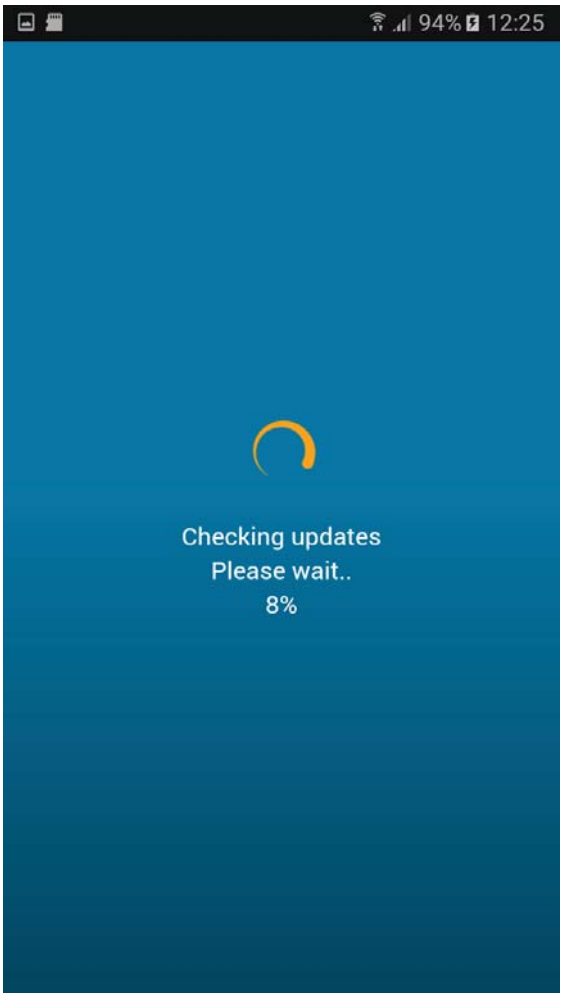

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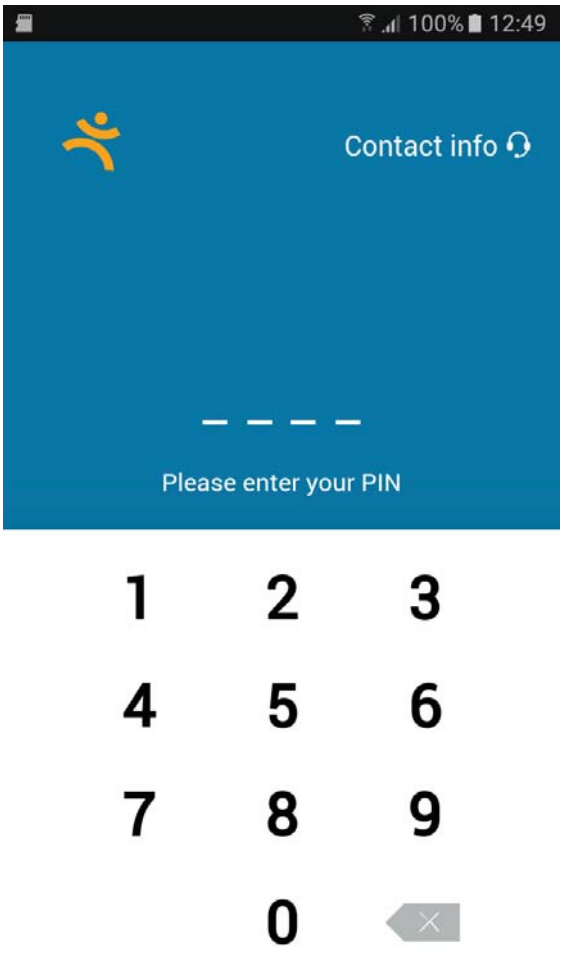

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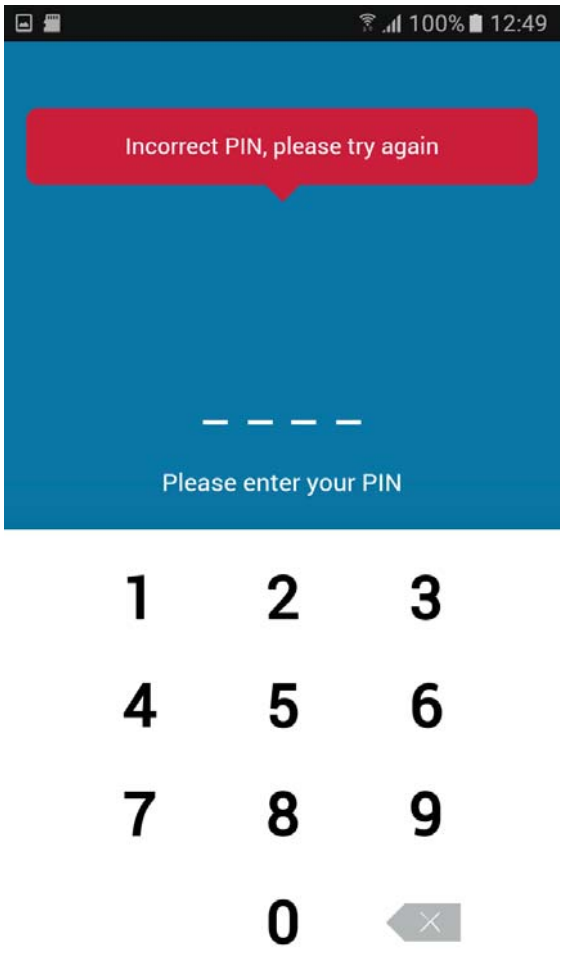

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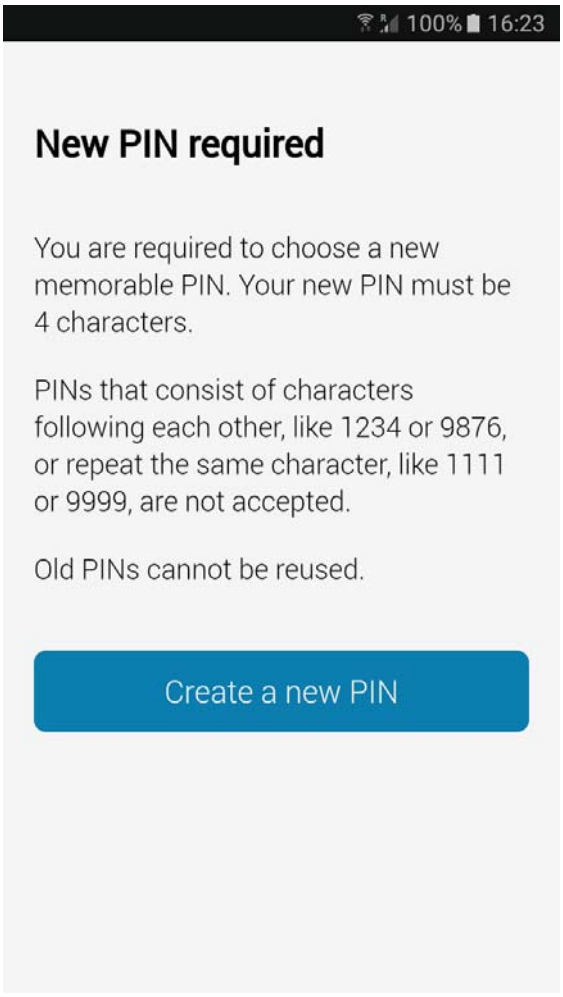

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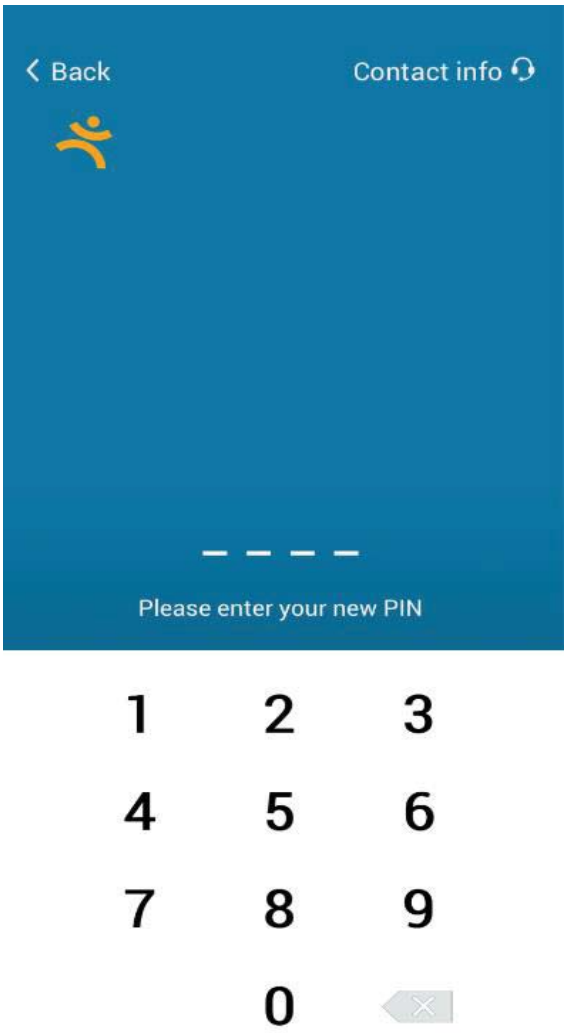

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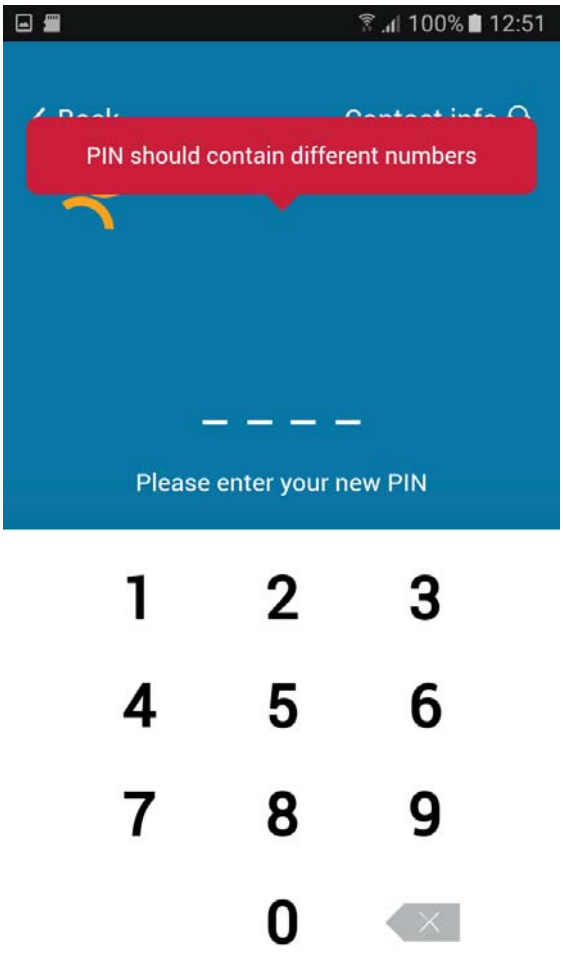

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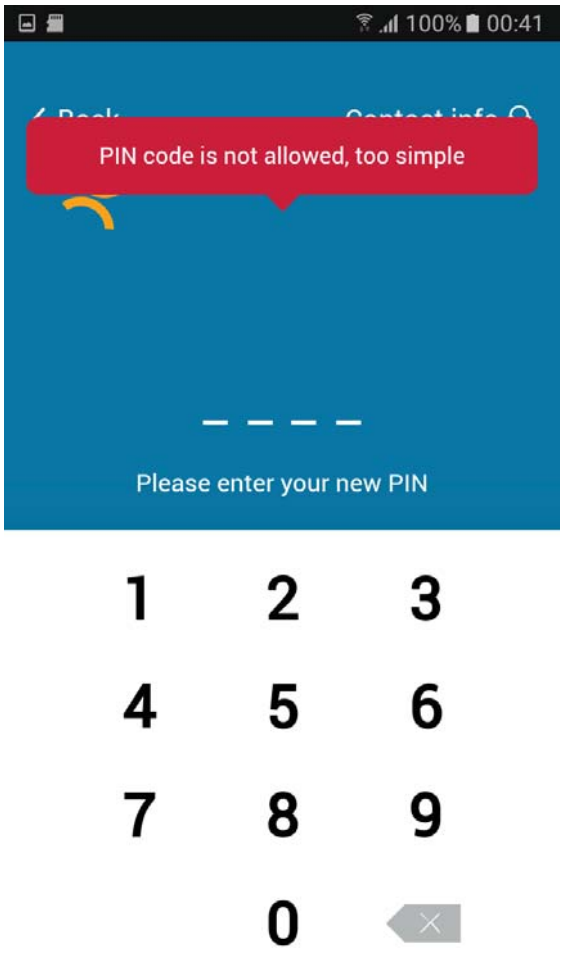

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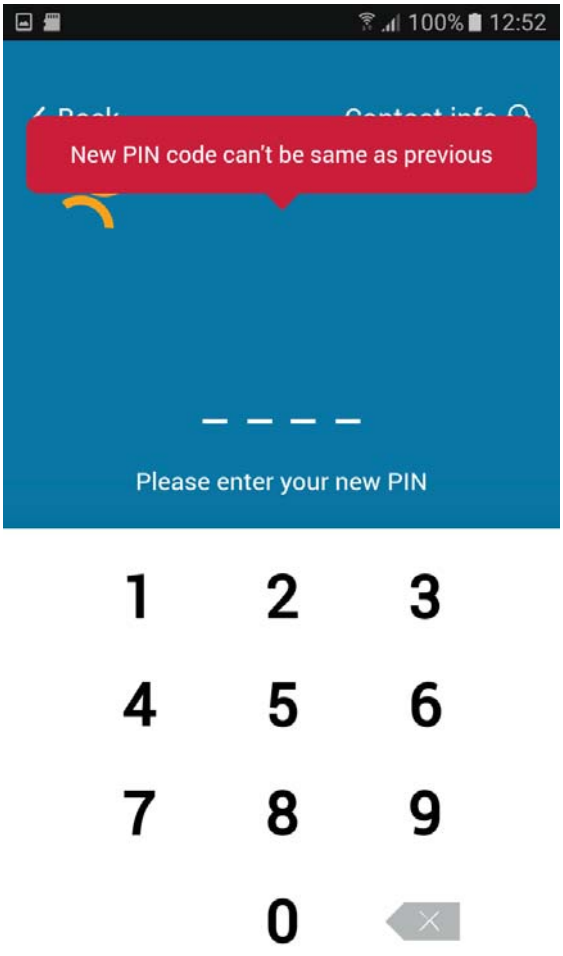

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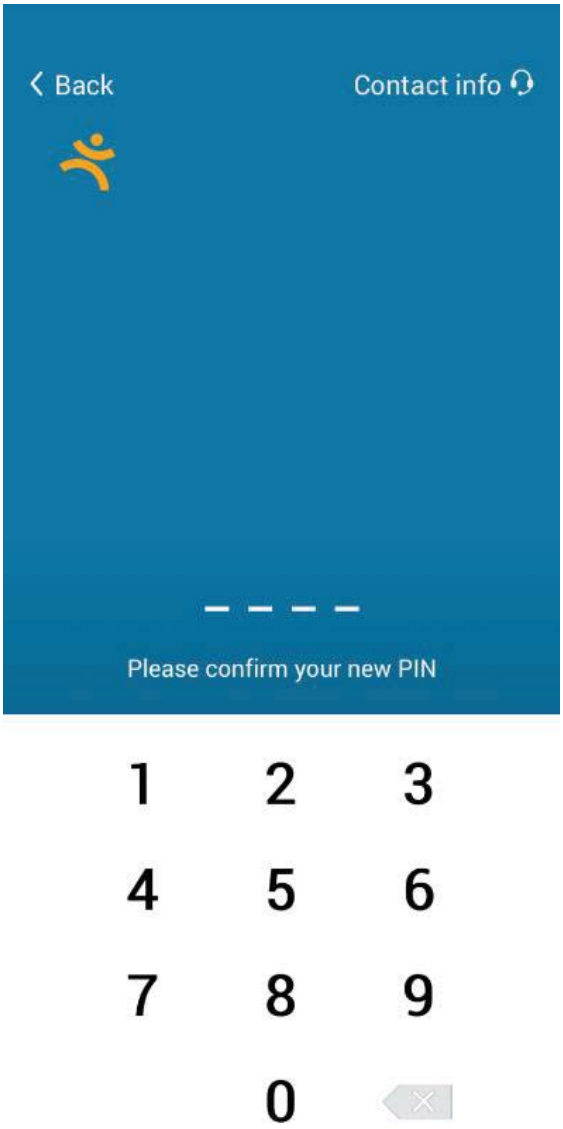

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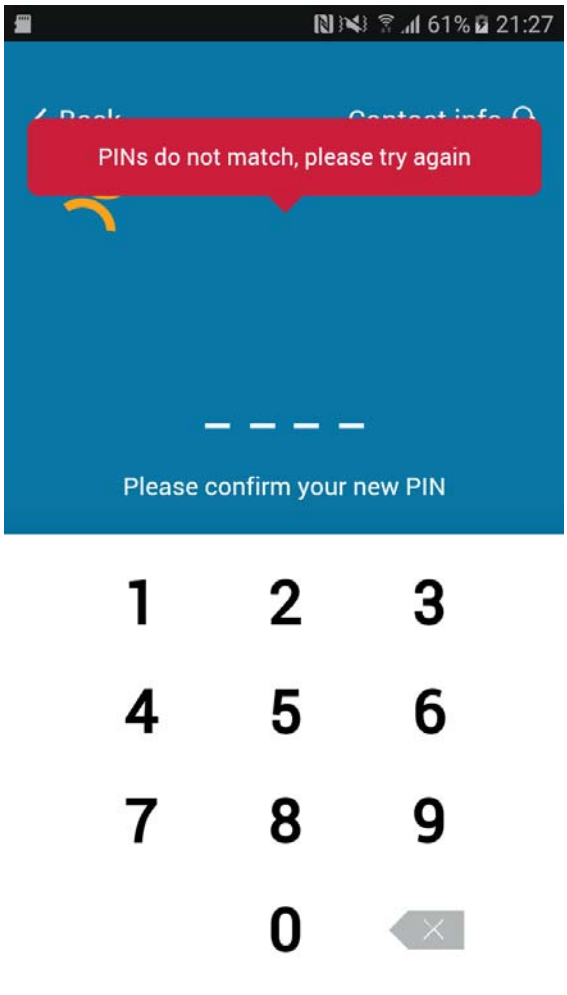
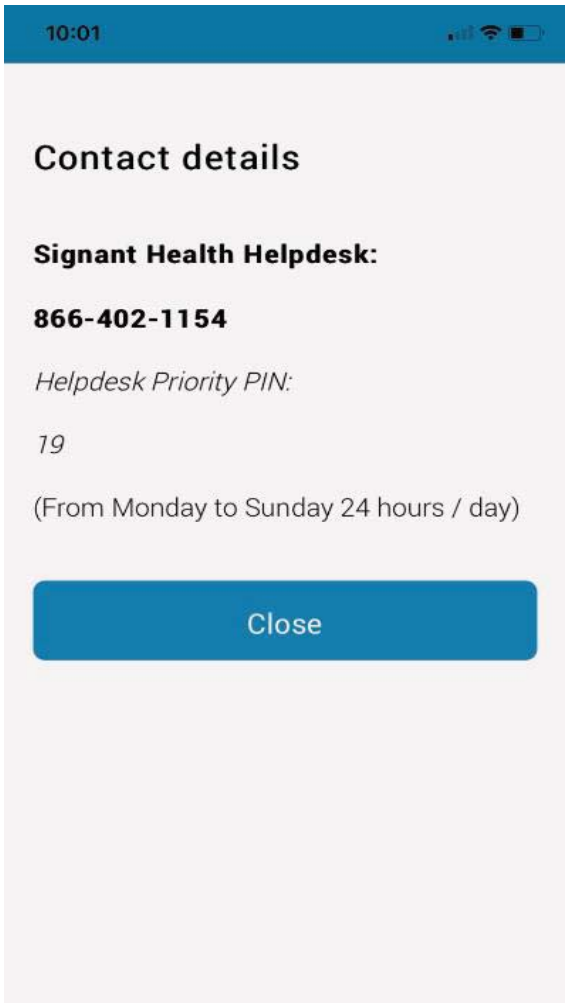


Screen 13

Screen 14



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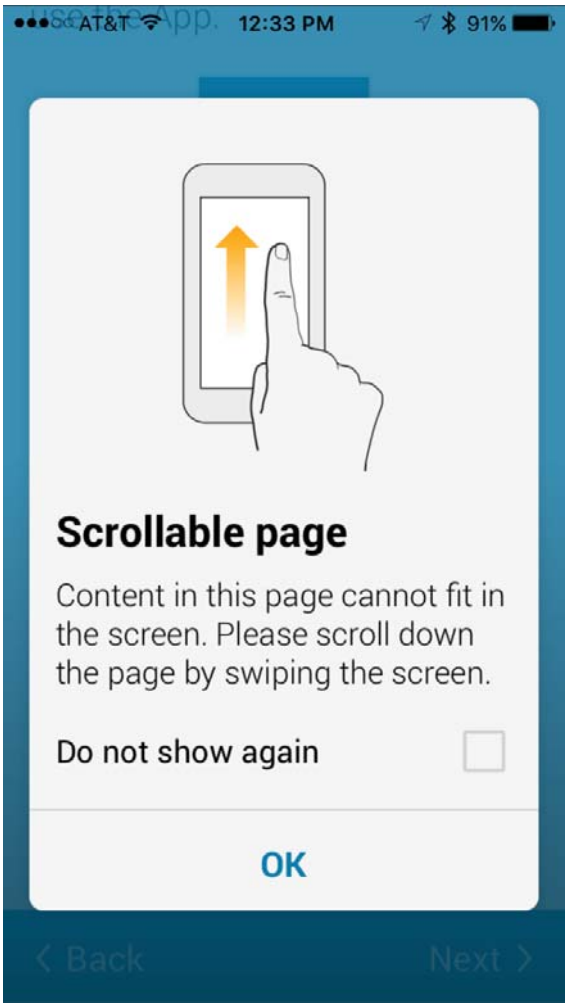

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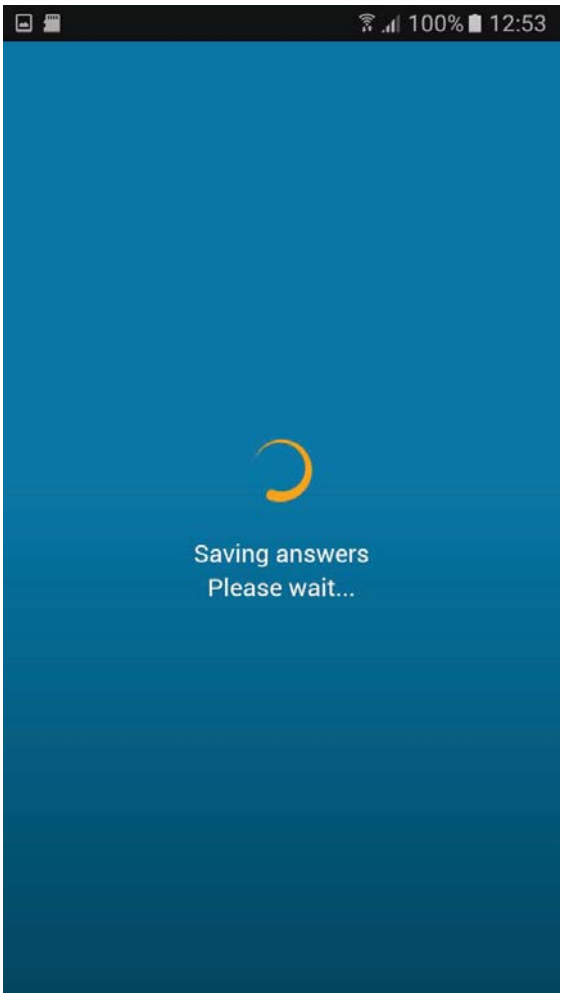

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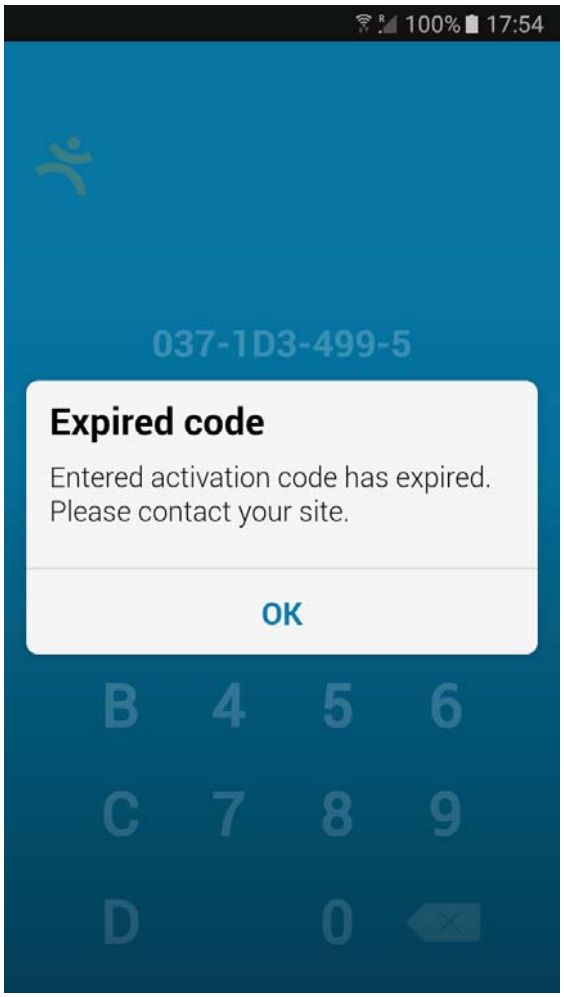

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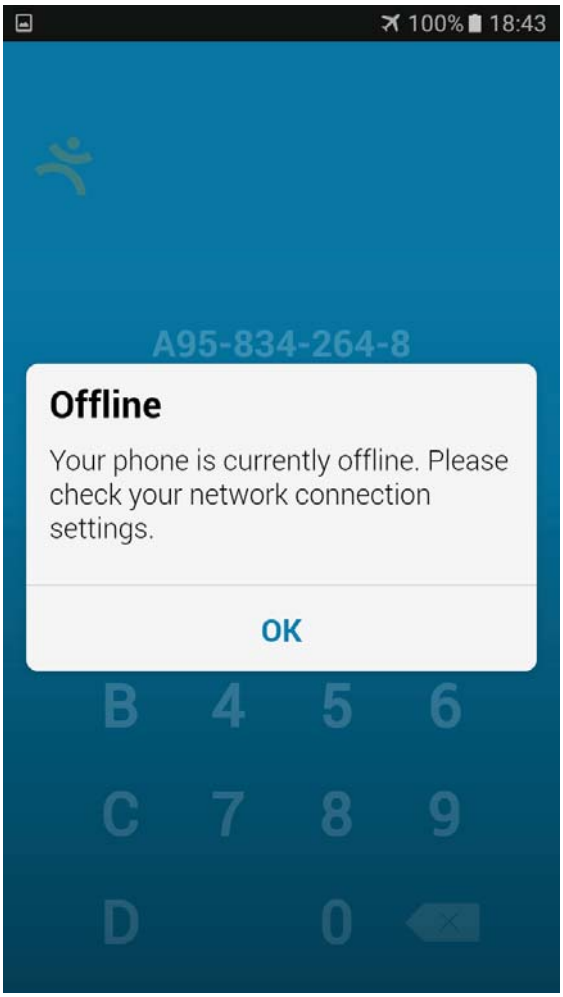

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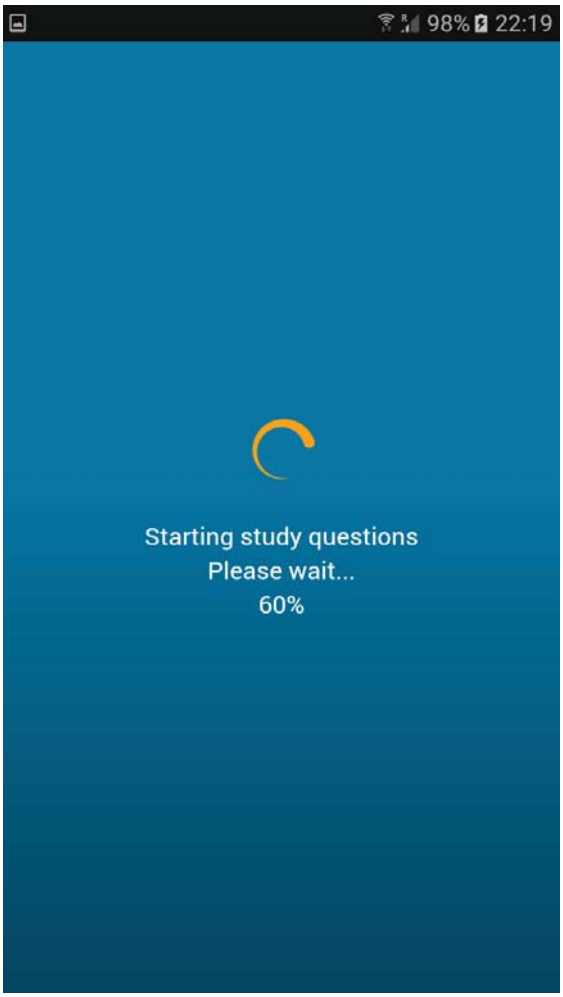
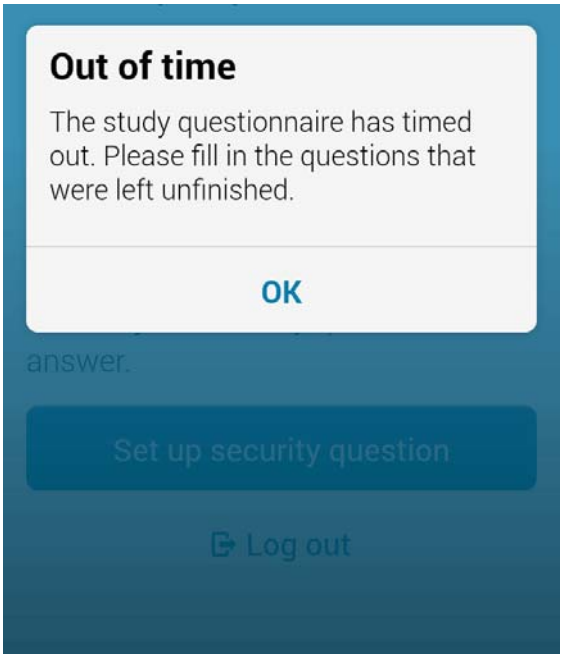
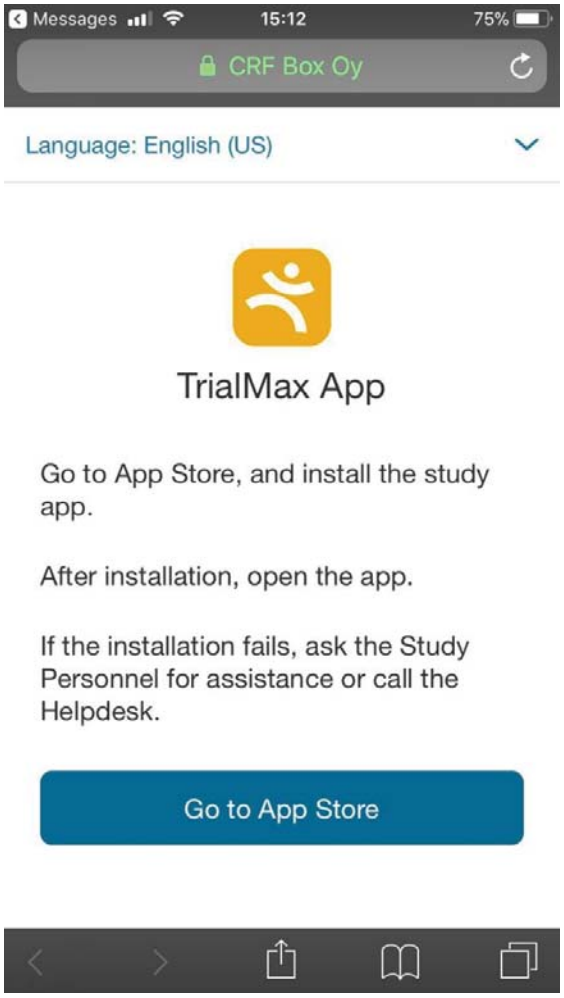


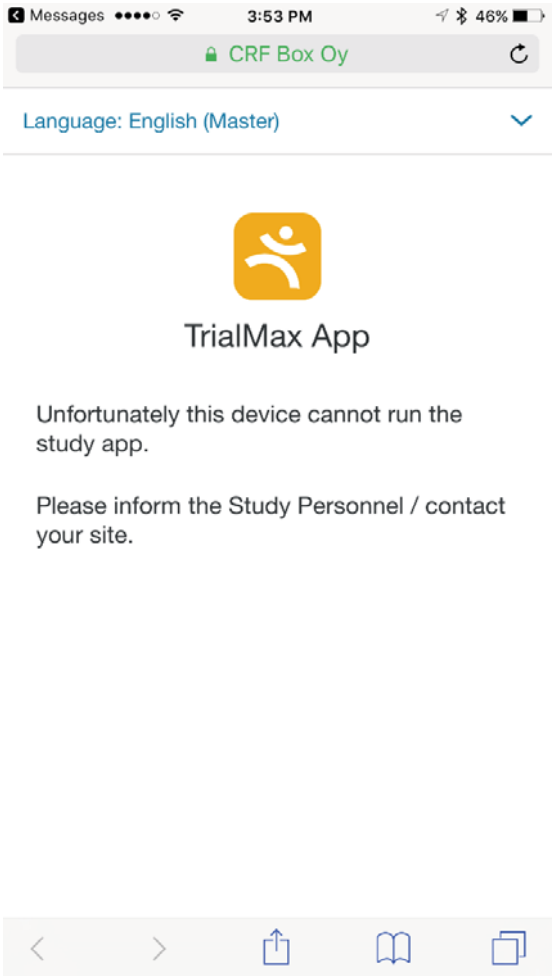
Screen 20



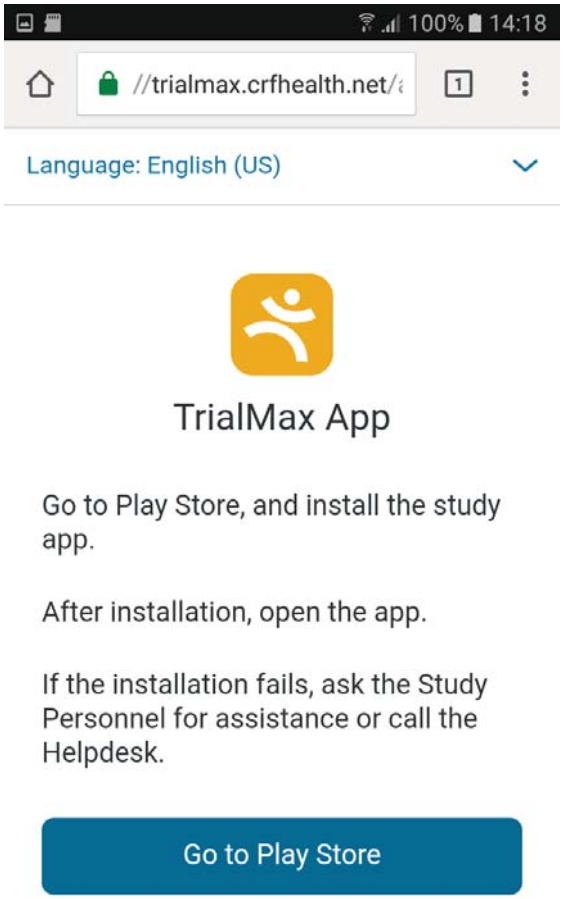
Screen 21



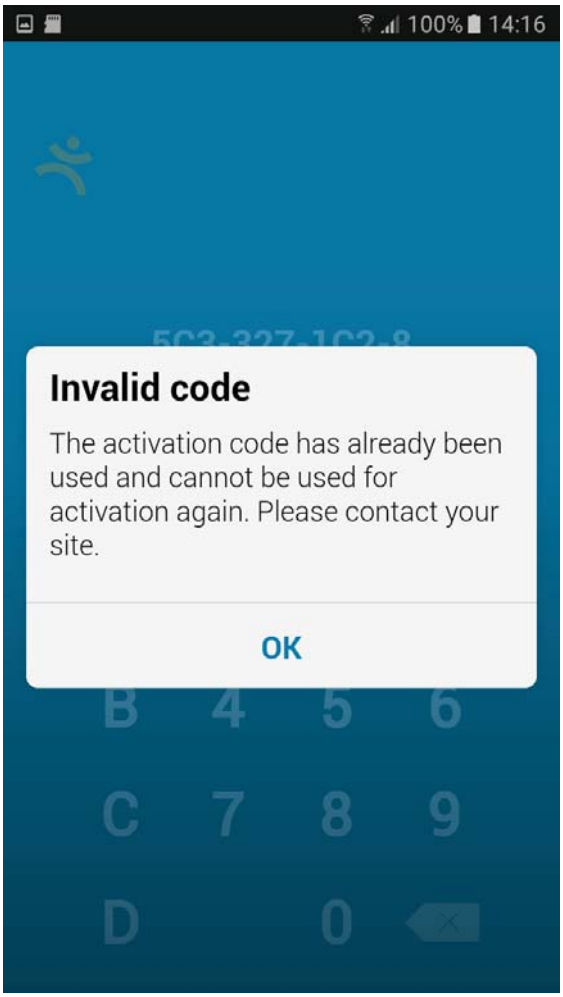
Screen 22



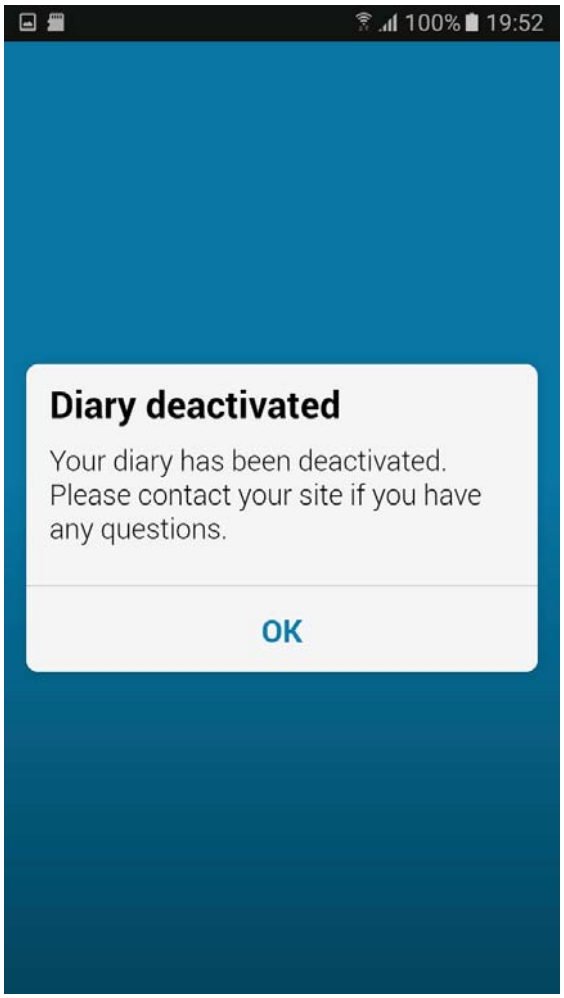
Screen 23



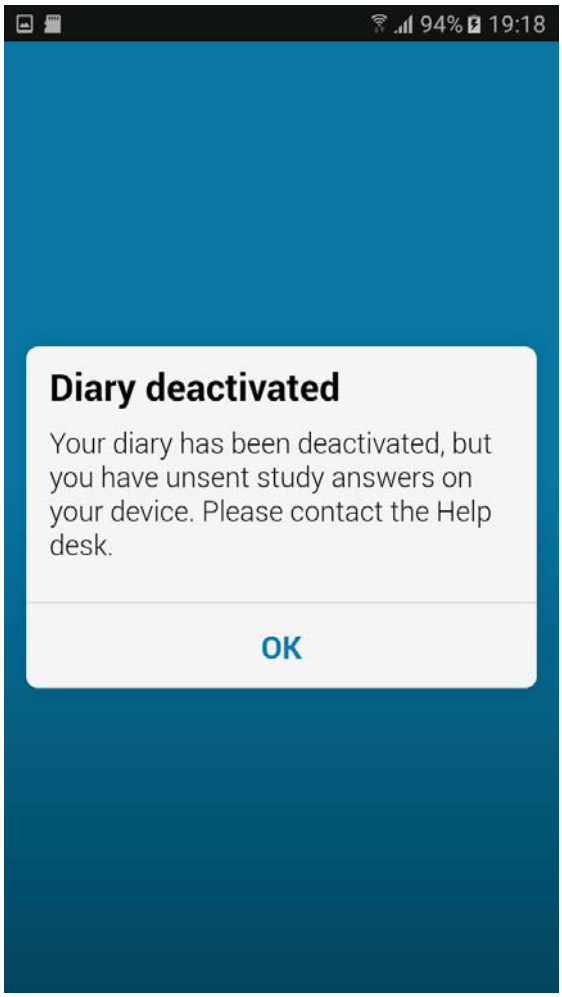
Screen 24



Screen 25

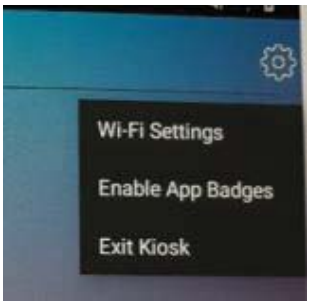


Screen 26

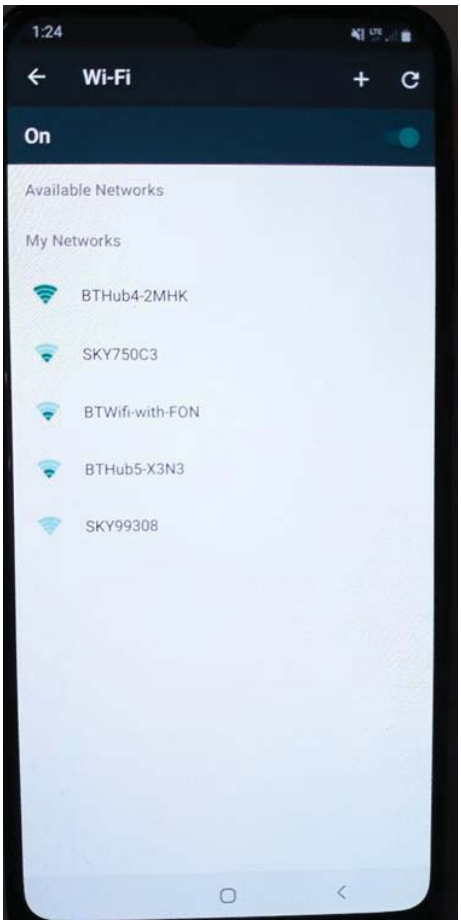


Screen 27

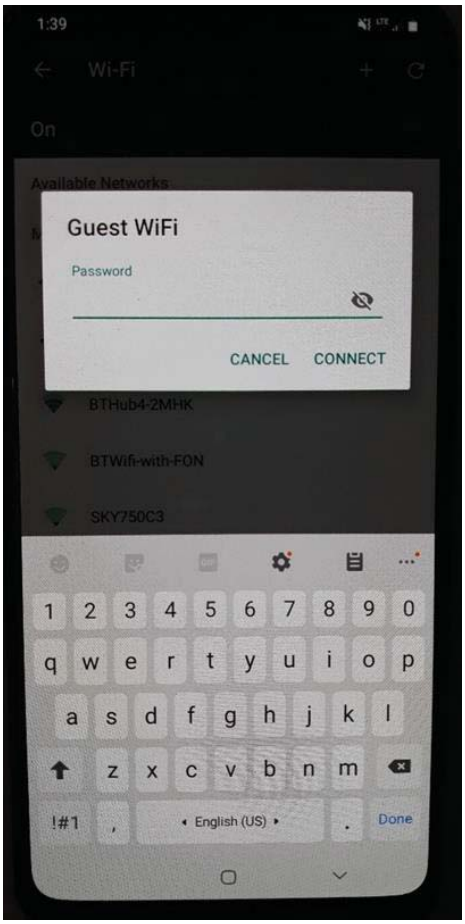
Screen 28



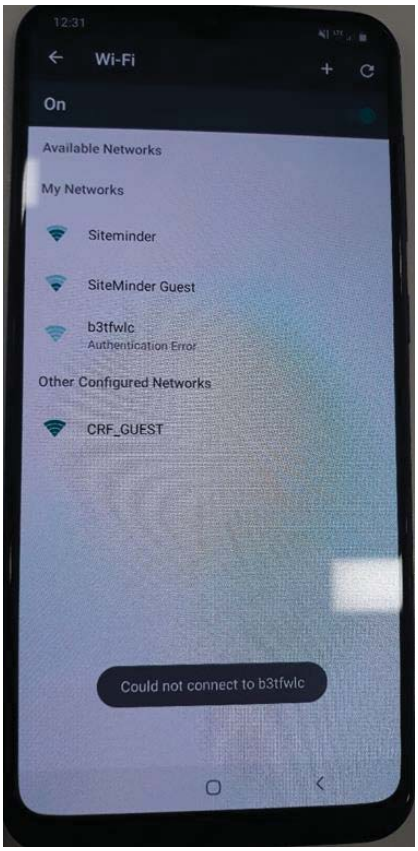
Screen 29



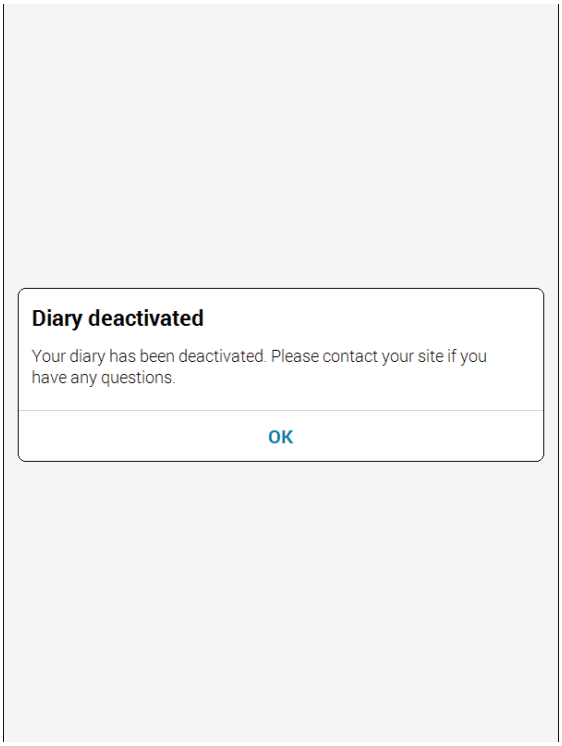
Screen 30



Screen 31



Screen 32



Message 1

Note: Other messages that could appear on the device include:

'Invalid PIN'

'Installing study questions'

'Securing study questions'

'Unsent answers'

'There are a lot of unsent study answers. Please make sure your device is connected to the Internet.'

'The limit of unsent study answers has been reached. Please connect your device to the Internet to fill in the diary again.'

'Oops!'

'Something went wrong, please try again or contact the Help desk.'

'Unsuccessful sending'

'Cannot safely send the study answers, please contact the Help desk.'

'Study ended'

'You no longer need to fill in the diary. Thank you for your help.'

'Updating'

'System is updating, please try again later.'

'Connection error'

'No Internet connection. Please check your Internet connection and try again.'

'Time out'

'Please check your Internet connection and try again.'

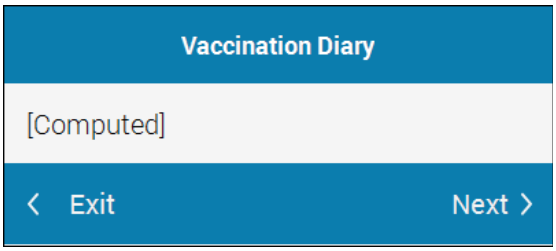
'Low storage space'

'Your device is running out of available storage. Please free some storage space and try again.'

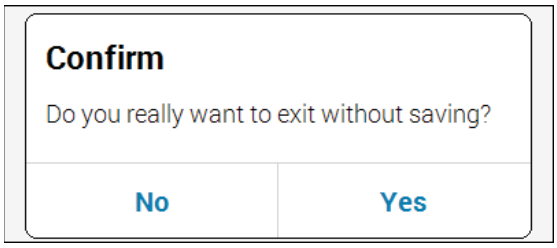
'Error'

'Something went wrong, please contact the Help desk or click OK to try again.'

3 Form: Vaccination Diary



Screen 1



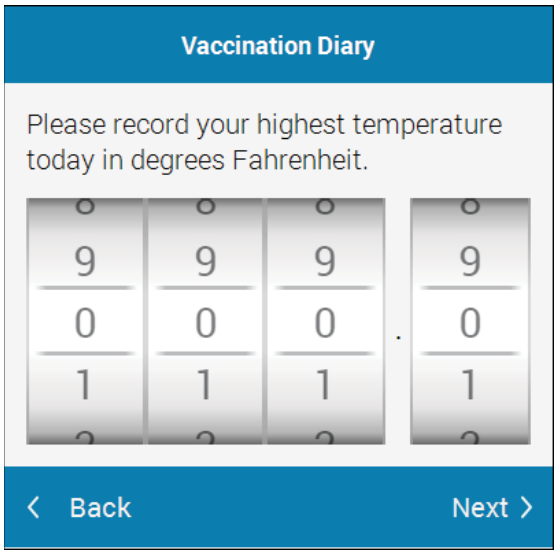
Message 1

[Computed] Text will display "Hello, welcome to the vaccination diary. You will be answering the following questions about how you have been feeling since your vaccination on {1}. You will answer these questions for {2} day(s)."

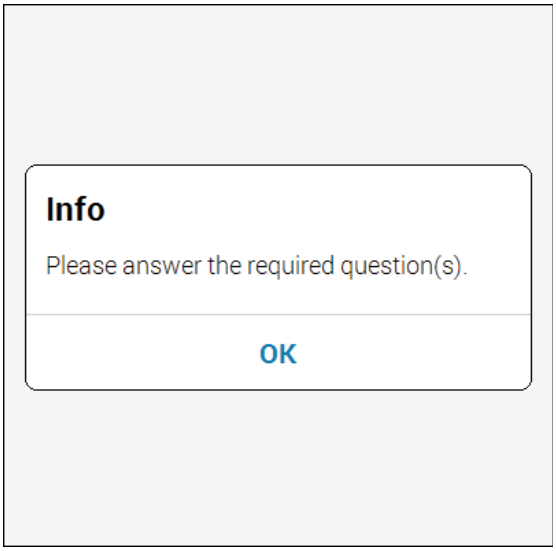
{1} Will display a date

{2} Will display a number of days.

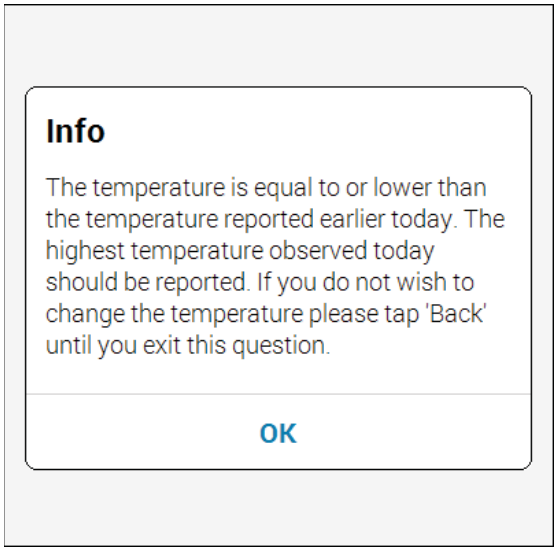
Example: Hello, welcome to the vaccination diary. You will be answering the following questions about how you have been feeling since your vaccination on Mar-27-2020. You will answer these questions for 7 day(s).



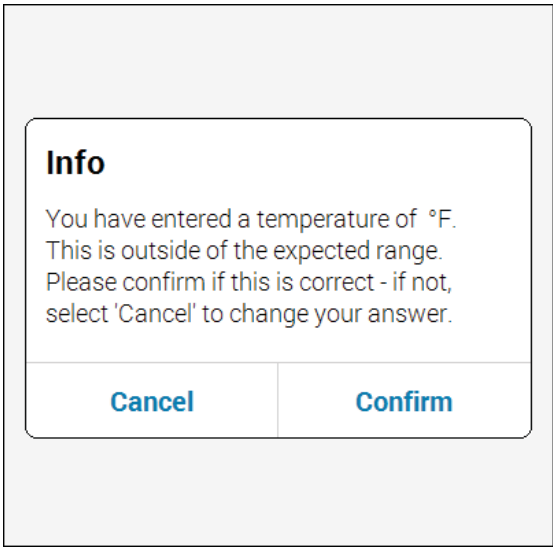
Screen 3



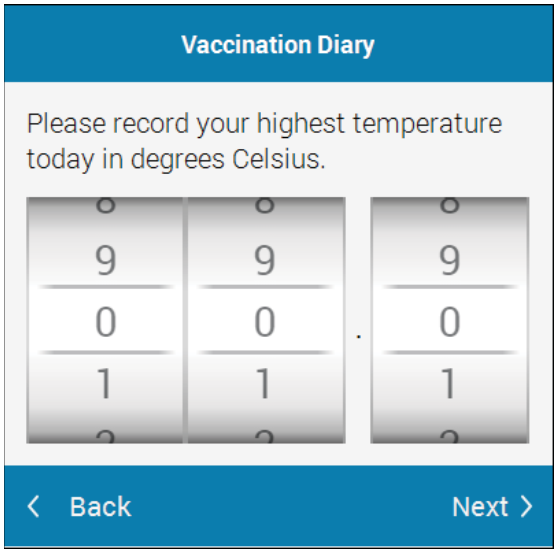
Message 1



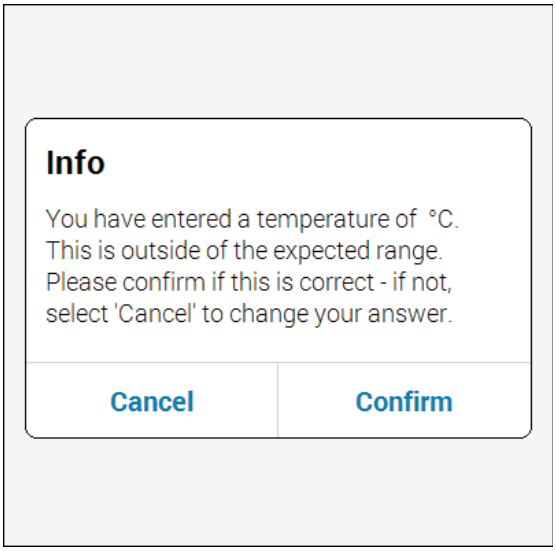
Message 2



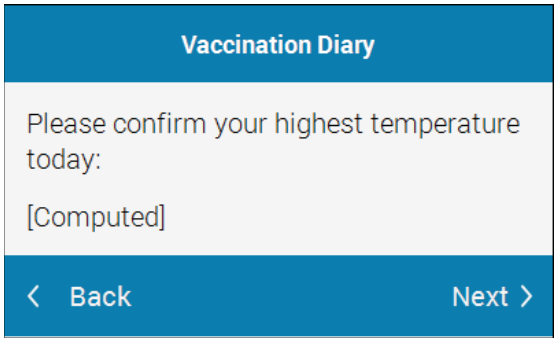
Message 3



Screen 4

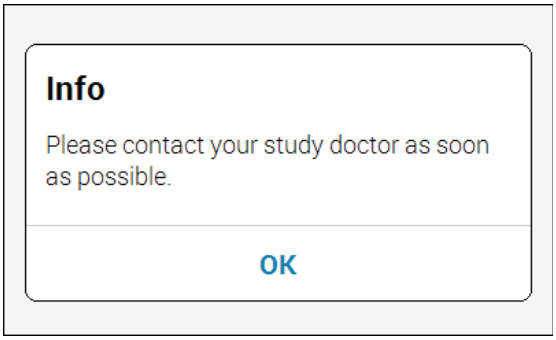


Message 3

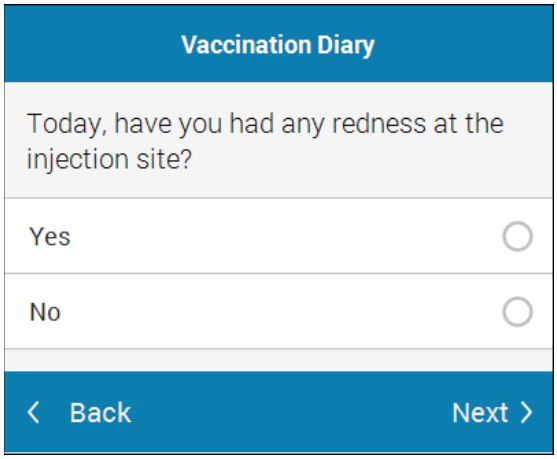


Screen 5

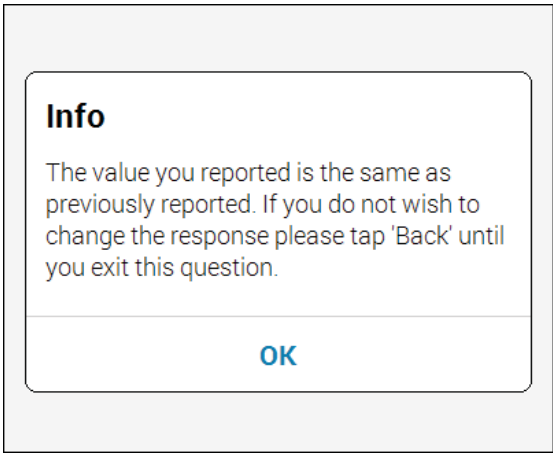
[Computed] will display the temperature selected on Screen 3 or Screen 4



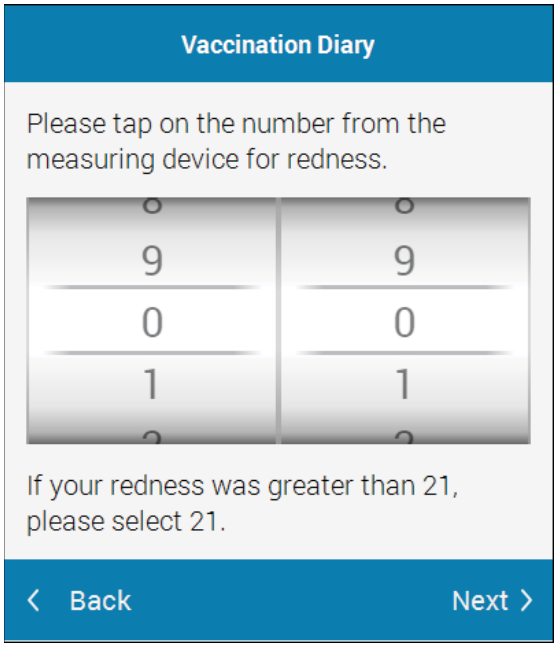
Message 1



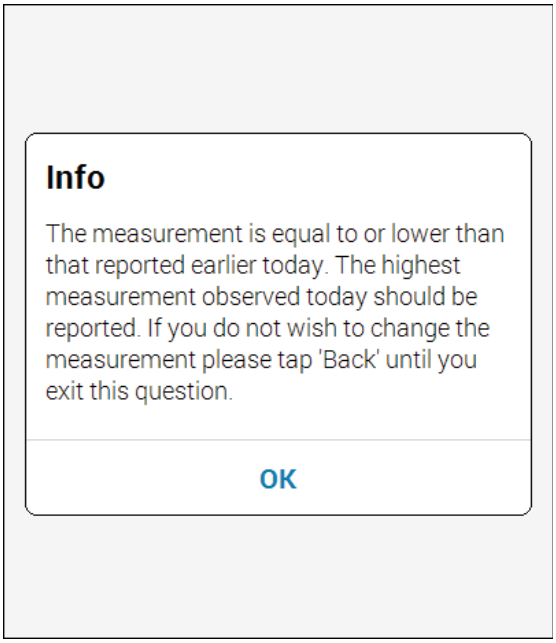
Screen 6



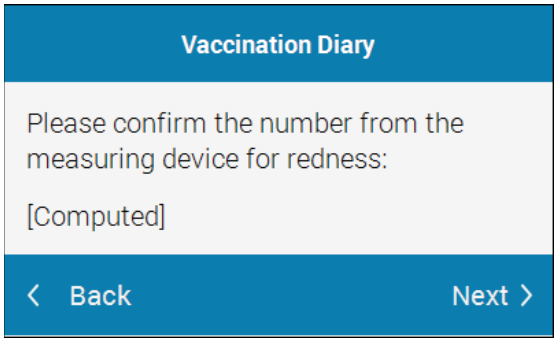
Message 2



Screen 7

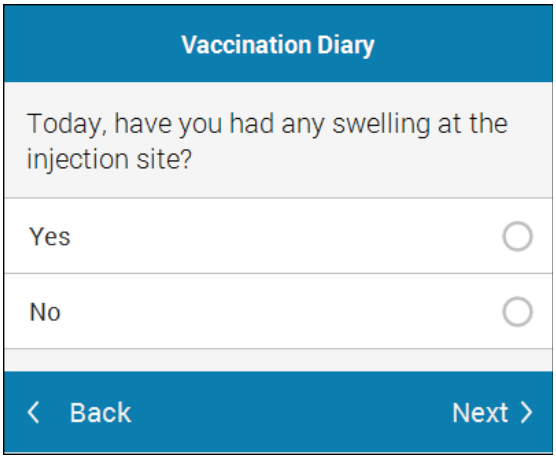


Message 2

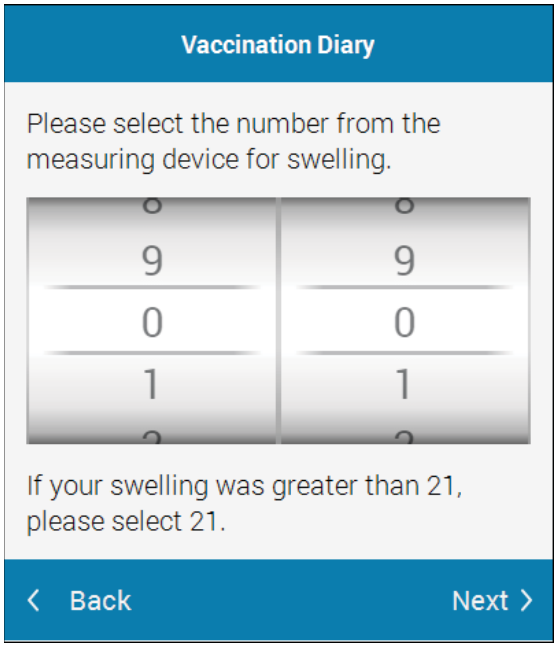


Screen 8

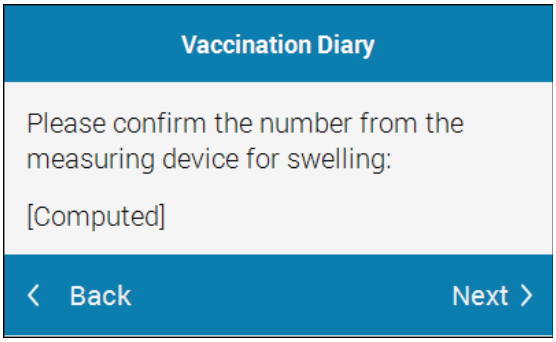
[Computed] will display the number selected on Screen 7.



Screen 9

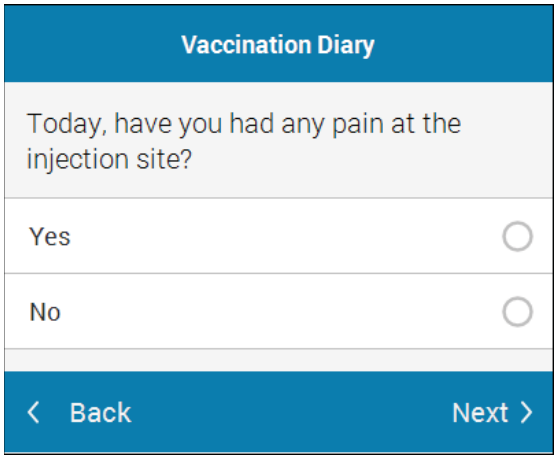


Screen 10

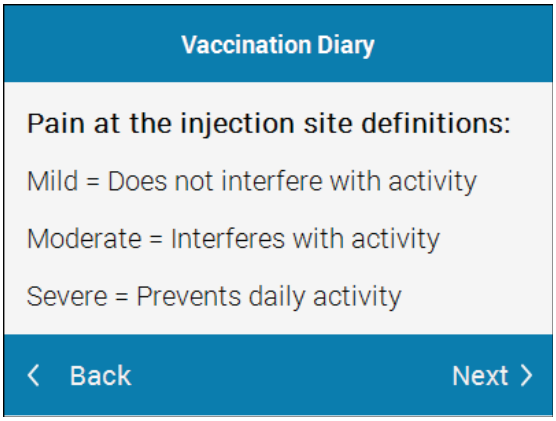


Screen 11

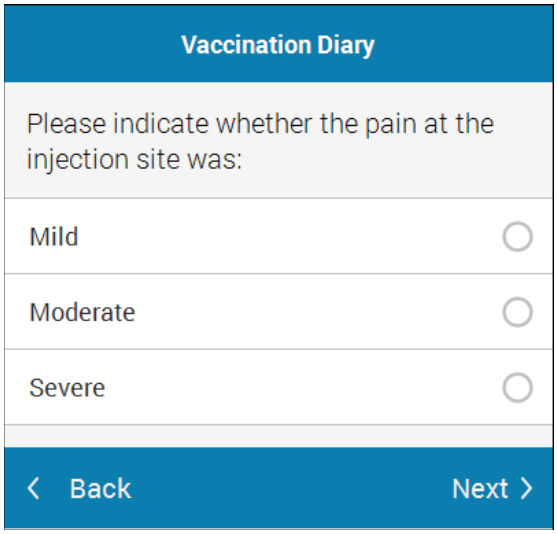
[Computed] will display the number selected on Screen 10.



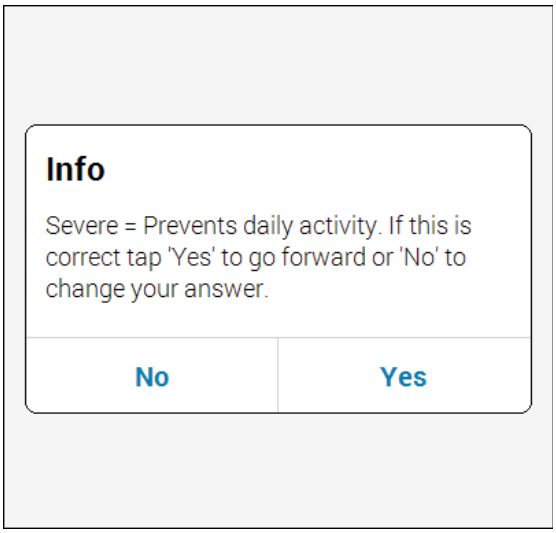
Screen 12



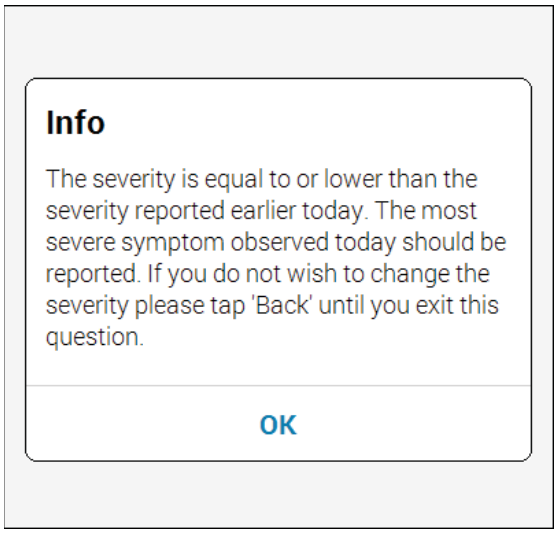
Screen 13



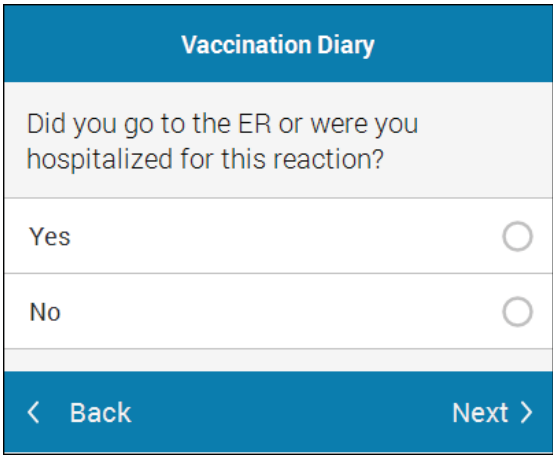
Screen 14



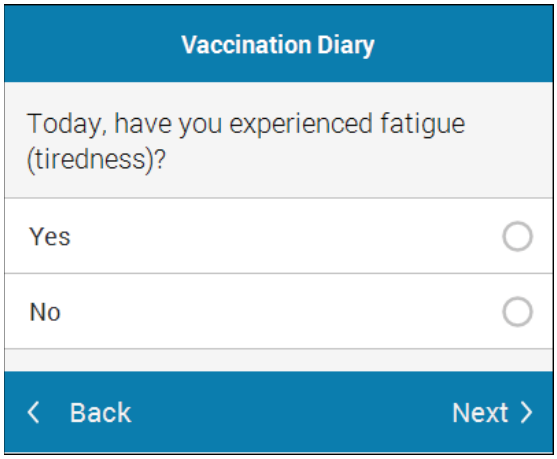
Message 2



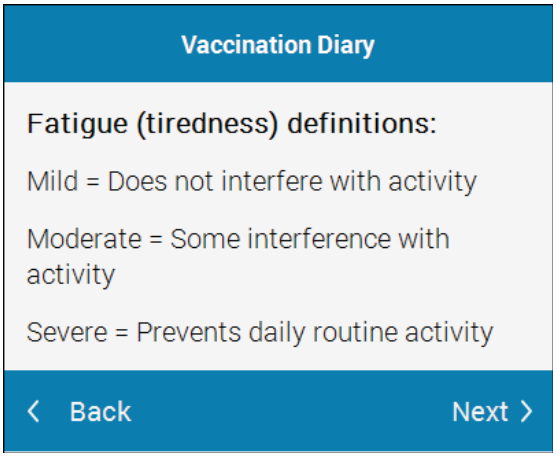
Message 4



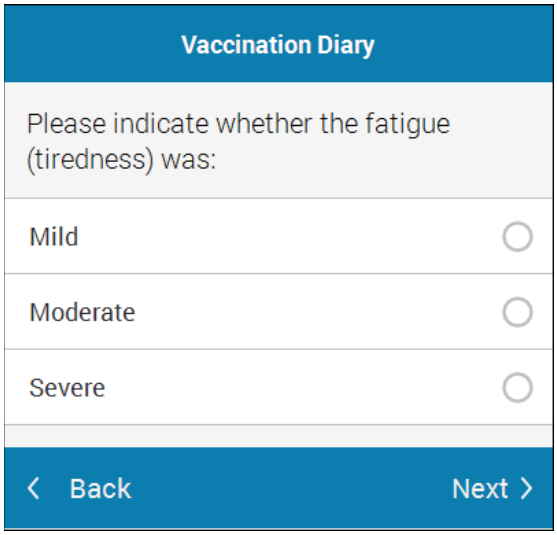
Screen 15



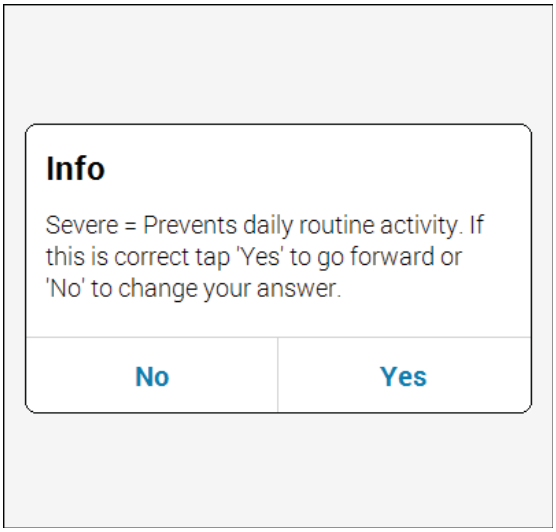
Screen 16



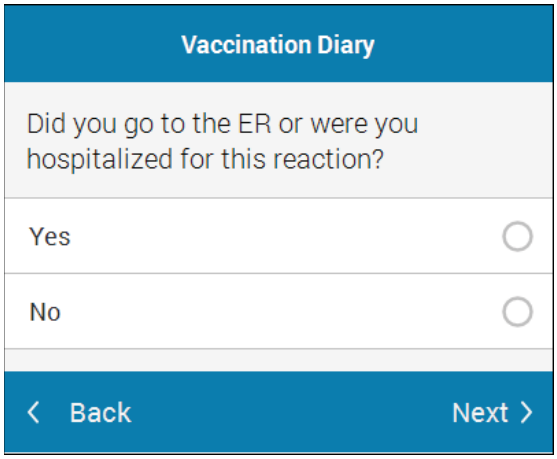
Screen 17



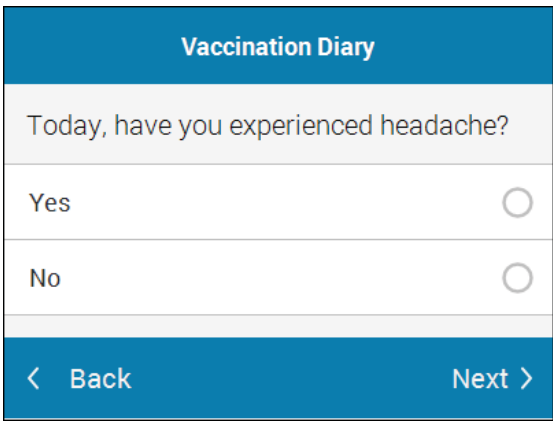
Screen 18



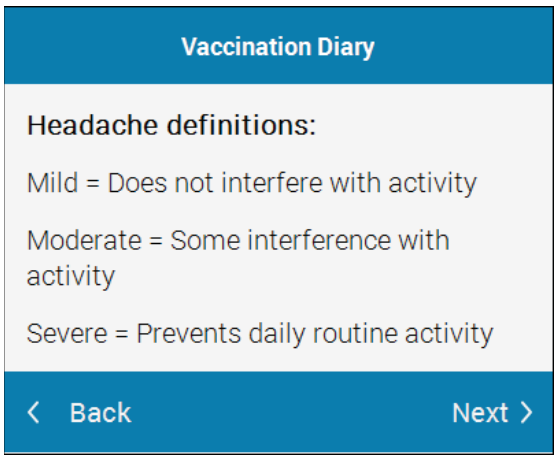
Message 2



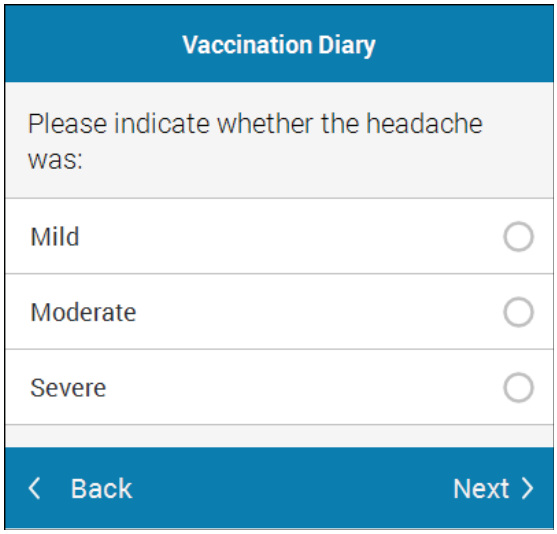
Screen 19



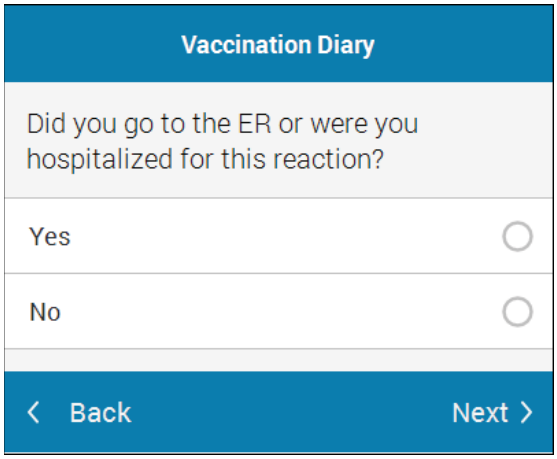
Screen 20



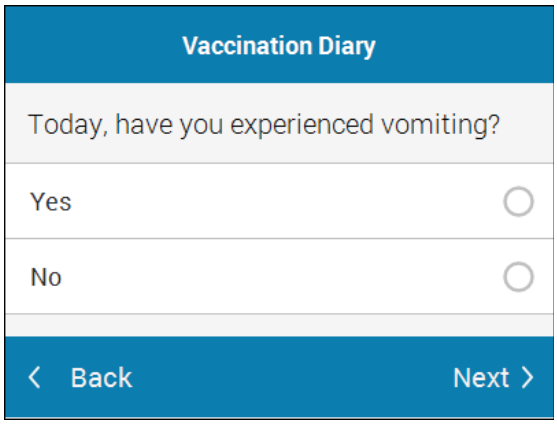
Screen 21



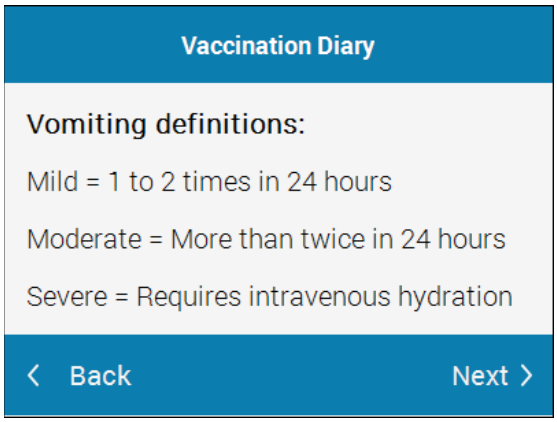
Screen 22



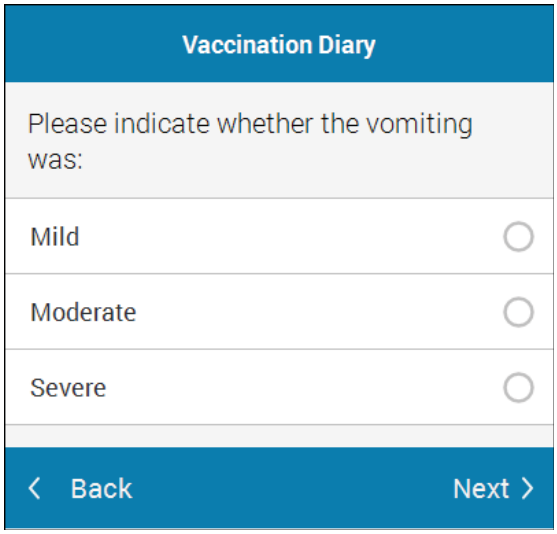
Screen 23



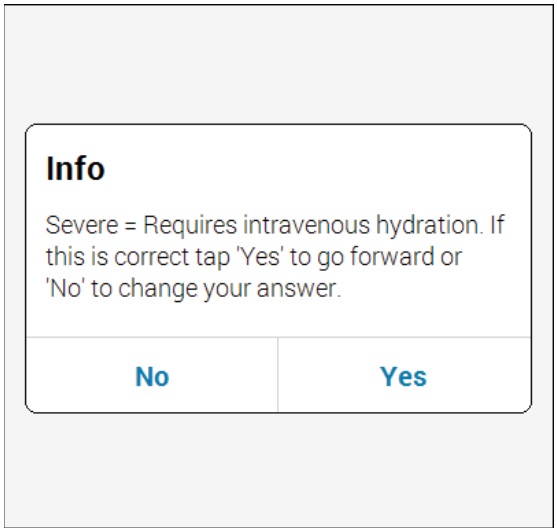
Screen 24



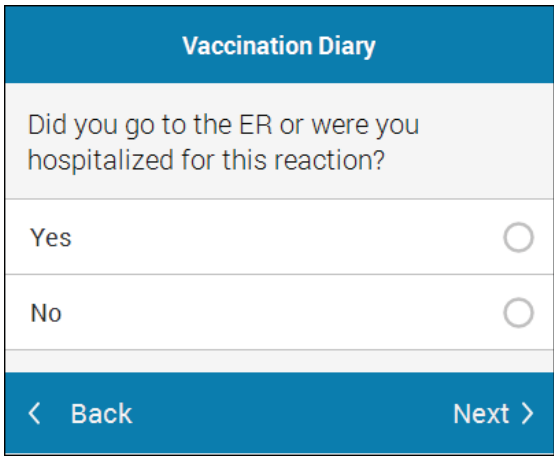
Screen 25



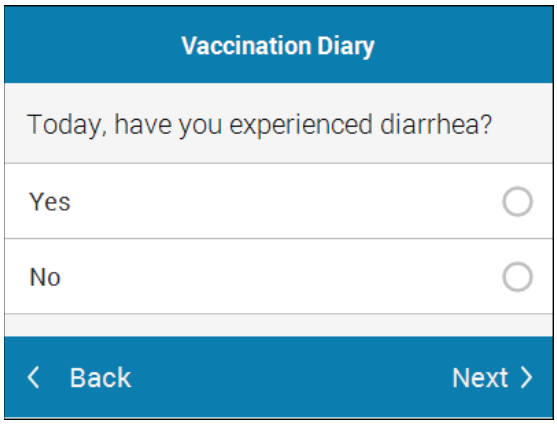
Screen 26



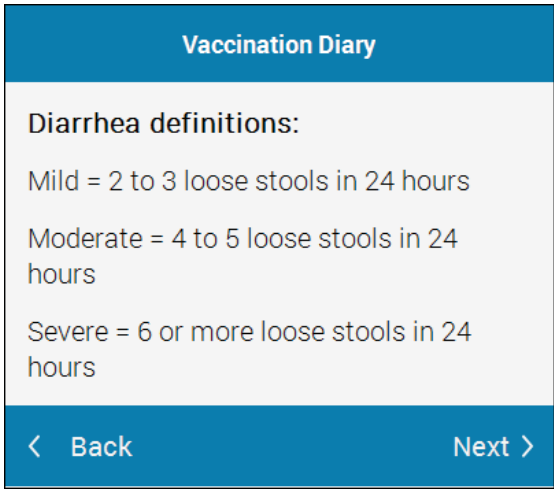
Message 2



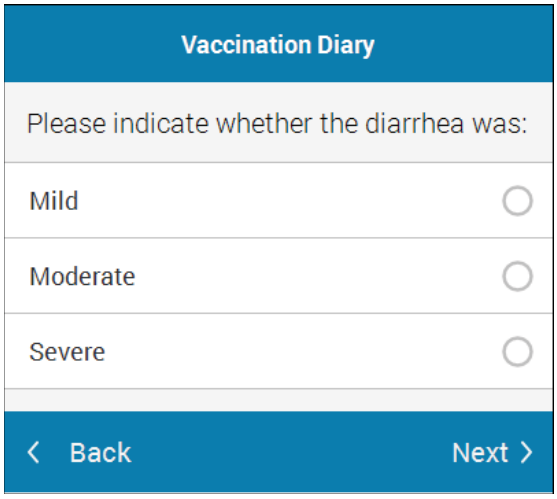
Screen 27



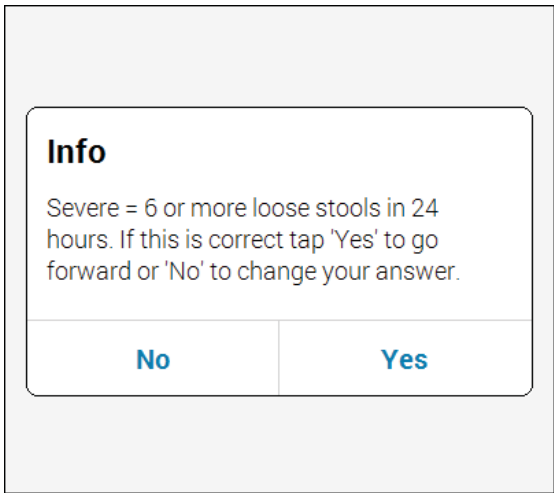
Screen 28



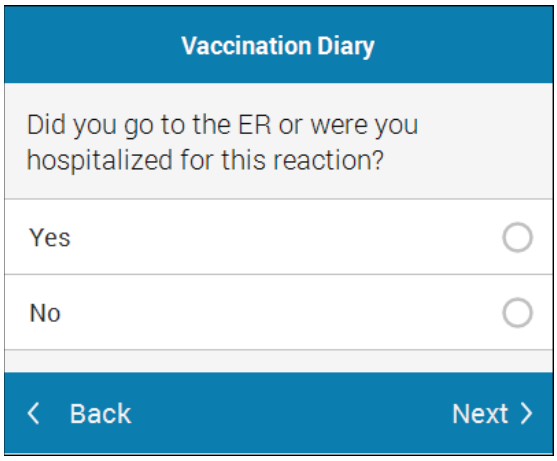
Screen 29



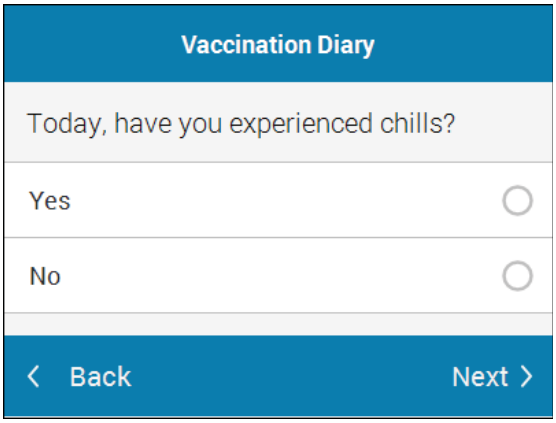
Screen 30



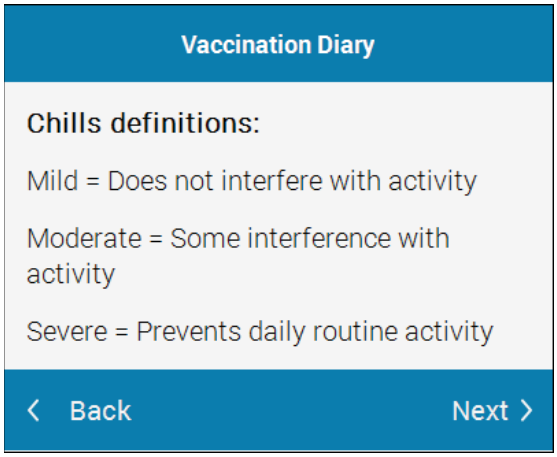
Message 2



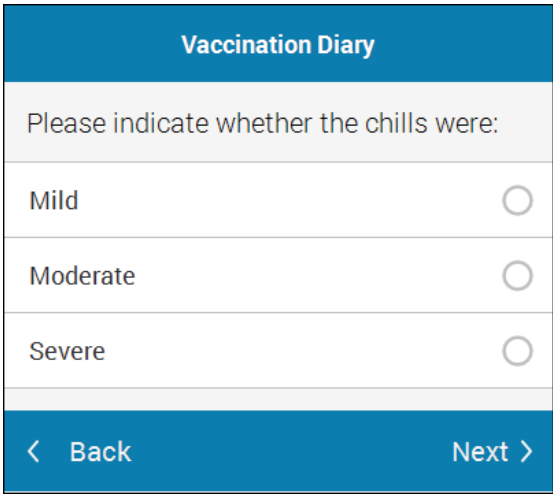
Screen 31



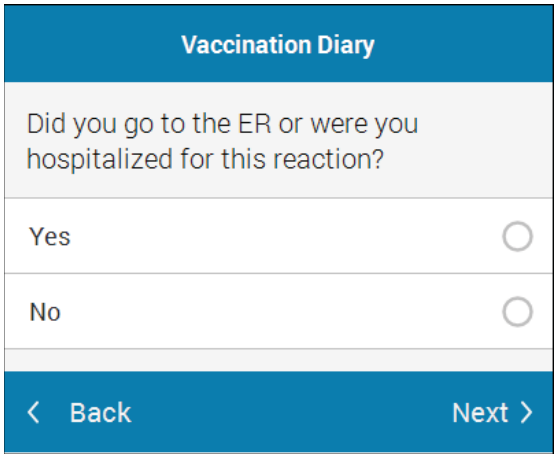
Screen 32



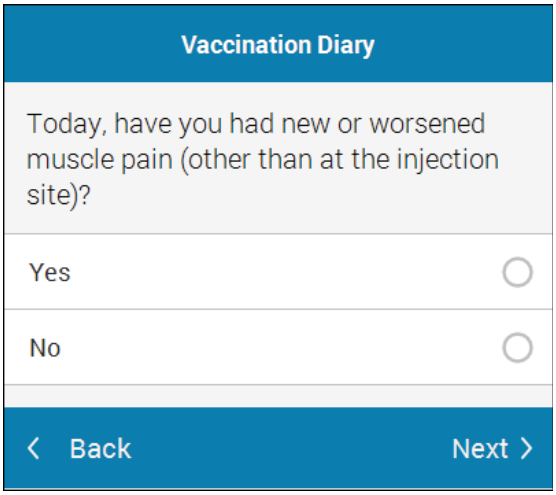
Screen 33



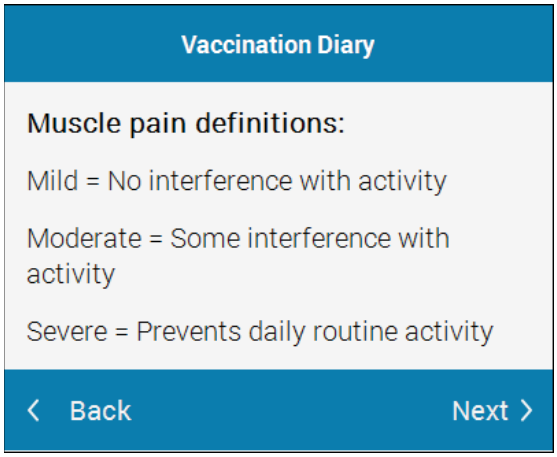
Screen 34



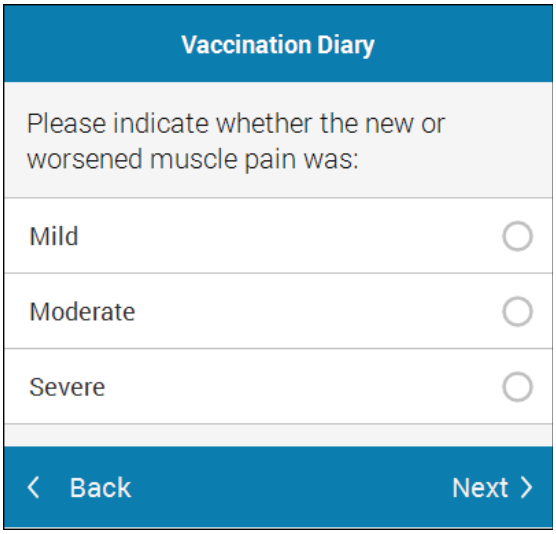
Screen 35



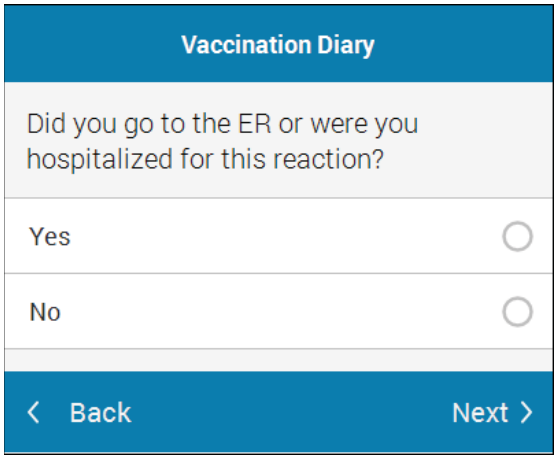
Screen 36



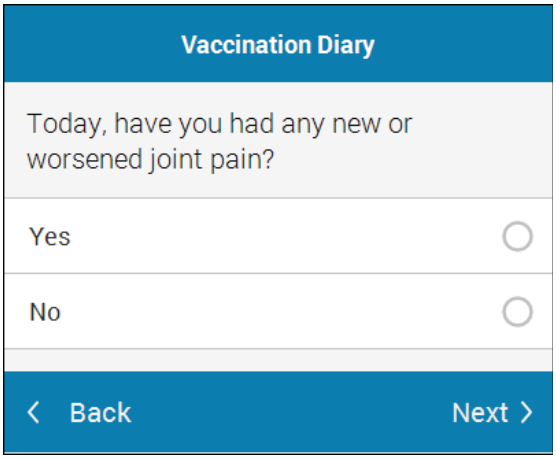
Screen 37



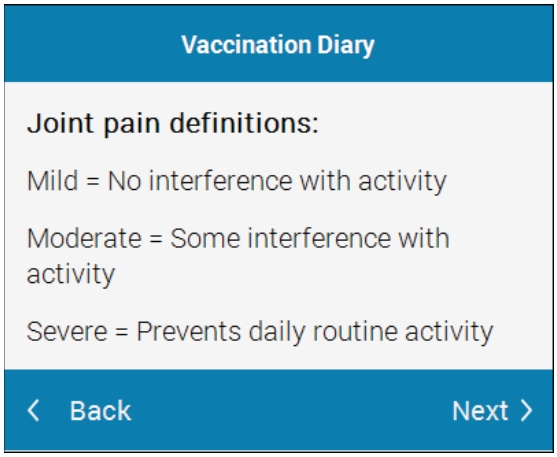
Screen 38



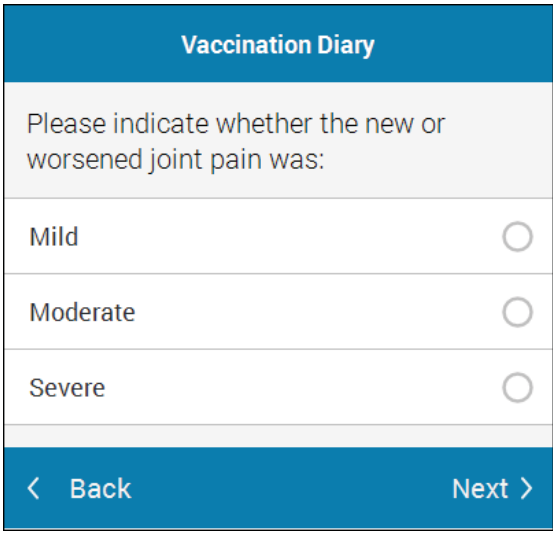
Screen 39



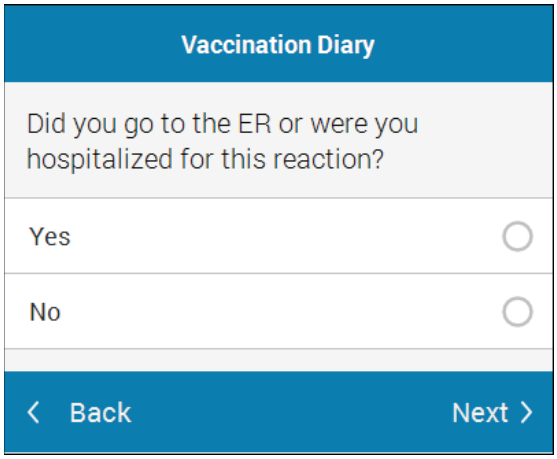
Screen 40



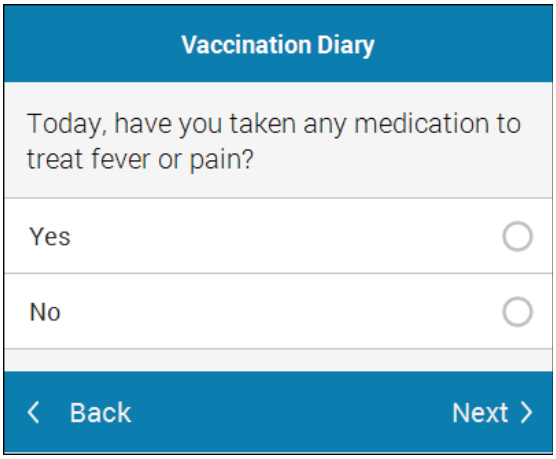
Screen 41



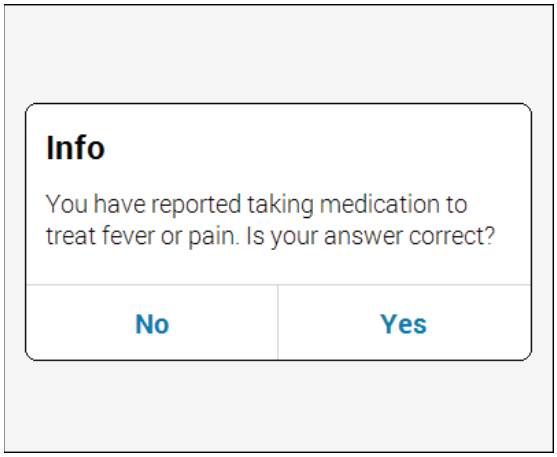
Screen 42



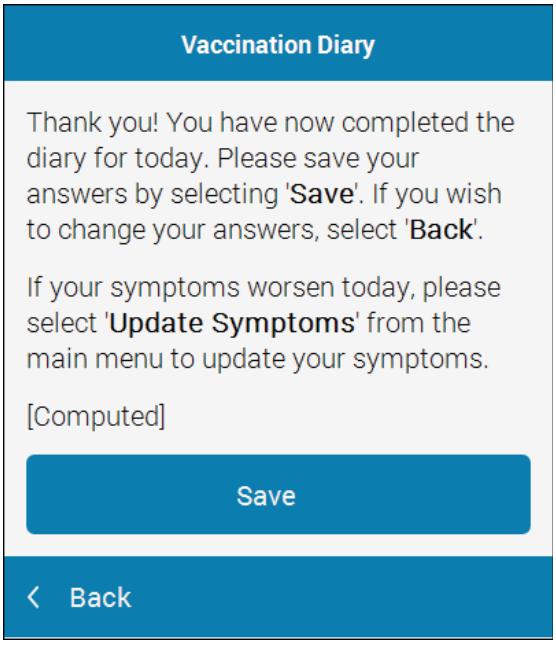
Screen 43



Screen 44



Message 2

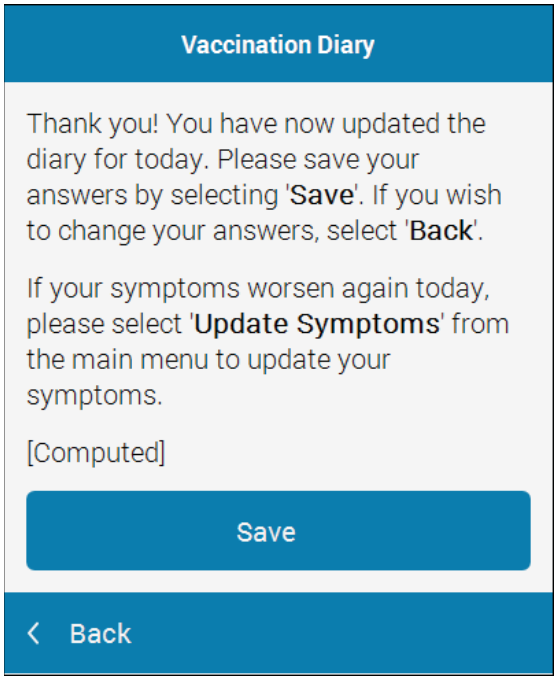


Screen 45

[Computed] will display "Please continue to fill out your diary for the next {1} day(s)."

Where {1} = a number of days

Example: Please continue to fill out your diary for the next 4 day(s).



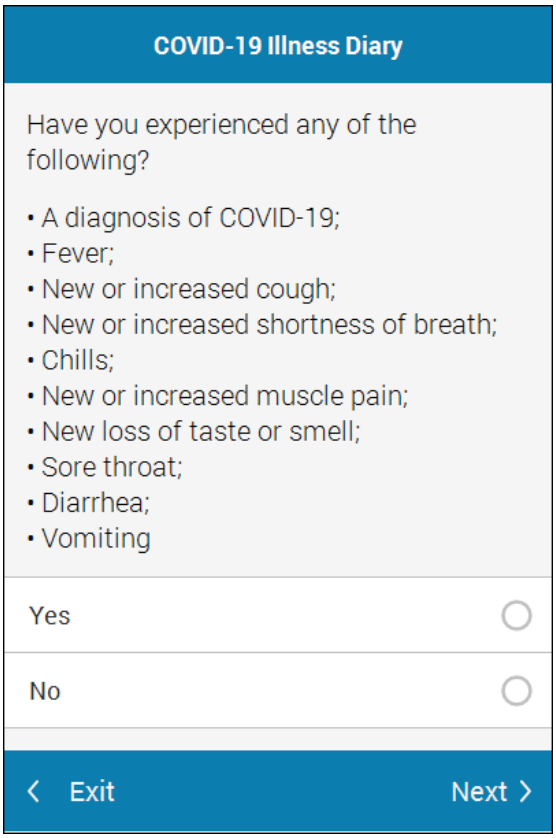
Screen 46

[Computed] will display "Please continue to fill out your diary for the next {1} day(s)."

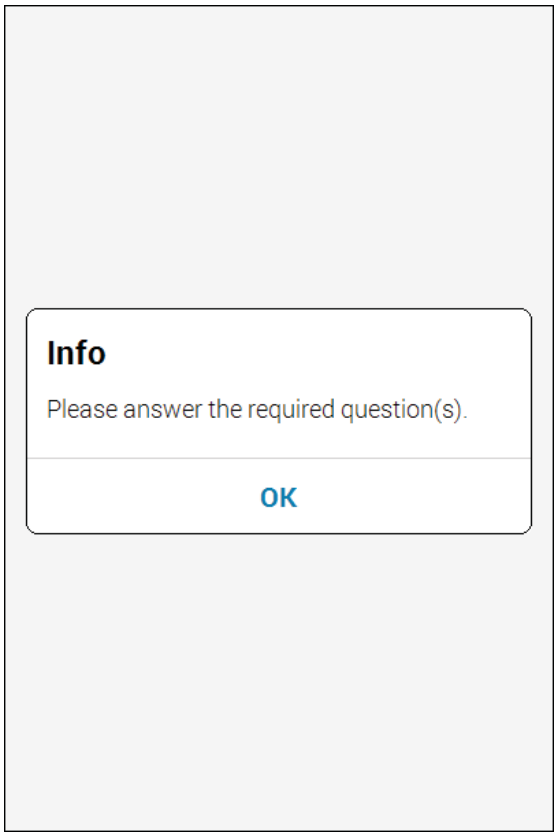
Where {1} = a number of days

Example: Please continue to fill out your diary for the next 4 day(s).

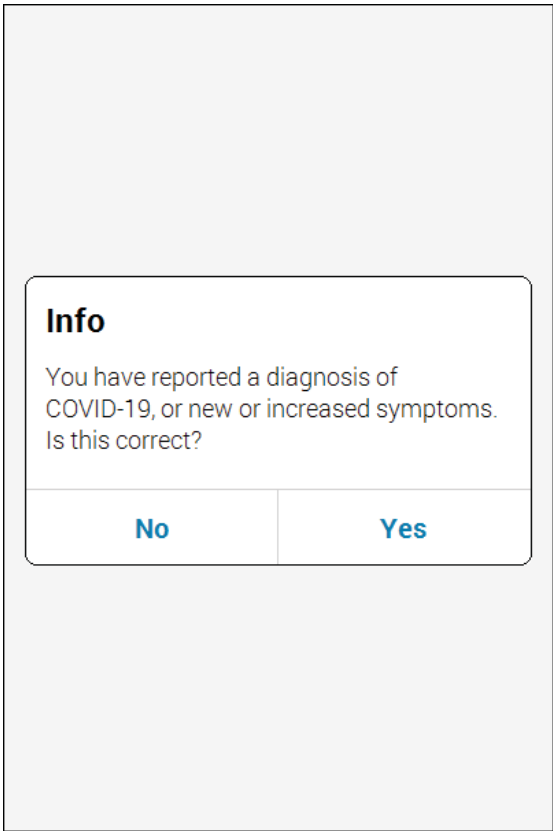
4 Form: COVID-19 Illness Diary



Screen 1

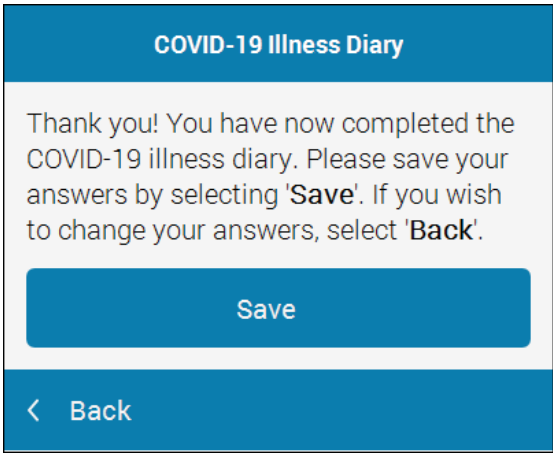


Message 1

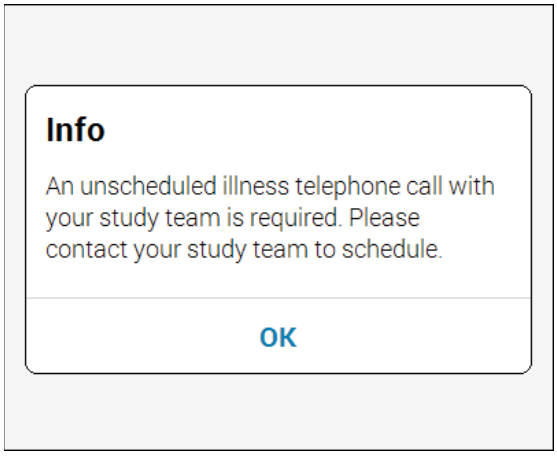


Message 2

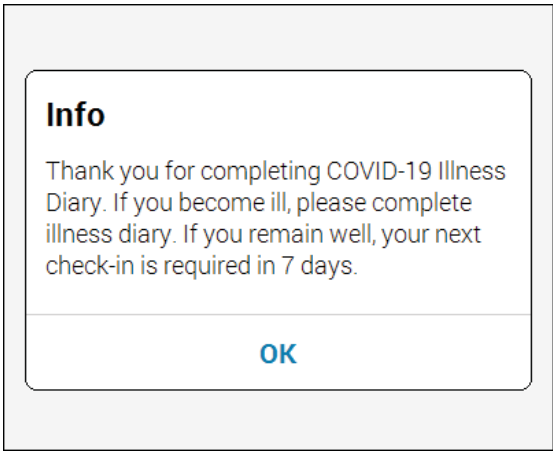
Message 3



Screen 2

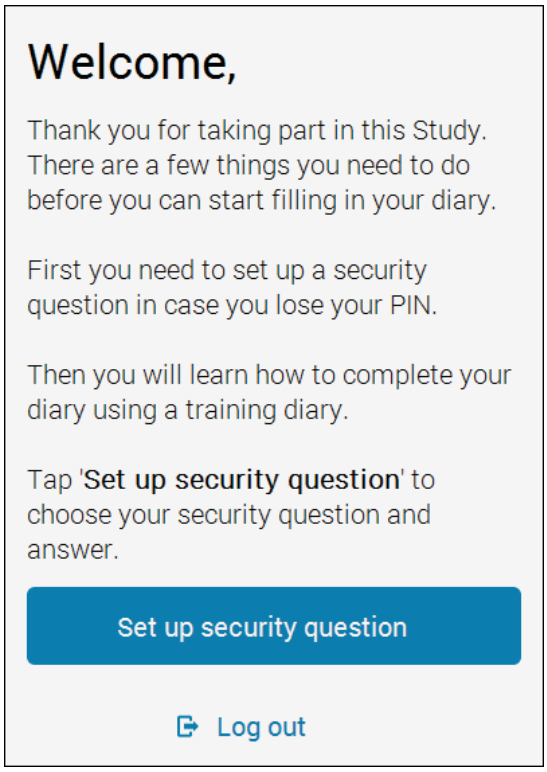


Message 1

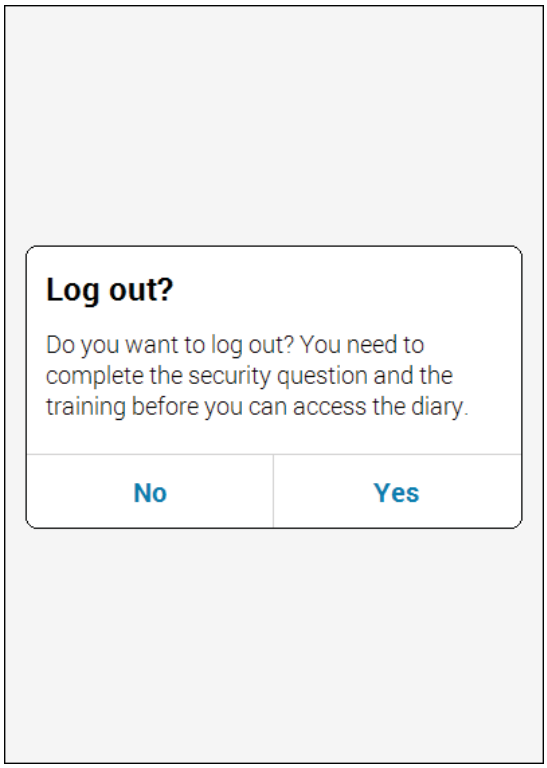


Message 2

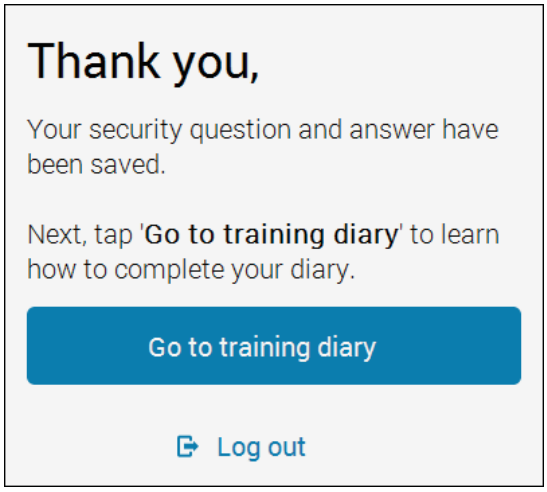
5 Form: Patient main menu



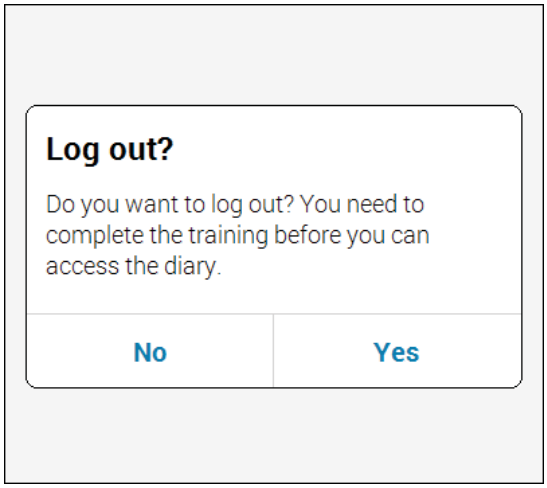
Screen 1



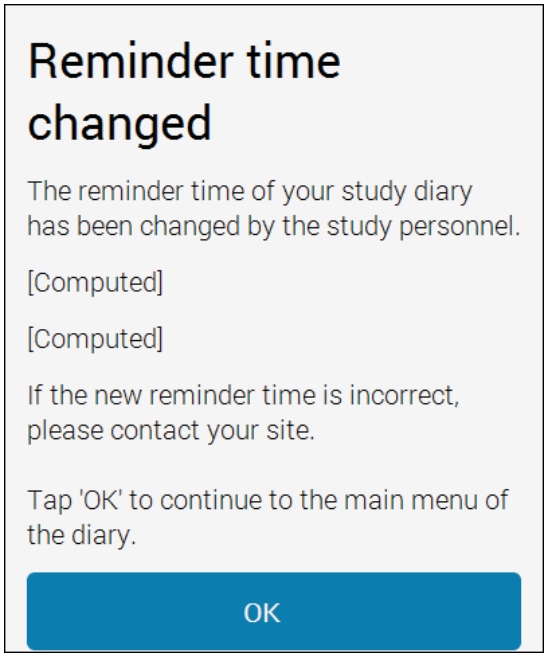
Message 1



Screen 2



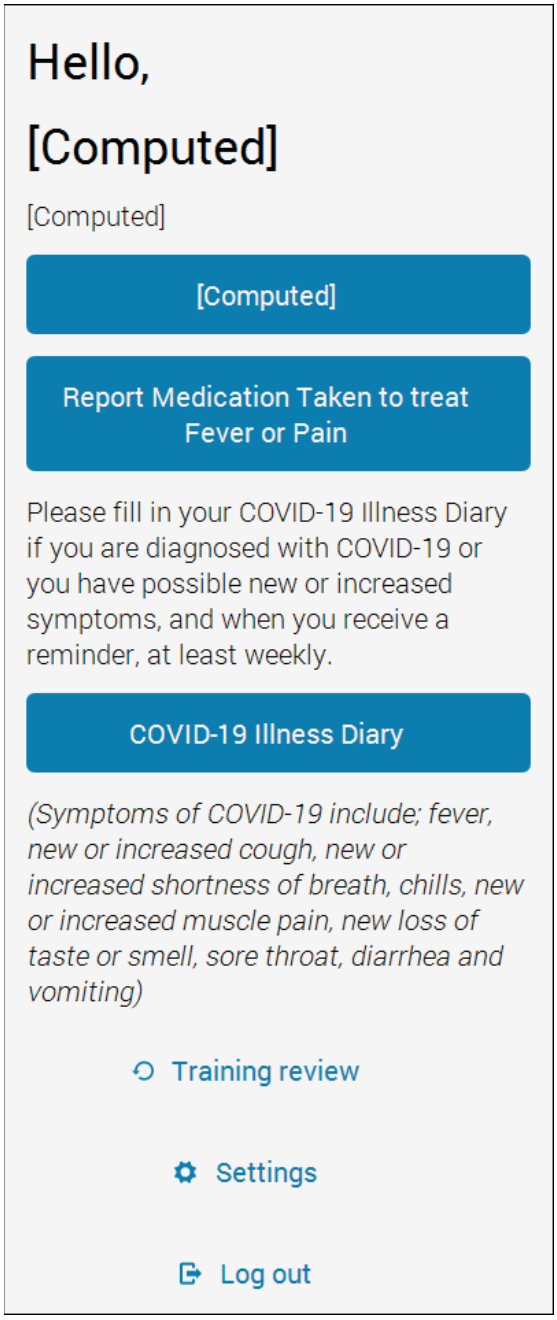
Message 1



Screen 3

First [Computed] will show 'Old reminder time: {1}' where {1} will be the old reminder time

Second [Computed] will show 'New reminder time: {1}' where {1} will be the new reminder time

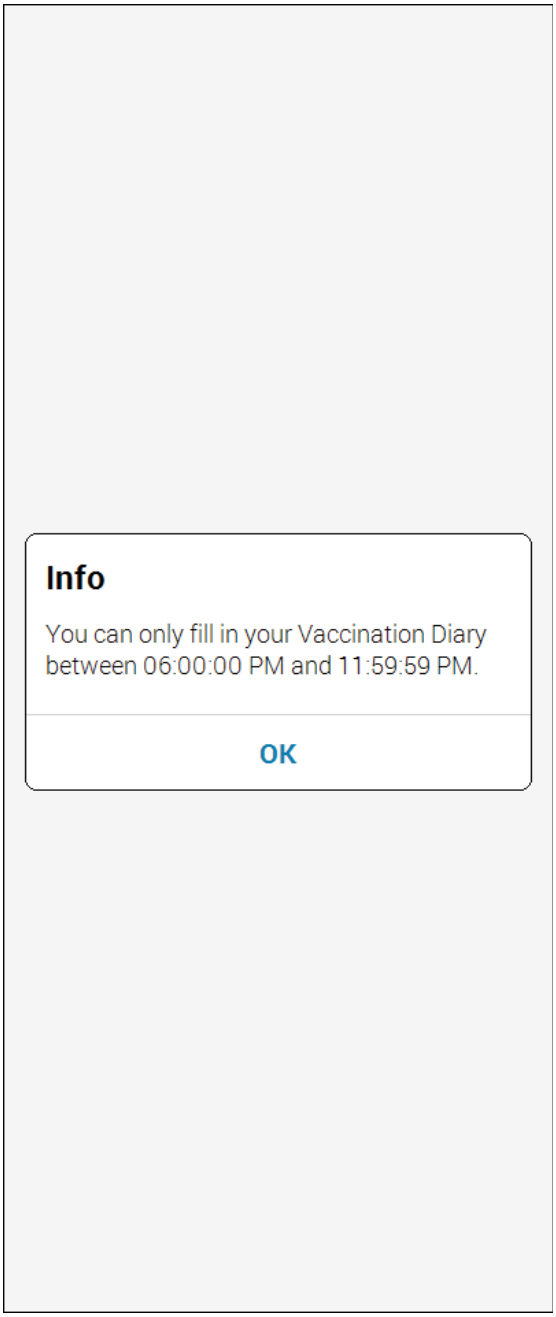


Screen 4

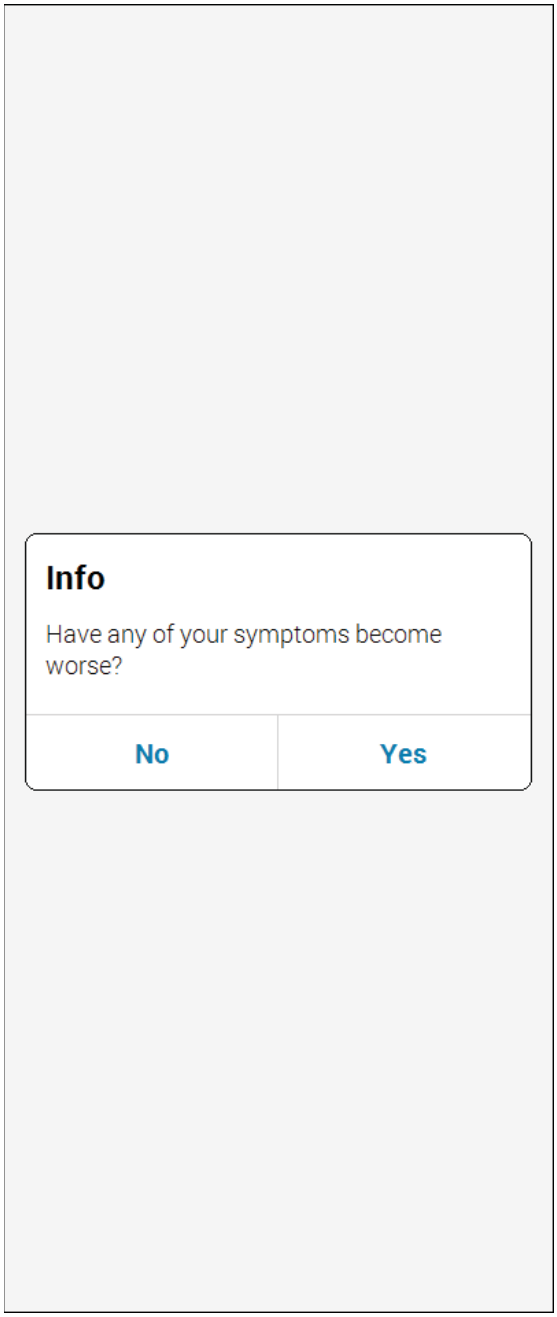
First [Computed] text below Hello, will either display: "You are being reminded to complete your weekly COVID-19 Illness Diary." or "You are being reminded to complete your daily <u>Vaccination Diary</u>."

Second [Computed] text below Hello, will either display: “You have completed today's Vaccination Diary.”, “You have completed today's Vaccination Diary. Please remember to log in again tomorrow." or “Please fill in your daily Vaccination Diary before midnight.”

[Computed] text within the button will read: “Update Symptoms” or “Vaccination Diary”

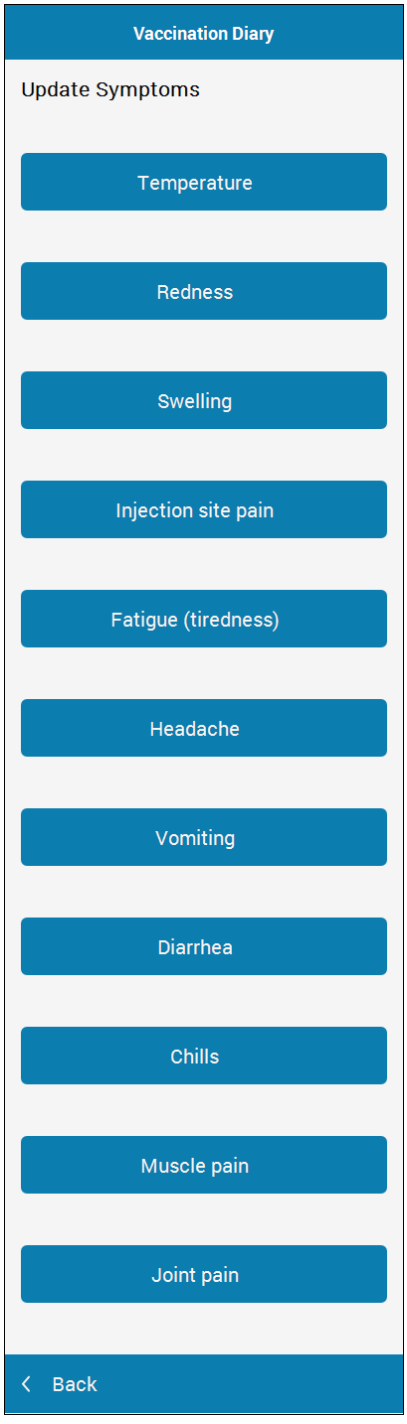


Message 1

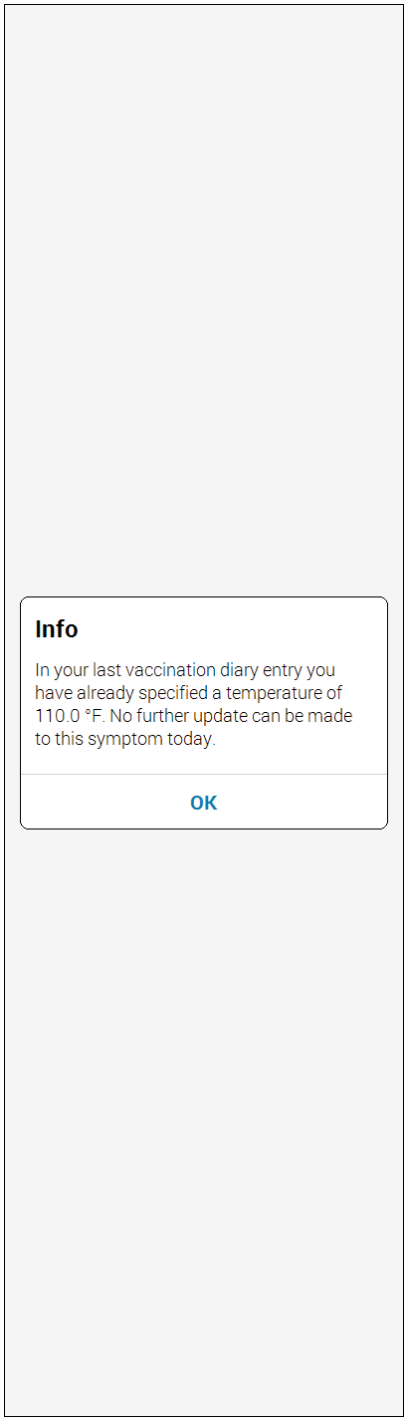


Message 2

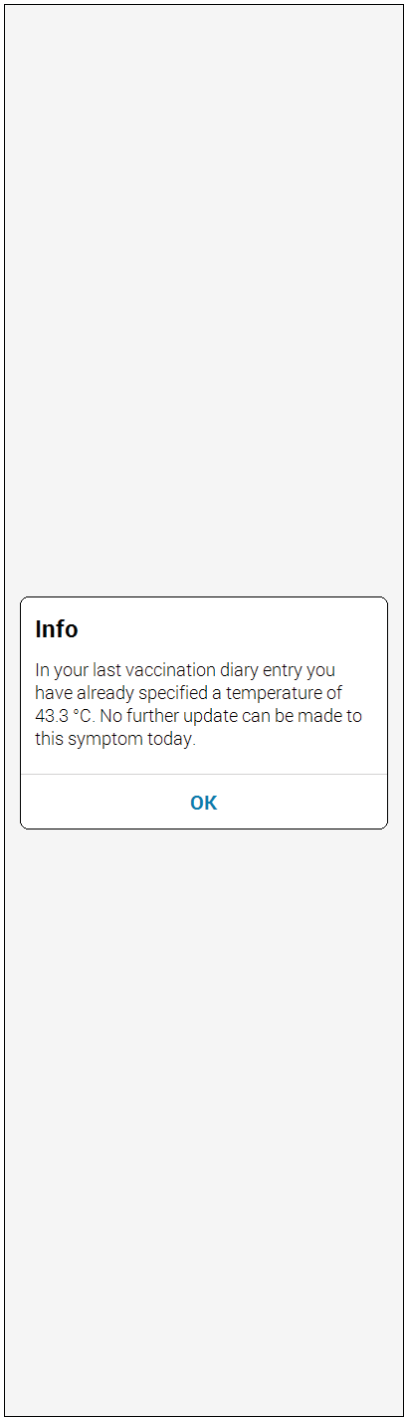
Device text will format out the leading 0's and seconds. Actual popup will read "6:00 PM and 11:59 PM"



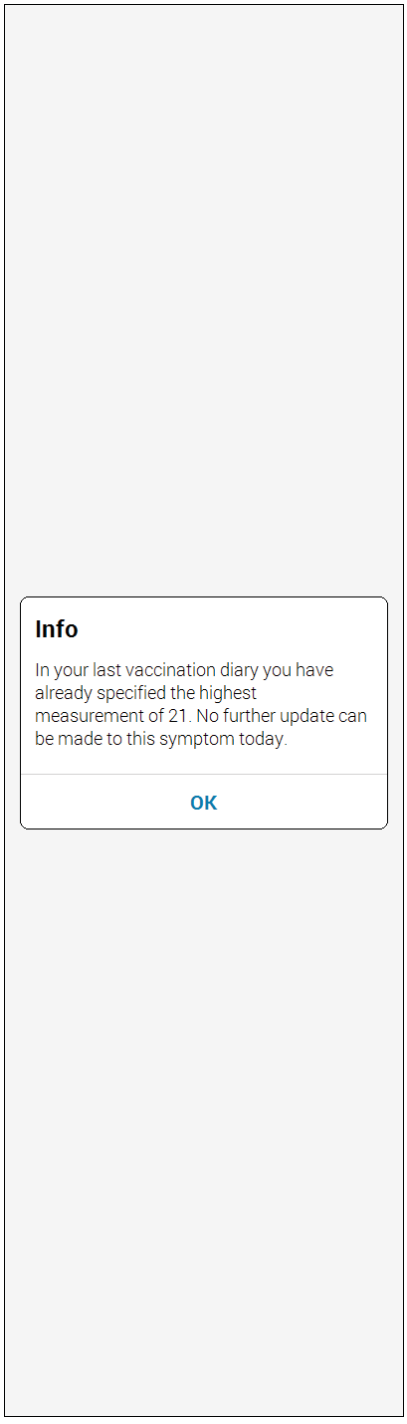
Screen 5



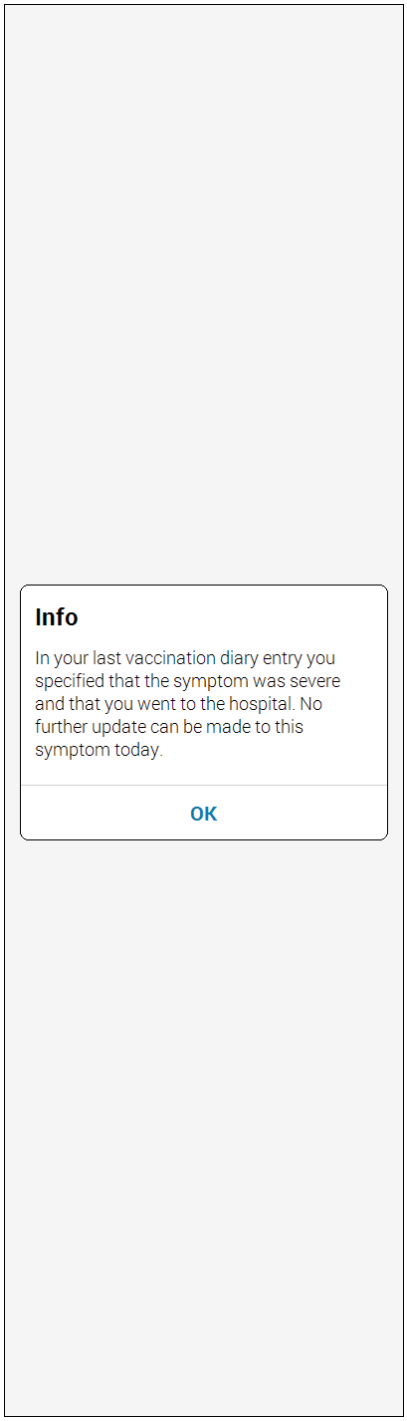
Message 2



Message 3

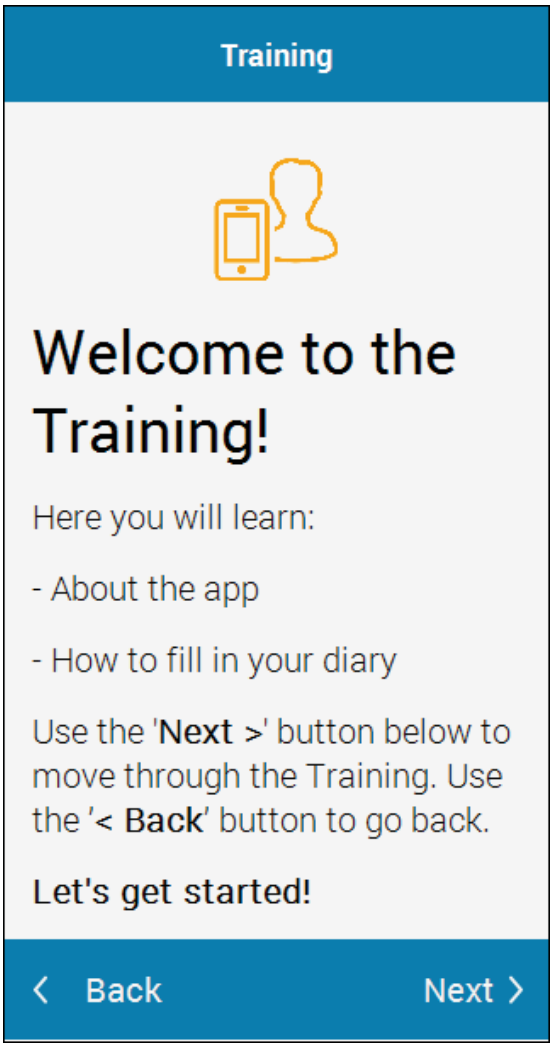


Message 5

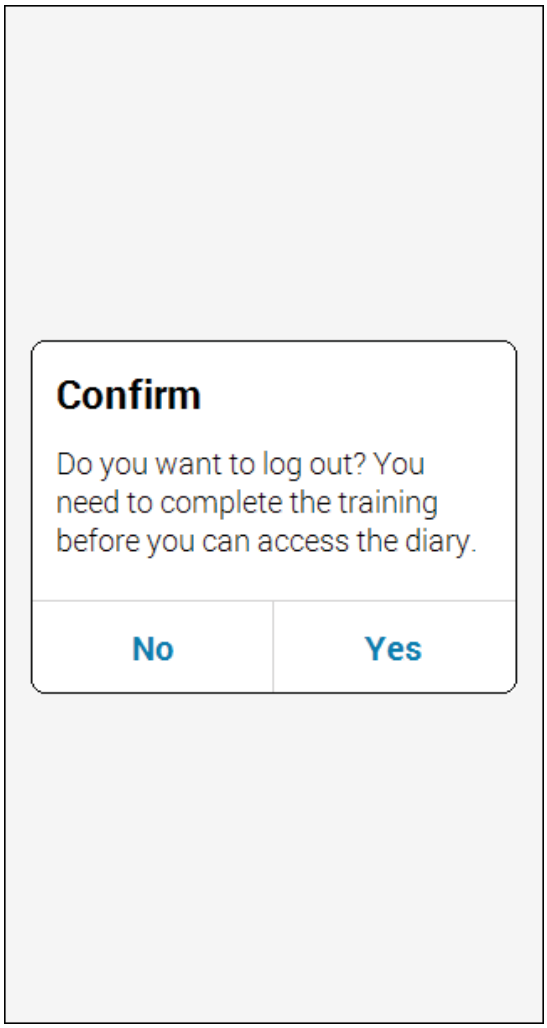


Message 9

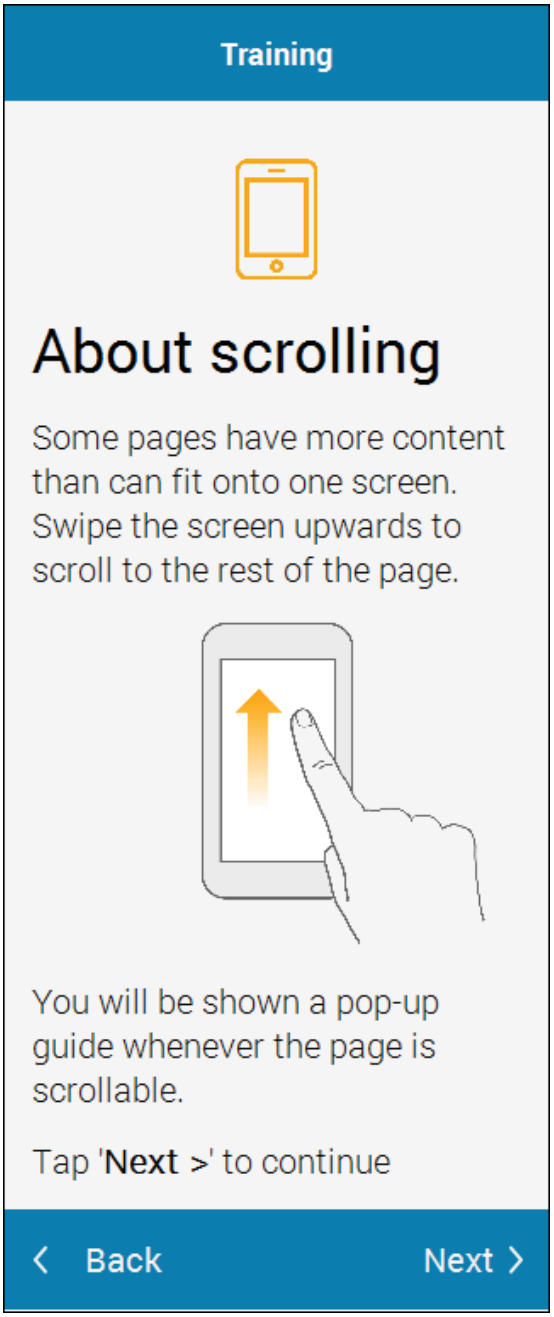
6 Form: Subject training diary



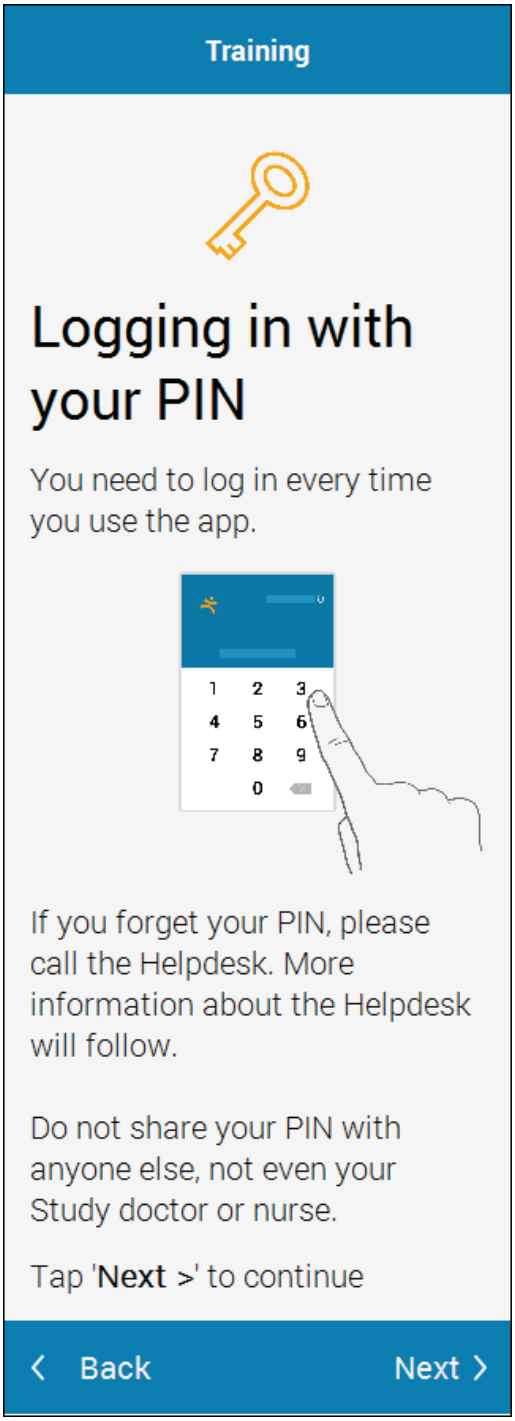
Screen 1



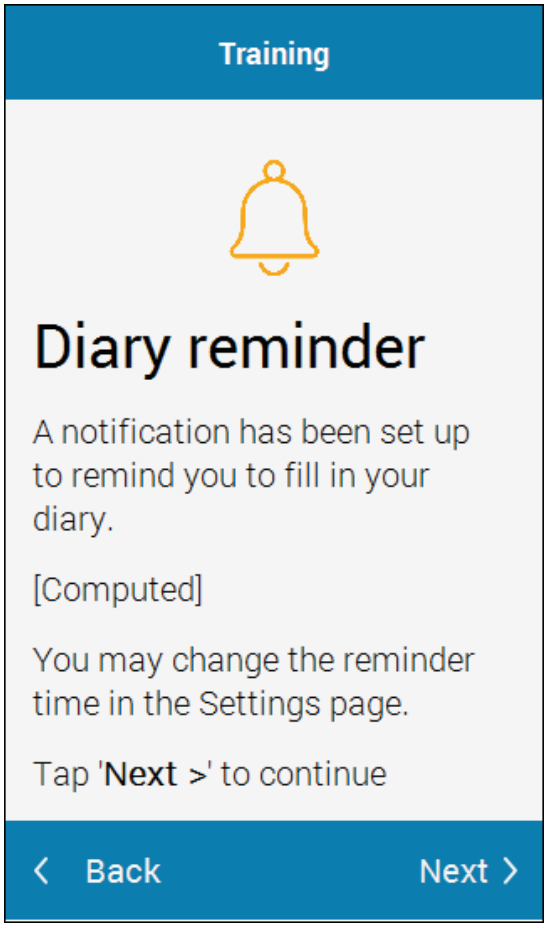
Message 1



Screen 2

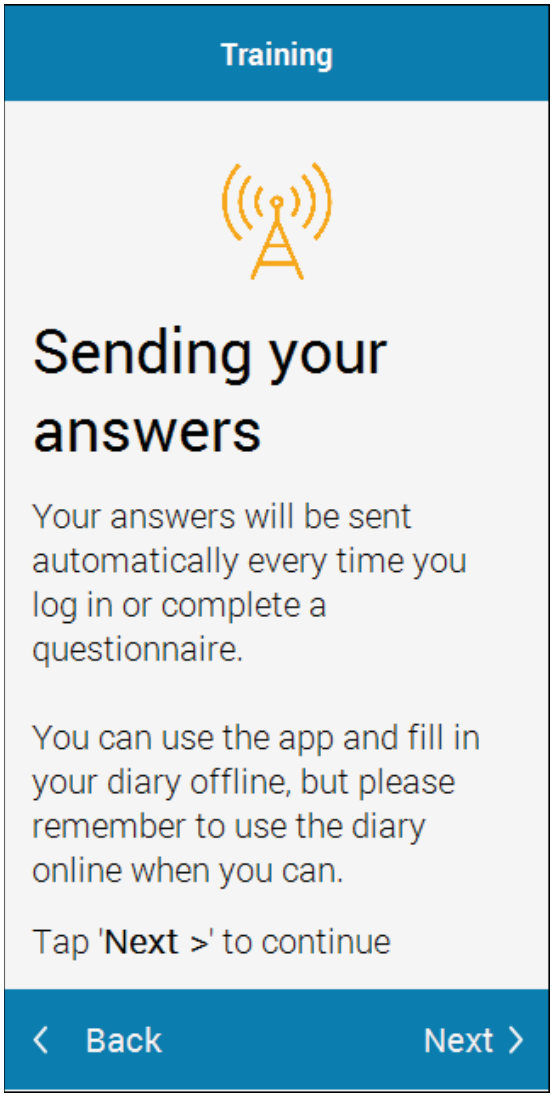


Screen 3

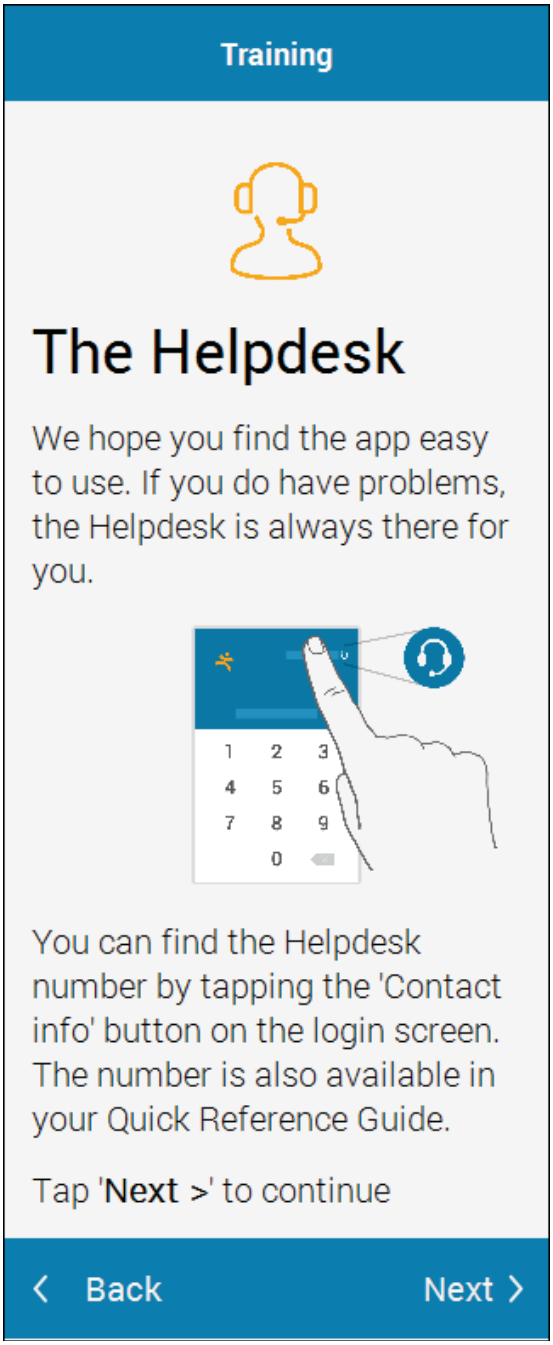


Screen 4

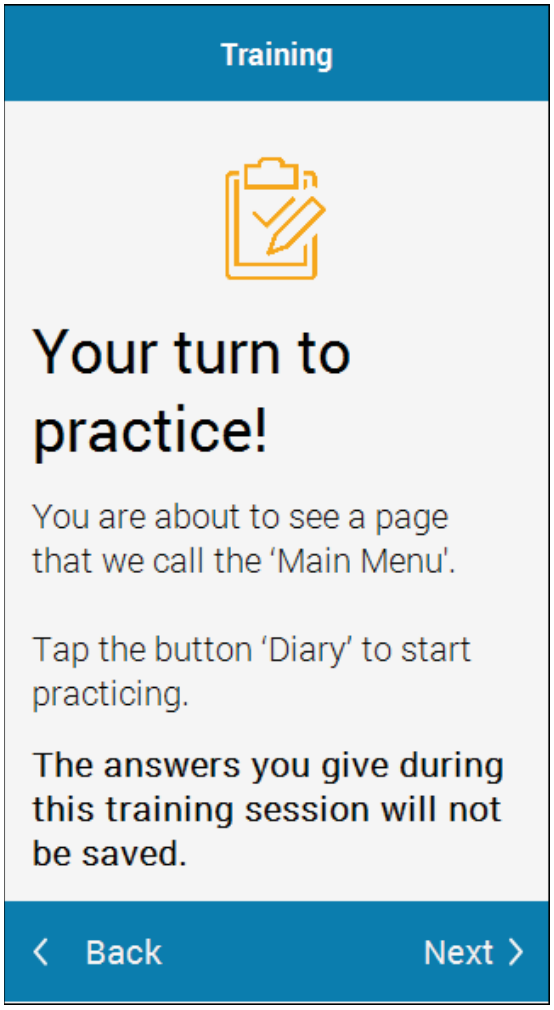
[Computed] will display 'Your reminder time is {1}.', where {1} will be the selected diary reminder time.



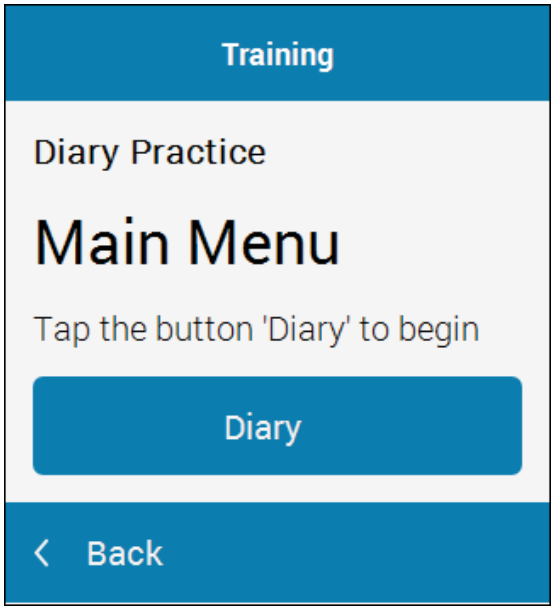
Screen 5



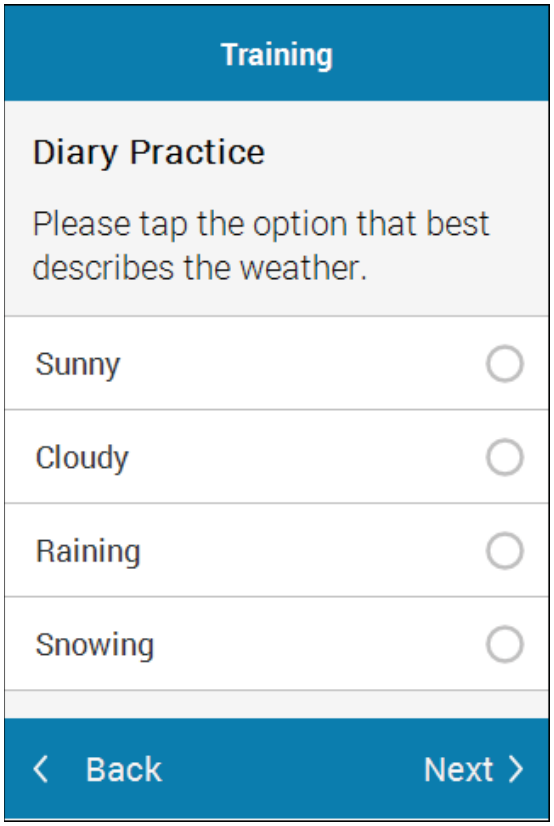
Screen 6



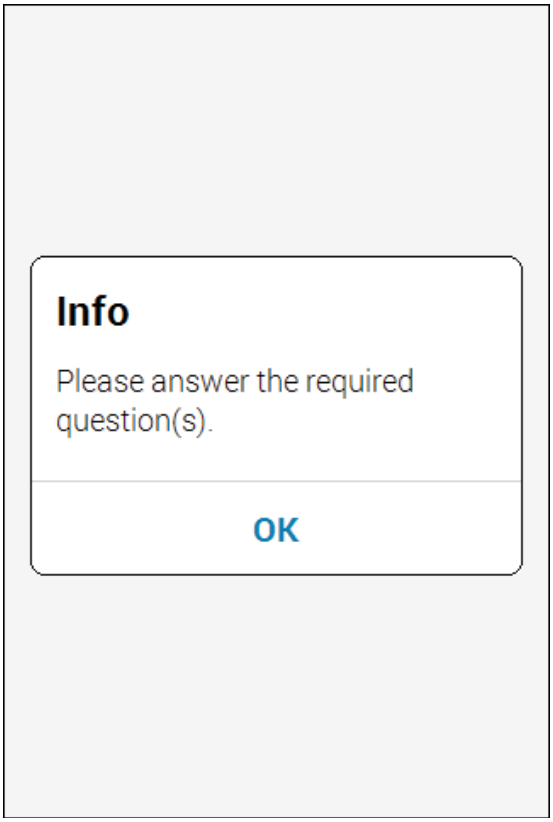
Screen 7



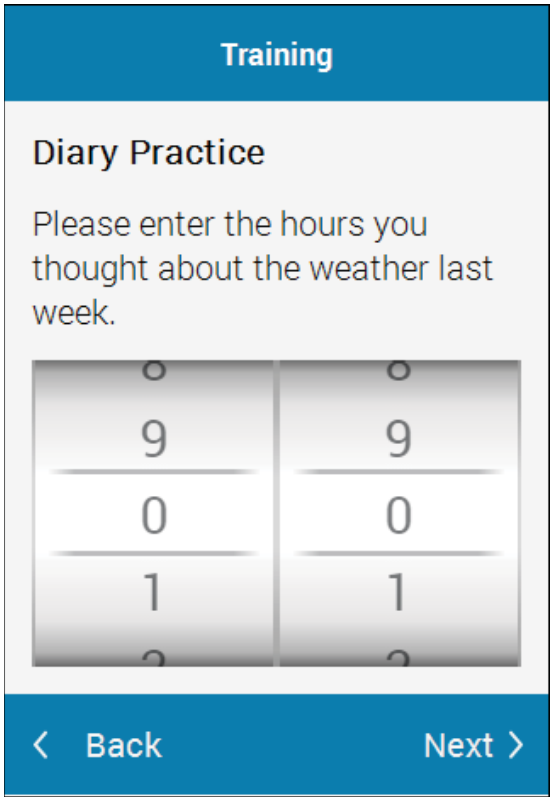
Screen 8



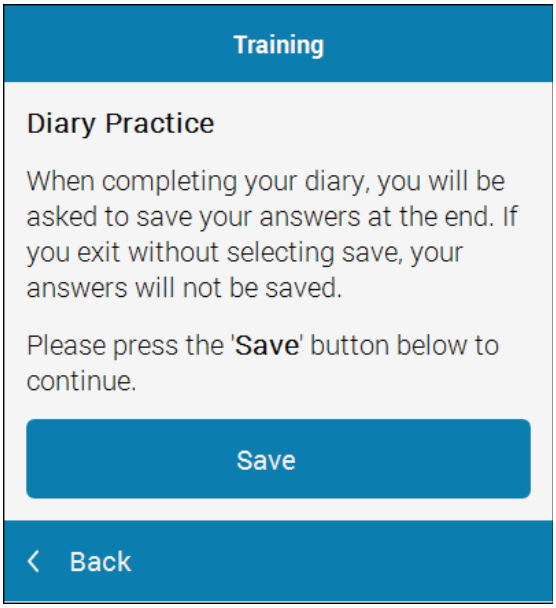
Screen 9



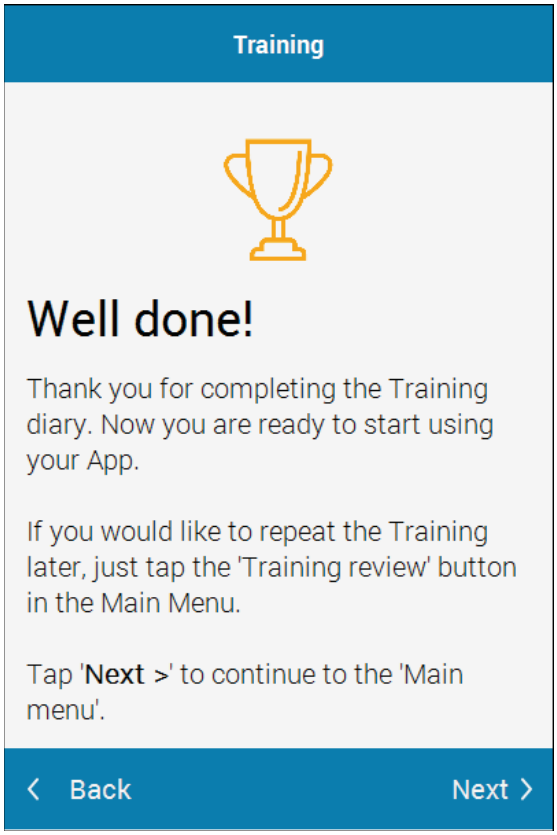
Message 1



Screen 10

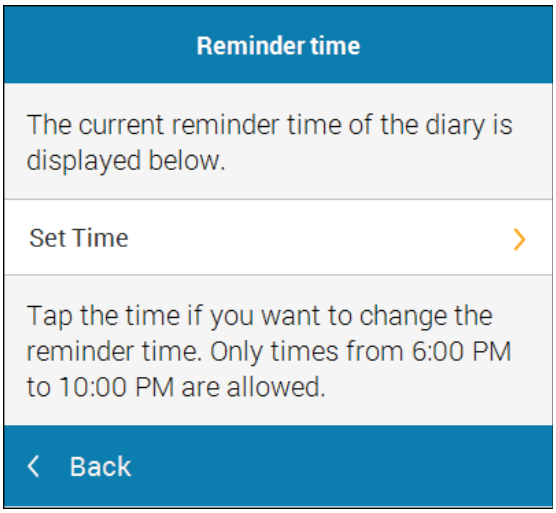


Screen 11

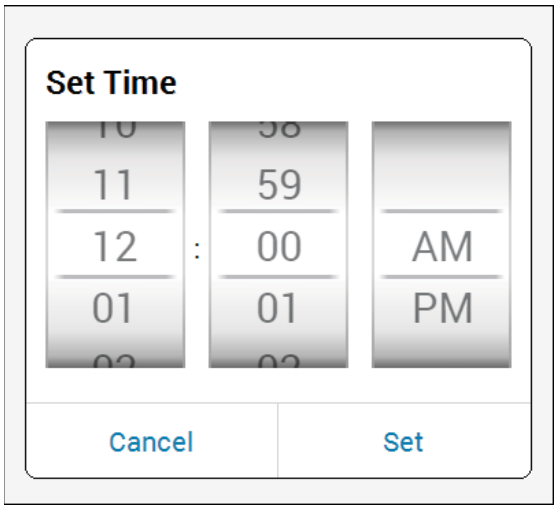


Screen 12

7 Form: Settings

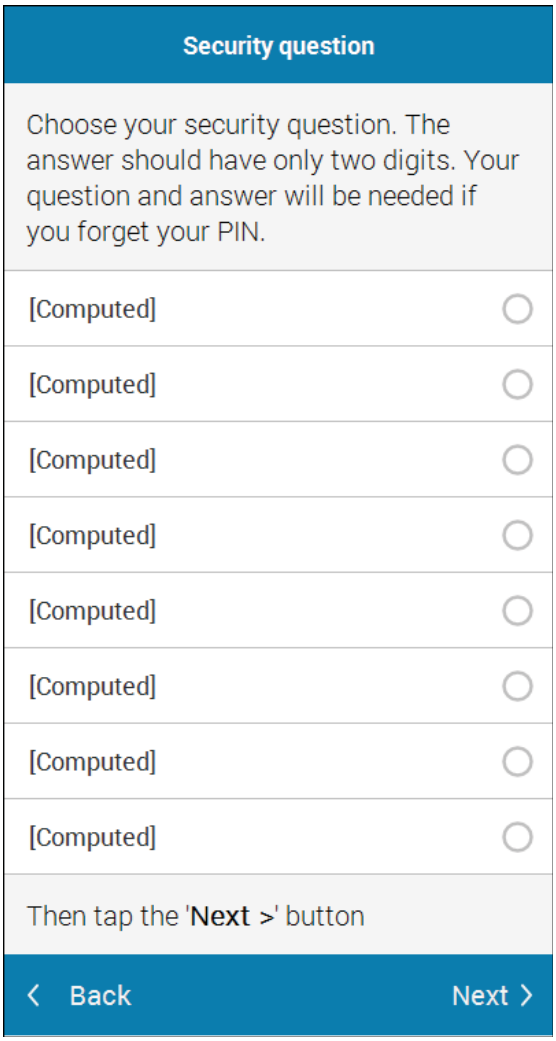


Screen 1

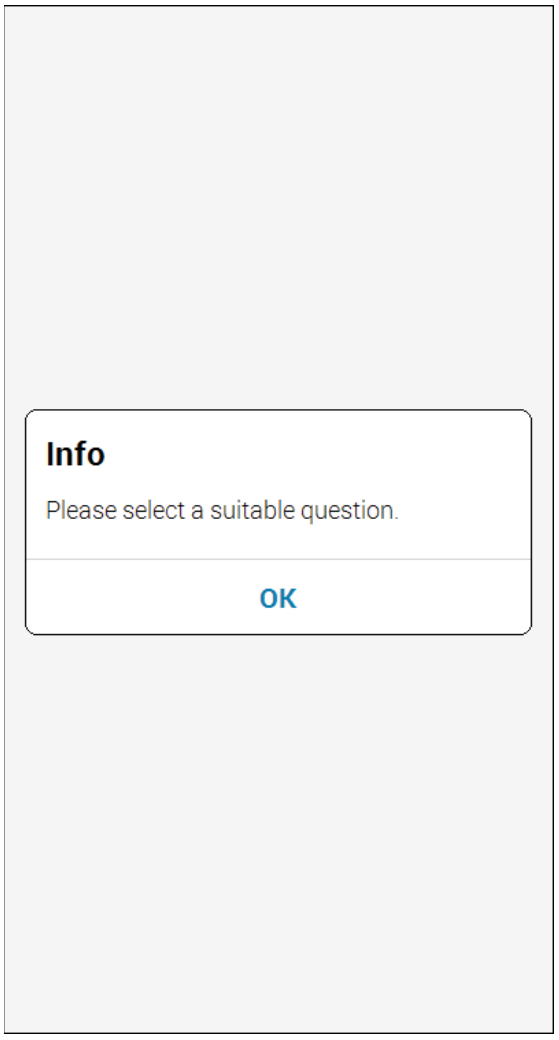


Popup input 1

8 Form: Security question



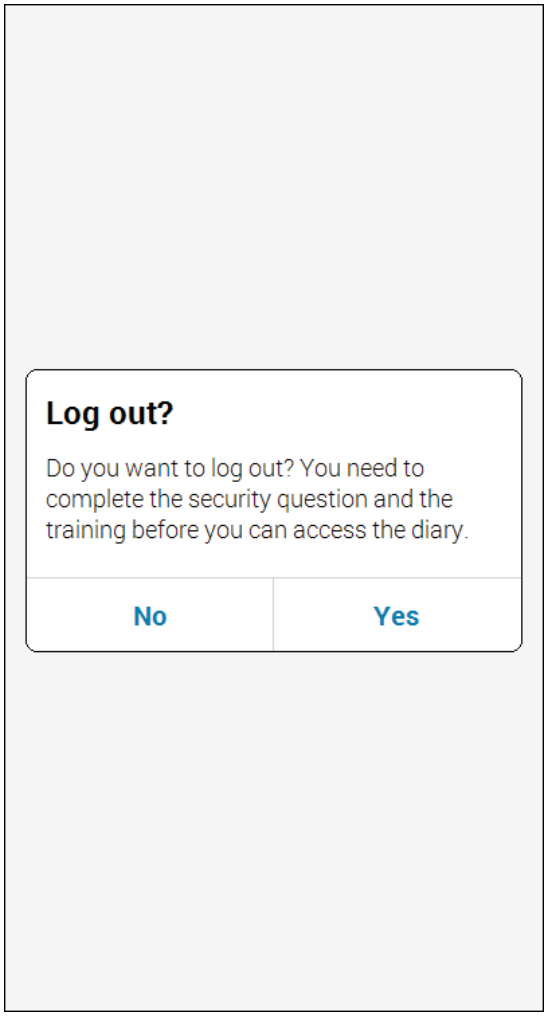
Screen 1



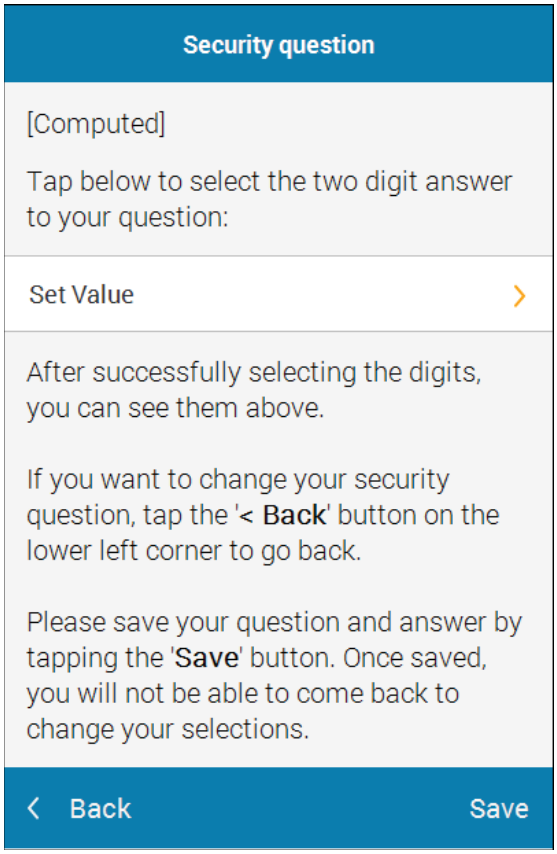
Message 1

[Computed] will show one of the following:

'Your oldest sibling's birth year (YY)'
'Your mother's birth year (YY)'
'Last two digits of your childhood phone number'
'Day of the month of your father's birthday'
'Day of the month of your mother's birthday'
'Childhood home door number (2 digits only)'
'How old were you when you passed your driving test?'
'The year you got married (YY)'



Message 2



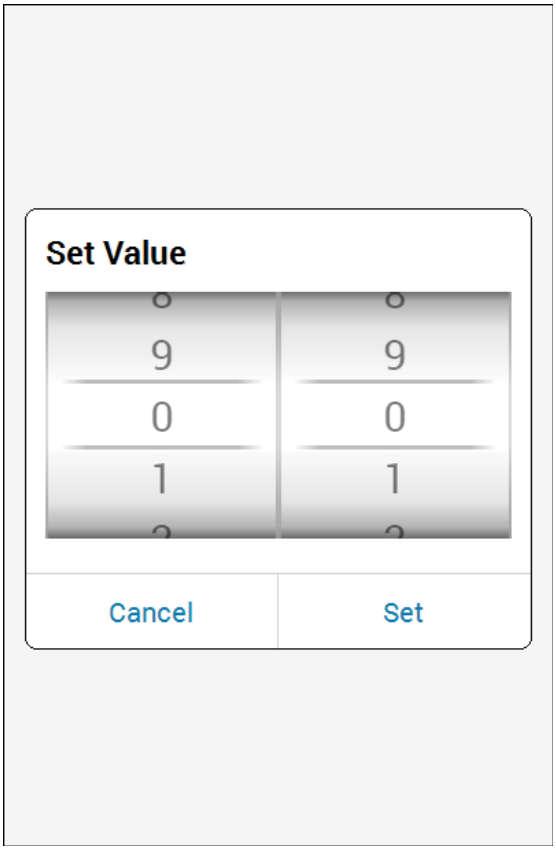
Screen 2

[Computed] will display

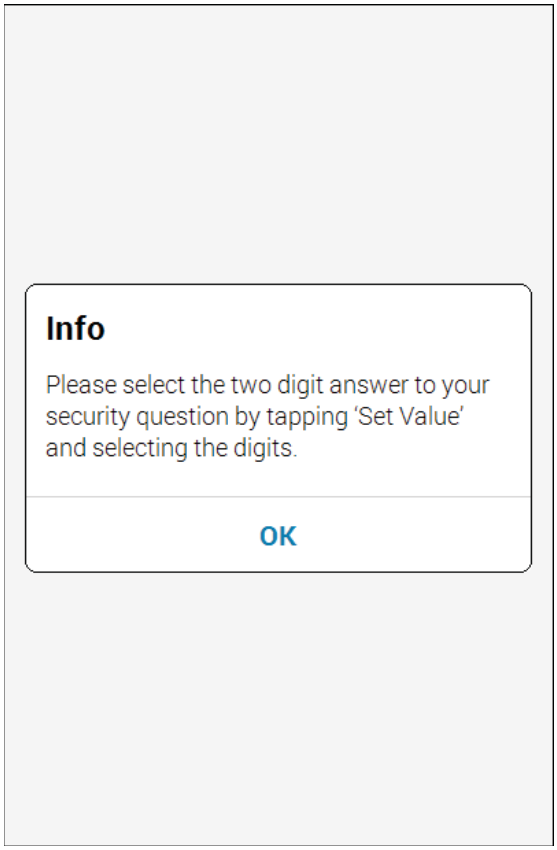
'Your question:

{1}'

{1} will show the question selected on Screen 1



Popup input 1



Message 1

MASTER SUBJECT SCREEN REPORT APPROVAL

Content for Approval					
Language	English for United States				
Subject screen report	A-1426-0086-5270SR-enUS	**Version**	4	**Date**	26-Oct-2020

CUSTOMER

Approval		
Name and Title: PPD		Signature: DocuSigned by: PPD
Company: Pfizer	Role: Study Manager	Date: 26-Oct-2020 | 16:47 EDT

SIGNANT HEALTH

Approval	
Name: PPD	Signature: DocuSigned by: PPD
Title: PPD	Date: 26-Oct-2020 | 15:29 EDT

Protocol C4591001

A PHASE 1/2/3, PLACEBO-CONTROLLED, RANDOMIZED, OBSERVER-BLIND, DOSE-FINDING STUDY TO EVALUATE THE SAFETY, TOLERABILITY, IMMUNOGENICITY, AND EFFICACY OF SARS-COV-2 RNA VACCINE CANDIDATES AGAINST COVID-19 IN HEALTHY INDIVIDUALS

Statistical Analysis Plan
(SAP)

Version: 8

Date: 11 Nov 2021

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LIST OF FIGURES

APPENDICES

1. VERSION HISTORY

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Summary and Rationale for Changes
1/ 20 May 2020	Protocol amendment 1, 13 May 2020	N/A
2/ 30 Jul 2020	Protocol amendment 5, 24 July 2020	Implemented the changes made in protocol amendments 2 through 5.
3/ 02 Nov 2020	Protocol amendment 9, 29 Oct 2020	Implemented the changes made in protocol amendments 6 through 9.
4/ 08 Jan 2021	Protocol amendment 11, 04 Jan 2021	Implemented the changes made in protocol amendments 10 and 11.
5/ 17 Mar 2021	Protocol amendment 14, 02 Mar 2021	Implemented the changes made in protocol amendments 12 through 14.
6/ 14 Jun 2021	Protocol amendment 16, 28 May 2021	Implemented the changes made in protocol amendments 15 and 16.
7/ 26 Jul 2021	Protocol amendment 17, 20 Jul 2021	Implemented the changes made in protocol amendment 17.
8/ 11 Nov 2021	Protocol amendment 18, 07 Sep 2021	Implemented the changes made in protocol amendment 18.

2. INTRODUCTION

This SAP provides the detailed methodology for summary and statistical analyses of the data collected in Study C4591001. This document may modify the plans outlined in the protocol; however, any major modifications of the primary endpoint definition or its analysis will also be reflected in a protocol amendment.

2.1. Study Objectives, Endpoints, and Estimands

The estimands corresponding to each primary, secondary, and tertiary/exploratory objective are described in Table 2 and Table 3 below.

In the primary safety objective evaluations, missing e-diary data will not be imputed. Missing AE dates will be imputed according to Pfizer safety rules. No other missing information will be imputed in the safety analysis.

The estimands to evaluate the immunogenicity objectives are based on evaluable populations for immunogenicity (see Section 4 for definition). These estimands estimate vaccine effect in the hypothetical setting where participants follow the study schedules and protocol requirements as directed. Missing antibody results will not be imputed. Immunogenicity results that are below the LLOQ will be set to 0.5 × LLOQ in the analysis; this may be adjusted once additional data on the assay characteristics become available.

The estimands to evaluate the efficacy objectives are based on evaluable populations for efficacy (see Section 4 for definition). These estimands estimate vaccine effect in the hypothetical setting where participants follow the study schedules and protocol requirements

as directed. In addition, VE will be analyzed by the all-available efficacy populations. Missing laboratory results will not be imputed for the primary analysis, but missing data imputation for the efficacy endpoint may be performed as a sensitivity analysis.

Table 2. List of Primary and Secondary Objectives, Estimands, and Endpoints for Phase 1

Objectives	Estimands	Endpoints
Primary:	**Primary:**	**Primary:**
To describe the safety and tolerability profiles of prophylactic BNT162 vaccines in healthy adults after 1 or 2 doses	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 • Adverse events (AEs) from Dose 1 to 1 month after the last dose • Serious AEs (SAEs) from Dose 1 to 6 months after the last dose	• 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
	In addition, the percentage of participants with: • Abnormal hematology and chemistry laboratory values 1 and 7 days after Dose 1; and 7 days after Dose 2 • Grading shifts in hematology and chemistry laboratory assessments between baseline and 1 and 7 days after Dose 1; and before Dose 2 and 7 days after Dose 2	Hematology and chemistry laboratory parameters detailed in the protocol, Section 10.2.
Secondary:	**Secondary:**	**Secondary:**
To describe the immune responses elicited by prophylactic BNT162 vaccines in healthy adults after 1 or 2 doses	In participants complying with the key protocol criteria (evaluable participants) at the following time points after receipt of study intervention: 7 and 21 days after Dose 1; 7 and 14 days and 1, 6, 12, and 24 months after Dose 2	
	• Geometric mean titers (GMTs) at each time point • Geometric mean fold rise (GMFR) from before vaccination to each subsequent time point after vaccination • Proportion of participants achieving ≥4-fold rise from before vaccination to each subsequent time point after vaccination	SARS-CoV-2 neutralizing titers

Table 2. List of Primary and Secondary Objectives, Estimands, and Endpoints for Phase 1

Objectives	Estimands	Endpoints
	• Geometric mean concentrations (GMCs) at each time point • GMFR from prior to first dose of study intervention to each subsequent time point • Proportion of participants achieving ≥4-fold rise from before vaccination to each subsequent time point after vaccination	S1-binding IgG levels and RBD-binding IgG levels
	• Geometric mean ratio (GMR), estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers to the geometric mean of binding IgG levels at each time point	• SARS-CoV-2 neutralizing titers • S1-binding IgG levels • RBD-binding IgG levels
Exploratory:	**Exploratory:**	**Exploratory:**
To describe the immune responses elicited by a third dose of prophylactic BNT162b2 administered to healthy adults 6 to 12 months after the second dose of either BNT162b1 or BNT162b2	• GMCs/GMTs at the time of Dose 3 and 7 days and 1 month after Dose 3 • GMFRs from before Dose 3 to 7 days and 1 month after Dose 3	• SARS-CoV-2 reference-strain neutralizing titers • SARS-CoV-2 SA-variant neutralizing titers • Full-length S-binding or S1-binding IgG levels
	• GMR of SARS-CoV-2 reference-strain neutralizing titers 1 month after Dose 3 to 1 month after Dose 2	• SARS-CoV-2 reference-strain neutralizing titers
	• GMR of SARS-CoV-2 SA-variant neutralizing titers 1 month after Dose 3 to SARS-CoV-2 reference-strain neutralizing titers 1 month after Dose 2	• SARS-CoV-2 reference-strain neutralizing titers • SARS-CoV-2 SA-variant neutralizing titers
To describe the safety profile of a third dose of prophylactic BNT162b2 administered to healthy adults 6 to 12 months after the second dose of either BNT162b1 or BNT162b2	In participants receiving a third dose of BNT162b2, the percentage of participants reporting: • Local reactions for up to 7 days after Dose 3 • Systemic events for up to 7 days after Dose 3 • AEs and SAEs from Dose 3 to 1 month after Dose 3	• 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

Table 3. List of Primary, Secondary, and Tertiary/Exploratory Objectives, Estimands, and Endpoints for Phase 2/3

Objectives[a]	Estimands	Endpoints
Primary Efficacy		
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 7 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 7 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants with no serological or virological evidence (up to 7 days after receipt of the second dose) of past SARS-CoV-2 infection
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 7 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 7 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT
Primary Safety		
To define the safety profile of prophylactic BNT162b2 in the first 360 participants randomized (Phase 2)	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 7 days after the second dose • SAEs from Dose 1 to 7 days after the second dose	• 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
To define the safety profile of prophylactic BNT162b2 in all participants randomized in Phase 2/3	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	• AEs • SAEs • In a subset of at least 6000 participants: o Local reactions (pain at the injection site, redness, and swelling) o Systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain)
To define the safety profile of prophylactic BNT162b2 in participants 12 to 15 years of age in Phase 3	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	• 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

Table 3. List of Primary, Secondary, and Tertiary/Exploratory Objectives, Estimands, and Endpoints for Phase 2/3

Objectives[a]	Estimands	Endpoints
To describe the safety and tolerability profile of BNT162b2$_{SA}$ given as 1 or 2 doses to BNT162b2-experienced participants, or as 2 doses to BNT162b2-naïve participants To describe the safety and tolerability profile of BNT162b2 given as a third dose to BNT162b2-experienced participants in the subset for evaluation of boostability and protection against emerging VOCs	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 last dose • SAEs from Dose 1 to 5 or 6 months after the last dose	• 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
To describe the safety and tolerability profile of BNT162b2 given as a third dose at least 6 months after the second dose of BNT162b2 (or BNT162b2$_{SA}$) for participants who received a third dose as part of protocol amendment 18	In participants receiving at least 1 dose of study intervention, the percentage of participants reporting: • AEs from Dose 3 to 1 month after Dose 3 • SAEs from Dose 3 to 6 months after Dose 3	• AEs • SAEs
Primary Immunogenicity ***BNT162b2-experienced participants***		
To demonstrate the noninferiority of the anti–reference strain immune response after a third dose of BNT162b2 at 30 µg compared to after 2 doses of BNT162b2, in the same individuals	GMR of reference strain NT 1 month after the third dose of BNT162b2 at 30 µg to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the reference strain at 1 month after the third dose of BNT162b2 at 30 µg and 1 month after the second dose of BNT162b2	SARS-CoV-2 reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the third dose of BNT162b2 at 30 µg) of past SARS-CoV-2 infection
To demonstrate the noninferiority of the anti-SA immune response after 1 dose of BNT162b2$_{SA}$ compared to the anti–reference strain immune response after 2 doses of BNT162b2, in the same individuals	GMR of SA NT 1 month after 1 dose of BNT162b2$_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after 1 dose of BNT162b2$_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of 1 dose of BNT162b2$_{SA}$) of past SARS-CoV-2 infection

Table 3. List of Primary, Secondary, and Tertiary/Exploratory Objectives, Estimands, and Endpoints for Phase 2/3

Objectives[a]	Estimands	Endpoints
BNT162b2-naïve participants		
To demonstrate the noninferiority of the anti-SA immune response after 2 doses of BNT162b2$_{SA}$ compared to the anti–reference strain immune response after 2 doses of BNT162b2	GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$ or BNT162b2 as appropriate) of past SARS-CoV-2 infection
Secondary Efficacy		
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 14 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants with no serological or virological evidence (up to 14 days after receipt of the second dose) of past SARS-CoV-2 infection
To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 14 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT
To evaluate the efficacy of prophylactic BNT162b2 against confirmed severe COVID-19 occurring from 7 days and from 14 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	Confirmed severe COVID-19 incidence per 1000 person-years of follow-up in participants with no serological or virological evidence (up to 7 days and up to 14 days after receipt of the second dose) of past SARS-CoV-2 infection
To evaluate the efficacy of prophylactic BNT162b2 against confirmed severe COVID-19 occurring from 7 days and from 14 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	Confirmed severe COVID-19 incidence per 1000 person-years of follow-up

Table 3. List of Primary, Secondary, and Tertiary/Exploratory Objectives, Estimands, and Endpoints for Phase 2/3

Objectives[a]	Estimands	Endpoints
To describe the efficacy of prophylactic BNT162b2 against confirmed COVID-19 (according to the CDC-defined symptoms) occurring from 7 days and from 14 days after the second dose in participants without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants with no serological or virological evidence (up to 7 days and up to 14 days after receipt of the second dose) of past SARS-CoV-2 infection
To describe the efficacy of prophylactic BNT162b2 against confirmed COVID-19 (according to the CDC-defined symptoms) occurring from 7 days and from 14 days after the second dose in participants with and without evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) • at least 7 days and • at least 14 days after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT
To evaluate the efficacy of prophylactic BNT162b2 against non-S seroconversion to SARS-CoV-2 in participants without evidence of infection or confirmed COVID-19	In participants complying with the key protocol criteria (evaluable participants): 100 × (1 – IRR) [ratio of active vaccine to placebo]	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on N-binding antibody seroconversion in participants with no serological or virological evidence of past SARS-CoV-2 infection or confirmed COVID-19
To evaluate the efficacy of prophylactic BNT162b2 against asymptomatic SARS-CoV-2 infection in participants without evidence of infection up to the start of the asymptomatic surveillance period	In participants complying with the key protocol criteria (evaluable participants): 100 × (1 – IRR) [ratio of active vaccine to placebo]	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on central laboratory–confirmed NAAT in participants with no serological or virological evidence (up to the start of the asymptomatic surveillance period) of past SARS-CoV-2 infection
Secondary Immunogenicity		
To demonstrate the noninferiority of the immune response to prophylactic BNT162b2 in participants 12 to 15 years of age compared to participants 16 to 25 years of age	GMR, estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in the 2 age groups (12-15 years of age to 16-25 years of age) 1 month after completion of vaccination	SARS-CoV-2 neutralizing titers in participants with no serological or virological evidence (up to 1 month after receipt of the second dose) of past SARS-CoV-2 infection
BNT162b2-experienced participants		
To demonstrate the noninferiority of the anti-SA immune response after a third dose of BNT162b2 at 30 µg compared to the anti–reference strain immune response after 2 doses of BNT162b2, in the same individuals	GMR of SA NT 1 month after the third dose of BNT162b2 at 30 µg to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the third dose of BNT162b2 at 30 µg and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the third dose of BNT162b2 at 30 µg) of past SARS-CoV-2 infection

Table 3. List of Primary, Secondary, and Tertiary/Exploratory Objectives, Estimands, and Endpoints for Phase 2/3

Objectives[a]	Estimands	Endpoints
To demonstrate the noninferiority of the anti–reference strain immune response after 1 dose of BNT162b2$_{SA}$ compared to after 2 doses of BNT162b2, in the same individuals	GMR of reference strain NT 1 month after 1 dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the reference strain at 1 month after 1 dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2	SARS-CoV-2 reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of 1 dose of BNT162b2$_{SA}$) of past SARS-CoV-2 infection
To descriptively compare the anti-SA immune response after 1 dose of BNT162b2$_{SA}$ and a third dose of BNT162b2 at 30 µg	GMR of SA NT 1 month after 1 dose of BNT162b2$_{SA}$ to 1 month after the third dose of BNT162b2 at 30 µg The difference in percentages of participants with seroresponse to the SA strain at 1 month after 1 dose of BNT162b2$_{SA}$ and 1 month after the third dose of BNT162b2 at 30 µg	SARS-CoV-2 SA NT in participants with no serological or virological evidence (up to 1 month after receipt of 1 dose of BNT162b2$_{SA}$ or the third dose of BNT162b2 at 30 µg) of past SARS-CoV-2 infection
To descriptively compare the anti-SA immune response after 2 doses of BNT162b2$_{SA}$ and the anti–reference strain immune response after 2 doses of BNT162b2, in the same individuals	GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2	SARS-CoV-2 SA and reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$) of past SARS-CoV-2 infection
BNT162b2-naïve participants		
To demonstrate a statistically greater anti-SA immune response after 2 doses of BNT162b2$_{SA}$ compared to after 2 doses of BNT162b2	GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2	SARS-CoV-2 SA NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$ or BNT162b2 as appropriate) of past SARS-CoV-2 infection
To descriptively compare the anti–reference strain immune response after 2 doses of BNT162b2$_{SA}$ and after 2 doses of BNT162b2	GMR of reference strain NT 1 month after the second dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 The difference in percentages of participants with seroresponse to the reference strain at 1 month after the second dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2	SARS-CoV-2 reference strain NTs in participants with no serological or virological evidence (up to 1 month after receipt of the second dose of BNT162b2$_{SA}$ or BNT162b2 as appropriate) of past SARS-CoV-2 infection

Table 3. List of Primary, Secondary, and Tertiary/Exploratory Objectives, Estimands, and Endpoints for Phase 2/3

Objectives[a]	Estimands	Endpoints
Exploratory		
To describe the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 7 days after the second dose through the blinded follow-up period in participants without, and with and without, evidence of infection before vaccination	In participants complying with the key protocol criteria (evaluable participants) after receipt of the second dose of study intervention: 100 × (1 – IRR) [ratio of active vaccine to placebo]	• COVID-19 incidence per 1000 person-years of blinded follow-up based on central laboratory or locally confirmed NAAT
To describe the incidence of confirmed COVID-19 through the entire study follow-up period prior to receiving the third dose of BNT162b2 in participants who received BNT162b2 at initial randomization or subsequently	In participants who received BNT162b2 (at initial randomization or subsequently): Incidence per 1000 person-years of follow-up	• COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT
To describe the incidence of confirmed COVID-19 after receiving the third dose of BNT162b2	In participants who received the third dose of BNT162b2: Incidence per 1000 person-years of follow-up	• COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT
To evaluate the immune response over time to prophylactic BNT162b2 and persistence of immune response in participants with and without serological or virological evidence of SARS-CoV-2 infection before vaccination	GMC/GMT and GMFR at baseline and 1, 6, 12, and 24 months after completion of vaccination	• Full-length S-binding or S1-binding IgG levels • SARS-CoV-2 neutralizing titers
To describe the incidence of non-S seroconversion to SARS-CoV-2 through the entire study follow-up period in participants who received BNT162b2 at initial randomization	In participants who received BNT162b2 at initial randomization: Incidence per 1000 person-years of follow-up	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on N-binding antibody seroconversion in participants with no serological or virological evidence of past SARS-CoV-2 infection or confirmed COVID-19
To describe the efficacy of prophylactic BNT162b2 against asymptomatic SARS-CoV-2 infection in participants with evidence of infection up to the start of the asymptomatic surveillance period	In participants complying with the key protocol criteria (evaluable participants): 100 × (1 – IRR) [ratio of active vaccine to placebo]	Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on central laboratory–confirmed NAAT in participants with serological or virological evidence (up to the start of the asymptomatic surveillance period) of past SARS-CoV-2 infection
To describe the serological responses to the BNT vaccine candidate and characterize the SARS-CoV-2 isolate in cases of: • Confirmed COVID-19 • Confirmed severe COVID-19 • SARS-CoV-2 infection without confirmed COVID-19		• Full-length S-binding or S1-binding IgG levels • SARS-CoV-2 neutralizing titers • Identification of SARS-CoV-2 variant(s)

Table 3. List of Primary, Secondary, and Tertiary/Exploratory Objectives, Estimands, and Endpoints for Phase 2/3

Objectives[a]	Estimands	Endpoints
To describe the safety, immunogenicity, and efficacy of prophylactic BNT162b2 in individuals with confirmed stable HIV disease		• All safety, immunogenicity, and efficacy endpoints described above
To describe the safety and immunogenicity of prophylactic BNT162b2 in individuals 16 to 55 years of age vaccinated with study intervention produced by manufacturing "Process 1" or "Process 2"[b]		• AEs • SAEs • SARS-CoV-2 neutralizing titers
To describe the immune response to any VOCs not already specified	Geometric mean NT for any VOCs not already specified, after any dose of BNT162b2$_{SA}$ or BNT162b2	• SARS-CoV-2 NTs for any VOCs not already specified
To describe the immune response to a third dose of BNT162b2 (at 30 µg or a lower dose of 5 or 10 µg) or a third or fourth dose of BNT162b2$_{SA}$	GMTs at Dose 3 and subsequent time points GMFRs from Dose 3 to subsequent time points	• SARS-CoV-2 reference strain NTs
To describe the cell-mediated immune response, and additional humoral immune response parameters, to the reference strain and SA in a subset of participants: • 7 Days and 1 and 6 months after BNT162b2$_{SA}$ given as 1 or 2 doses to BNT162b2-experienced participants • 7 Days and 1 and 6 months after BNT162b2$_{SA}$ given as 2 doses to BNT162b2-naïve participants • 7 Days and 1 and 6 months after BNT162b2 given as a third dose to BNT162b2-experienced participants		

a. HIV-positive participants in Phase 3 will not be included in analyses of the objectives, with the exception of the specific exploratory objective.
b. See the protocol, Section 6.1.1, for description of the manufacturing process.

2.2. Study Design

2.2.1. Overall Design

This is a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate–selection, and efficacy study in healthy individuals.

The study consists of 2 parts. Phase 1: to identify preferred vaccine candidate(s) and dose level(s); Phase 2/3: an expanded cohort and efficacy part. These parts, and the progression between them, are detailed in the schema (see protocol, Section 1.2).

The study will evaluate the safety, tolerability, and immunogenicity of 2 different SARS-CoV-2 RNA vaccine candidates against COVID-19 and the efficacy of 1 candidate:

- As a 2-dose (separated by 21 days) schedule;
- At various different dose levels in Phase 1;
- As a booster;
- In 3 age groups (Phase 1: 18 to 55 years of age, 65 to 85 years of age; Phase 2/3: ≥12 years of age [stratified as 12-15, 16-55, or >55 years of age]).

Dependent upon safety and/or immunogenicity data generated during the course of this study, or the BioNTech study conducted in Germany (BNT162-01), it is possible that groups in Phase 1 may be started at the next highest dose, groups may not be started, groups may be terminated early, and/or groups may be added with dose levels below the lowest stated dose or intermediate between the lowest and highest stated doses.

The study is observer-blinded, as the physical appearance of the investigational vaccine candidates and the placebo may differ. The participant, investigator, study coordinator, and other site staff will be blinded. At the study site, only the dispenser(s)/administrator(s) are unblinded.

To facilitate rapid review of data in real time, sponsor staff will be unblinded to vaccine allocation for the participants in Phase 1.

In order to describe the boostability of BNT162, an additional dose of BNT162b2 at 30 µg will be given to Phase 1 participants approximately 6 to 12 months after their second dose of BNT162b1 or BNT162b2. This will provide an early assessment of the safety of a third dose of BNT162, as well as its immunogenicity. The assessment of boostability will be further expanded in a subset of Phase 3 participants at selected sites in the US who will receive a third dose of BNT162b2 at 30 µg or a third and potentially a fourth dose of prototype $BNT162b2_{VOC}$ at 30 µg (based upon the South African variant and hereafter referred to as $BNT162b2_{SA}$). A further subset of Phase 3 participants will receive a third, lower, dose of BNT162b2 at 5 or 10 µg.

To further describe potential homologous and heterologous protection against emerging SARS-CoV-2 VOCs, a new cohort of participants will be enrolled who are COVID-19 vaccine–naïve (ie, BNT162b2-naïve) and have not experienced COVID-19. They will receive $BNT162b2_{SA}$ given as a 2-dose series, separated by 21 days.

2.2.2. Phase 1

Each group (vaccine candidate/dose level/age group) will comprise 15 participants; 12 participants will be randomized to receive active vaccine and 3 to receive placebo.

For each vaccine candidate/dose level/age group, the following apply:

- Additional safety assessments (see protocol, Section 8.2).
- Controlled enrollment (required only for the first candidate and/or dose level studied):
  - No more than 5 participants (4 active, 1 placebo) can be vaccinated on the first day.
  - The first 5 participants must be observed by blinded site staff for at least 4 hours after vaccination for any acute reactions.
  - Vaccination of the remaining participants will commence no sooner than 24 hours after the fifth participant received his or her vaccination.
- Application of stopping rules.
- IRC review of safety data to determine escalation to the next dose level in the 18- to 55-year age cohort:
  - Escalation between dose levels will be based on IRC review of at least 7-day post–Dose 1 safety data in this study and/or the BioNTech study conducted in Germany (BNT162-01).
  - Note that, since both candidates are based upon the same RNA platform, dose escalation for the second candidate studied may be based upon the safety profile of the first candidate studied being deemed acceptable at the same, or a higher, dose level by the IRC.

Groups of participants 65 to 85 years of age will not be started until safety data for the RNA platform have been deemed acceptable at the same, or a higher, dose level in the 18- to 55-year age cohort by the IRC.

In this phase, 13 groups will be studied, corresponding to a total of 195 participants.

The IRC will select 1 vaccine candidate that, in Phase 1, has an established dose level per age group based on induction of a post–Dose 2 immune response, including neutralizing antibodies, which is expected to be associated with protection against COVID-19, for progression into Phase 2/3.

Participants who originally received placebo and become eligible for receipt of BNT162b2 or another COVID-19 vaccine according to recommendations detailed separately, and available in the electronic study reference portal, will have the opportunity to receive BNT162b2 in a phased manner as part of the study. The investigator will ensure the participant meets at least 1 of the recommendation criteria.

Any Phase 1 placebo recipient who has not already been offered the opportunity to receive BNT162b2 will be given this opportunity no later than at the approximate time participants in Phase 2/3 reach Visit 4.

Any participant who originally received placebo but then goes on to receive BNT162b2 will move to a new visit schedule (protocol, Section 1.3.3).

In order to describe the boostability of BNT162, and potential heterologous protection against emerging SARS-CoV-2 VOCs, an additional dose of BNT162b2 at 30 µg will be given to Phase 1 participants approximately 6 to 12 months after their second dose of BNT162b1 or BNT162b2.

Phase 1 participants who originally received BNT162b1 or BNT162b2 at dose levels of 10, 20, or 30 µg at Doses 1 and 2 will be offered an additional dose of BNT162b2 at 30 µg approximately 6 to 12 months after their second dose of BNT162.

Participants are expected to participate for up to a maximum of approximately 26 months.

2.2.3. Phase 2/3

On the basis of safety and/or immunogenicity data generated during the course of this study, and/or the BioNTech study conducted in Germany (BNT162-01), 1 vaccine candidate was selected to proceed into Phase 2/3. Participants in this phase will be ≥12 years of age, stratified as follows: 12 to 15 years, 16 to 55 years, or >55 years. The 12- to 15-year stratum will comprise up to approximately 2000 participants enrolled at selected investigational sites. It is intended that a minimum of 40% of participants will be in the >55-year stratum. Commencement of each age stratum will be based upon satisfactory post–Dose 2 safety and immunogenicity data from the 18- to 55-year and 65- to 85-year age groups in Phase 1, respectively. The vaccine candidate selected for Phase 2/3 evaluation is BNT162b2 at a dose of 30 µg.

Phase 2/3 is event-driven. Under the assumption of a true VE rate of ≥60%, after the second dose of study intervention, a target of 164 primary-endpoint cases of confirmed COVID-19 due to SARS-CoV-2 occurring at least 7 days following the second dose of the primary series of the candidate vaccine will be sufficient to provide 90% power to conclude true VE >30% with high probability. The total number of participants enrolled in Phase 2/3 may vary depending on the incidence of COVID-19 at the time of the enrollment, the true underlying VE, and a potential early stop for efficacy or futility.

Assuming a COVID-19 attack rate of 1.3% per year in the placebo group, accrual of 164 first primary-endpoint cases within 6 months, an estimated 20% nonevaluable rate, and 1:1 randomization, the BNT162b2 vaccine candidate selected for Phase 2/3 is expected to comprise approximately 21,999 vaccine recipients. This is the number of participants initially targeted for Phase 2/3 and may be adjusted based on advice from DMC analyses of case accumulation and the percentage of participants who are seropositive at baseline. Dependent upon the evolution of the pandemic, it is possible that the COVID-19 attack rate may be much higher, in which case accrual would be expected to be more rapid, enabling the study's primary endpoint to be evaluated much sooner.

The first 360 participants enrolled (180 to active vaccine and 180 to placebo, stratified equally between 18 to 55 years and >55 to 85 years) will comprise the "Phase 2" portion. Safety data through 7 days after Dose 2 and immunogenicity data through 1 month after Dose 2 from these 360 participants will be analyzed by the unblinded statistical team, reviewed by the DMC, and submitted to appropriate regulatory authorities for review. Enrollment may continue during this period and these participants would be included in the efficacy evaluation in the "Phase 3" portion of the study.

In Phase 3, up to approximately 2000 participants, enrolled at selected sites, are anticipated to be 12 to 15 years of age. Noninferiority of immune response to prophylactic BNT162b2 in participants 12 to 15 years of age to response in participants 16 to 25 years of age will be assessed based on the GMR of SARS-CoV-2 neutralizing titers using a 1.5-fold margin. A sample size of 225 evaluable participants (or 280 vaccine recipients) per age group will provide a power of 90.4% to declare the noninferiority in terms of GMR (lower limit of 95% CI for GMR >0.67). A random sample of 280 participants from each of the 2 age groups (12 to 15 years and 16 to 25 years) will be selected as an immunogenicity subset for the noninferiority assessment.

The initial BNT162b2 was manufactured using "Process 1"; however, "Process 2" was developed to support an increased scale of manufacture. In the study, each lot of "Process 2"-manufactured BNT162b2 will be administered to approximately 250 participants 16 to 55 years of age. The safety and immunogenicity of prophylactic BNT162b2 in individuals 16 to 55 years of age vaccinated with "Process 1" and each lot of "Process 2" study intervention will be described. A random sample of 250 participants from those vaccinated with study intervention produced by manufacturing "Process 1" will be selected for this descriptive analysis.

For evaluation of boostability and protection against emerging VOCs, 600 existing Phase 3 participants 18 to 55 years of age will be rerandomized in a 1:1 ratio to receive either a third dose of BNT162b2 at 30 µg or a third dose of BNT162b2$_{SA}$.

A further group of approximately 144 existing Phase 3 participants 18 years of age and older will be enrolled to receive a third, lower, dose of BNT162b2 of either 5 or 10 µg.

Approximately 24 participants 18 to 55 years of age and 48 participants >55 years of age will be enrolled in each dose group.

An additional group of 30 existing Phase 3 participants 18 to 55 years of age will be enrolled to receive a third and fourth dose of BNT162b2$_{SA}$. For these 30 participants, through 1 month after their first dose of BNT162b2$_{SA}$ the participants will be blinded to their vaccine allocation, but the investigator and sponsor will not be. Serum samples from these participants may be used for assay development purposes and, except for objectives relating to response to a fourth dose, their results will be analyzed separately from the main immunogenicity analyses.

Three hundred participants 18 to 55 years of age who are COVID-19 vaccine–naïve (ie, BNT162b2-naïve) and have not experienced COVID-19 will be enrolled as a new cohort of participants to receive BNT162b2$_{SA}$ given as a 2-dose series.

Participants are expected to participate for up to a maximum of approximately 26 months. The duration of study follow-up may be shorter among participants enrolled in Phase 1 dosing arms that are not evaluated in Phase 2/3.

Participants who originally received placebo and become eligible for receipt of BNT162b2 according to recommendations detailed separately, and available in the electronic study reference portal, will have the opportunity to receive BNT162b2 in a phased manner as part of the study. The investigator will ensure the participant meets at least 1 of the recommendation criteria.

Any Phase 2/3 placebo recipient who has not already been offered the opportunity to receive BNT162b2 will be given this opportunity no later than 6 months after Vaccination 2 (at the time of the originally planned Visit 4).

Any participant who originally received placebo but then goes on to receive BNT162b2 will move to a new visit schedule (protocol, Section 1.3.3).

The changes to the protocol as part of protocol amendment 14 to assess boostability and homologous/heterologous protection against emerging VOCs allow the evaluation of safety and immunogenicity of BNT162b2$_{SA}$:

- When given as a third dose to C4591001 Phase 3 participants who received a second dose of BNT162b2 approximately 6 months previously (ie, BNT162b2-experienced) and have not experienced COVID-19.

- In a small separate group of individuals who previously received 2 doses of BNT162b2 followed by 1 dose of BNT162b2$_{SA}$, a second BNT162b2$_{SA}$ dose will also be given 1 month after Dose 1 of BNT162b2$_{SA}$.

- When given as a 2-dose series, separated by 21 days, in newly recruited participants who are COVID-19 vaccine–naïve (ie, BNT162b2-naïve) and have not experienced COVID-19.

In addition, a group of C4591001 Phase 3 participants who received a second dose of BNT162b2 approximately 6 months previously will receive a third dose of BNT162b2.

This approach will allow an evaluation of immunogenicity against the reference ancestral SARS-CoV-2 strain (Wuhan-Hu-1/USA-WA1) and the selected South African VOC, using a noninferiority approach based on neutralizing antibody titers in prior BNT162b2 vaccinees who receive either a homologous boost (with BNT162b2) or a heterologous boost (with BNT162b2$_{SA}$), as well as new vaccinees receiving 2 doses of BNT162b2$_{SA}$.

As part of protocol amendment 18, to reflect current and anticipated recommendations for COVID-19 vaccine boosters, participants in Study C4591001 who meet specified recommendations (detailed separately and available in the electronic study portal) and have not already received one will be offered a third dose of BNT162b2 after their second dose of BNT162. The opportunity to receive a third dose of BNT162b2 will be offered as part of the study, according to recommendations detailed separately, and available in the electronic study reference portal. This opportunity is only for those participants who received their first 2 doses of BNT162 (including BNT162b1, BNT162b2, or BNT162b2$_{SA}$) as part of the study.

An intensive period of surveillance to evaluate the efficacy of BNT162b2 against asymptomatic SARS-CoV-2 infection may be conducted at selected sites among Phase 2/3 participants following approval of protocol amendment 11. After an initial in-person visit where a blood sample will be collected and a nasal (midturbinate) swab obtained, nasal (midturbinate) swabs will be obtained from consented participants every 2 weeks until Visit 4, or a sufficient number of cases of SARS-CoV-2 infection have accrued to evaluate this objective, whichever is sooner, per the SoA in the protocol, Section 1.3.6. The swabs will be tested at a central laboratory using NAAT to detect SARS-CoV-2. Participants who are unblinded because they become potentially eligible for receipt of BNT162b2 according to recommendations detailed separately, and available in the electronic study reference portal, will not participate in surveillance for asymptomatic SARS-CoV-2 infection. However, participants who provided additional consent to conduct biweekly swabbing for surveillance of asymptomatic infection should continue to swab even after unblinding if they originally received BNT162b2.

Surveillance for asymptomatic SARS-CoV-2 infection (swabbing) should cease in participants enrolled into the subset of participants who will receive an additional dose of BNT162b2 or BNT162b2$_{SA}$.

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoints

3.1.1. Safety Endpoints

For all participants in Phase 1, a subset of at least 6000 participants randomized in Phase 2/3, receiving at least 1 dose of study intervention, BNT162b2-experienced participants receiving 1 or 2 doses of BNT162b2$_{SA}$, BNT162b2-naïve participants receiving 2 doses of BNT162b2$_{SA}$, and BNT162b2-experienced participants receiving the third dose of BNT162b2 in the subset for evaluation of boostability and protection against emerging VOCs in Phase 3, below are the primary safety endpoints for local reactions and systemic events:

- Local reactions (pain at the injection site, redness, and swelling) within 7 days after each dose in each vaccine group.
- Systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain) within 7 days after each dose in each vaccine group.

For all participants randomized in Phase 1 and Phase 2/3, receiving at least 1 dose of study intervention, below are the primary safety endpoints for AEs and SAEs (the last dose in Phase 1 is the second dose):

- AEs from Dose 1 to 1 month after the second dose.
- SAEs from Dose 1 to 6 months after the second dose.

In addition, for the first 360 participants randomized in Phase 2/3 (Phase 2 portion), receiving at least 1 dose of study intervention, below are the primary safety endpoints for AEs and SAEs:

- AEs from Dose 1 to 7 days after the second dose.
- SAEs from Dose 1 to 7 days after the second dose.

For BNT162b2-experienced participants receiving 1 or 2 doses of BNT162b2$_{SA}$, BNT162b2-naïve participants receiving 2 doses of BNT162b2$_{SA}$, and BNT162b2-experienced participants receiving the third dose of BNT162b2 in the subset for evaluation of boostability and protection against emerging VOCs in Phase 3, below are the primary safety endpoints for AEs and SAEs:

- AEs from Dose 1 to 1 month after the last dose.
- SAEs from Dose 1 to 5 or 6 months after the last dose.

For the participants receiving BNT162b2 as a third dose at least 6 months after the second dose of BNT162b2 (or BNT162b2$_{SA}$) as part of protocol amendment 18, below are the primary safety endpoints for AEs and SAEs:

- AEs from Dose 3 to 1 month after Dose 3.
- SAEs from Dose 3 to 6 months after Dose 3.

3.1.1.1. Local Reactions

The local reactions assessed and reported in the e-diary are redness, swelling, and pain at the injection site, from Day 1 through Day 7 after each dose, where Day 1 is the day of each dose. This section describes derivations with details for the assessment of local reactions: presence, severity level, duration, and onset day.

Presence or Absence

For the data summary of the presence (yes or no) of a local reaction during the interval from Day 1 through Day 7 for each dose, where Day 1 is the day of each dose, the following variables are required in order to compute the proportions:

- Presence (yes or no) of each severe/Grade 4 local reaction on each day and any day (Day 1 through Day 7);
- Presence (yes or no) of each local reaction by maximum severity on any day (Day 1 through Day 7).

For each local reaction and any local reaction on any day, Table 4 explains the algorithm to derive the presence of a reaction (yes or no) during the interval from Day 1 through Day 7, where Day 1 is the day of each dose.

Table 4. Derived Variables for Presence of Each and Any Local Reaction Within 7 Days for Each Dose

Variable[a]	Yes (1)	No (0)	Missing (.)
Presence of each local reaction.	Participant reports the reaction as "yes" on any day (Day 1 through Day 7).	Participant reports the reaction as "no" on all 7 days (Day 1 through Day 7) or as a combination of "no" and missing on all 7 days (Day 1 through Day 7).	Participant does not report any data on all 7 days (Day 1 through Day 7) for the reaction.
Presence of any local reaction.	Participant reports any local reaction as "yes" on any day (Day 1 through Day 7).	For all 3 local reactions, participant reports "no" on all 7 days (Day 1 through Day 7) or as a combination of "no" and missing on all 7 days (Day 1 through Day 7).	Participant does not report any data for all 3 local reactions on all 7 days (Day 1 through Day 7).

a. The variables will be derived for each and any of the local reactions (redness, swelling, and pain at the injection site) and for each and any of the severe local reactions within the interval from Day 1 through Day 7 after each dose.

Severity and Maximum Severity

Redness and swelling will be measured and recorded in measuring device units (range: 1 to 21) and then categorized during analysis as absent, mild, moderate, or severe based on the grading scale in Table 5. Measuring device units can be converted to centimeters according to the following formula: 1 measuring device unit = 0.5 cm. Pain at the injection site will be assessed by the participant as absent, mild, moderate, or severe according the grading scale in Table 5.

Table 5. Local Reaction Grading Scale

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Pain at the injection site	Does not interfere with activity.	Interferes with activity.	Prevents daily activity.	Emergency room visit or hospitalization for severe pain.

Table 5. Local Reaction Grading Scale

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Redness	>2.0 cm to 5.0 cm (5 to 10 measuring device units).	>5.0 cm to 10.0 cm (11 to 20 measuring device units).	>10 cm (≥21 measuring device units).	Necrosis or exfoliative dermatitis.
Swelling	>2.0 cm to 5.0 cm (5 to 10 measuring device units).	>5.0 cm to 10.0 cm (11 to 20 measuring device units).	>10 cm (≥21 measuring device units).	Necrosis.

For each local reaction reported for each dose, the maximum severity grade will be derived for the e-diary collection period (Day 1 through Day 7, where Day 1 is the day of each dose) as follows:

> maximum severity grade = highest grade (maximum severity) within 7 days after vaccination (Day 1 through Day 7) among severity grades where the answers are neither "no" nor missing for at least 1 day during the interval from Day 1 through Day 7.

Duration (First to Last Day Reported)

For participants experiencing any local reactions (or those with a derived reaction as described in Table 5), the maximum duration (last day of reaction – first day of reaction + 1) will be derived for each study vaccination. Resolution of the reaction is the last day on which the reaction is recorded in the e-diary or the date the reaction ends if it is unresolved during the participant e-diary recording period (end date collected on the CRF), unless chronicity is established. If there is no known end date, the duration will be considered unknown and set to missing. However, if a reaction is ongoing at the time of a subsequent vaccination, the end date/day for the ongoing reaction would be the date/day that the next vaccine is administered, which will be used for the duration computation. Participants with no reported reaction have no duration.

Onset Day

The onset day of each local reaction will be derived. Onset day is defined as the first day of reporting any severity.

For the onset day of each local reaction, if participants report change in severity of the local reaction, only the first day of reporting that specific local reaction will be counted.

3.1.1.2. Systemic Events (Systemic Event Symptoms and Fever)

The systemic events assessed and recorded in the e-diary are vomiting, diarrhea, headache, fatigue, chills, new or worsened muscle pain, and new or worsened joint pain from Day 1 through Day 7, where Day 1 is the day of each dose. The derivations for systemic events will

be handled in a way similar to the way local reactions are handled for presence of event, severity level, duration, and onset day.

The variables associated with the systemic events will be computed in a way similar to the way local reactions are computed (see Section 3.1.1.1). Maximum temperature range over the period from Day 1 through Day 7 will be mapped into the ranges described in Table 7 for summary of maximum temperature.

The symptoms will be assessed by the participant as absent, mild, moderate, or severe according to the grading scale in Table 6.

Table 6. Systemic Event Grading Scale

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Vomiting	1-2 times in 24 hours.	>2 times in 24 hours.	Requires IV hydration.	Emergency room visit or hospitalization for hypotensive shock.
Diarrhea	2 to 3 loose stools in 24 hours.	4 to 5 loose stools in 24 hours.	6 or more loose stools in 24 hours.	Emergency room visit or hospitalization for severe diarrhea.
Headache	Does not interfere with activity.	Some interference with activity.	Prevents daily routine activity.	Emergency room visit or hospitalization for severe headache.
Fatigue	Does not interfere with activity.	Some interference with activity.	Prevents daily routine activity.	Emergency room visit or hospitalization for severe fatigue.
Chills	Does not interfere with activity.	Some interference with activity.	Prevents daily routine activity.	Emergency room visit or hospitalization for severe chills.
New or worsened muscle pain	Does not interfere with activity.	Some interference with activity.	Prevents daily routine activity.	Emergency room visit or hospitalization for severe new or worsened muscle pain.
New or worsened joint pain	Does not interfere with activity.	Some interference with activity.	Prevents daily routine activity.	Emergency room visit or hospitalization for severe new or worsened joint pain.

Abbreviation: IV = intravenous.

Oral temperature will be collected in the evening, daily, for 7 days following each dose (Days 1 through 7, where Day 1 is the day of each dose) and at any time during the 7 days that fever is suspected. Fever is defined as an oral temperature of ≥38.0°C (100.4°F). The highest temperature for each day will be recorded in the e-diary.

Temperature will be measured and recorded to 1 decimal place. Temperatures recorded in degrees Fahrenheit will be programmatically converted to degrees Celsius for reporting. Temperatures <35.0°C and >42.0°C will be excluded from the analysis. Fever will be grouped into ranges for the analysis according to Table 7 below.

Table 7. Scale for Fever

≥38.0°C to 38.4°C (100.4°F to 101.1°F)
>38.4°C to 38.9°C (101.2°F to 102.0°F)
>38.9°C to 40.0°C (102.1°F to 104.0°F)
>40.0°C (>104.0°F)

Note: Fever is defined as temperature ≥38.0°C (≥100.4°F).

3.1.1.3. Use of Antipyretic Medication

The use of antipyretic medication is also recorded in the e-diary from Day 1 through Day 7, where Day 1 is the day of each dose. For the use of antipyretic medication from Day 1 through Day 7 after each dose, the following endpoints and variables will be derived for analysis following the same rules as for local reactions (see Section 3.1.1.1), where applicable.

- Presence (yes or no) of use of antipyretic medication on each day (Day 1 through Day 7);
- Presence (yes or no) of use of antipyretic medication on any day (Day 1 through Day 7);
- Duration (first to last day reported) of use of antipyretic medication;
- Onset day of use of antipyretic medication.

The use of antipyretic medication will be summarized and included in the systemic event summary tables but will not be considered a systemic event.

3.1.1.4. Adverse Events

AEs will be assessed from the time of informed consent through 1 month after the second dose or 1 month after the last dose for the subset for evaluation of boostability and protection against emerging VOCs.

The primary endpoints "AEs from Dose 1 to 1 month after the second dose" and "AEs from Dose 1 to 1 month after the last dose," for evaluation of boostability and protection against emerging VOCs, and other AE endpoints will be summarized by SOC and PT at the participant level. For the subset for evaluation of boostability and protection against emerging VOCs, Dose 1 refers to the first dose of BNT162b2$_{SA}$ or first dose of BNT162b2 booster.

These primary endpoints will be supported by summaries and listings of related AEs, severe AEs, and immediate AEs (within the first 30 minutes after each dose).

AE reporting will be based on the specific reporting period. Standard algorithms for handling missing AE dates will be applied as described in the Pfizer Vaccine data standard rules.

For Phase 2/3 only, a 3-tier approach will be used to summarize AEs. Under this approach, AEs are classified into 1 of 3 tiers. Different analyses will be performed for different tiers:

- Tier 1 events: These are prespecified events of clinical importance and are identified in a list in the product's Safety Review Plan.
- Tier 2 events: These are events that are not Tier 1 but are considered "relatively common." A MedDRA PT is defined as a Tier 2 event if there are at least 1% participants with the AE term in at least 1 vaccine group.
- Tier 3 events: These are events that are neither Tier 1 nor Tier 2.

3.1.1.5. Serious Adverse Events

SAEs will be collected from the time the participant provides informed consent to approximately 6 months after the second dose of study intervention (Visit 8 for Phase 1 participants and Visit 4 for Phase 2/3 participants).

For BNT162b2-experienced participants in the subset for evaluation of boostability and protection against emerging VOCs, SAEs will be collected from the time the participant provides informed consent (for participation in the subset) through and including Visit 306 (5 or 6 months after the last dose, depending upon group).

For BNT162b2-naïve participants in the subset for evaluation of protection against emerging VOCs, SAEs will be collected from the time the participant provides informed consent through and including Visit 405 (6 months after the second dose).

The safety endpoints "SAEs from Dose 1 to 6 months after the second dose" and "SAEs from Dose 1 to 5 or 6 months after the last dose" for evaluation of boostability and protection against emerging VOCs will be summarized by SOC and PT at the participant level. For the subset for evaluation of boostability and protection against emerging VOCs, Dose 1 refers to the first dose of BNT162b2$_{SA}$ or first dose of BNT162b2 booster.

3.1.1.6. Hematology and Chemistry Laboratory Parameters (for Phase 1 Only)

For participants in Phase 1, below are the additional primary safety endpoints:

- Abnormal hematology and chemistry laboratory values 1 and 7 days after Dose 1; and 7 days after Dose 2.
- Grading shifts in hematology and chemistry laboratory assessments between baseline and 1 and 7 days after Dose 1; and before Dose 2 and 7 days after Dose 2.

The following safety laboratory tests will be performed at the times defined in the protocol, Section 1.3 (Schedule of Activities). Additional laboratory results may be reported on these samples as a result of the method of analysis or the type of analyzer used by the clinical laboratory, or as derived from calculated values. These additional tests would not require

additional collection of blood. Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety issues.

Hematology	Chemistry
Hemoglobin Hematocrit RBC count MCV MCH MCHC Platelet count WBC count Total neutrophils (Abs) Eosinophils (Abs) Monocytes (Abs) Basophils (Abs) Lymphocytes (Abs)	BUN and creatinine AST, ALT Total bilirubin Alkaline phosphatase

Clinically significant abnormal laboratory findings should be recorded in the AE CRF in accordance with the following grading scale (Table 8). Additionally, the primary criterion for abnormality will follow the Pfizer safety rule book.

Table 8. Laboratory Abnormality Grading Scale

Hematology	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Hemoglobin (Female) - g/dL	11.0 – 12.0	9.5 – 10.9	8.0 – 9.4	<8.0
Hemoglobin (Male) - g/dL	12.5 – 13.5	10.5 – 12.4	8.5 – 10.4	<8.5
WBC increase - cells/mm^3	10,800 – 15,000	15,001 – 20,000	20,001 – 25,000	>25,000
WBC decrease - cells/mm^3	2500 – 3500	1500 – 2499	1000 – 1499	<1000
Lymphocytes decrease - cells/mm^3	750 – 1000	500 – 749	250 – 499	<250
Neutrophils decrease - cells/mm^3	1500 – 2000	1000 – 1499	500 – 999	<500
Eosinophils - cells/mm^3	650 – 1500	1501 – 5000	>5000	Hypereosinophilic
Platelets decreased - cells/mm^3	125,000 – 140,000	100,000 – 124,000	25,000 – 99,000	<25,000
Chemistry	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**	**Potentially Life Threatening (Grade 4)**
BUN - mg/dL	23 – 26	27 – 31	>31	Requires dialysis
Creatinine - mg/dL	1.5 – 1.7	1.8 – 2.0	2.1 – 2.5	>2.5 or requires dialysis
Alkaline phosphate - increase by factor	1.1 – 2.0 × ULN	2.1 – 3.0 × ULN	3.1 – 10 × ULN	>10 × ULN

Table 8. Laboratory Abnormality Grading Scale

Liver function tests - ALT, AST increase by factor	1.1 – 2.5 × ULN	2.6 – 5.0 × ULN	5.1 – 10 × ULN	>10 × ULN
Bilirubin - when accompanied by any increase in liver function test - increase by factor	1.1 – 1.25 × ULN	1.26 – 1.5 × ULN	1.51 – 1.75 × ULN	>1.75 × ULN
Bilirubin - when liver function test is normal - increase by factor	1.1 – 1.5 × ULN	1.6 – 2.0 × ULN	2.0 – 3.0 × ULN	>3.0 × ULN

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; ULN = upper limit of normal; WBC = white blood cell.

3.1.2. Immunogenicity Endpoints (for the Phase 2/3 Subset for Evaluation of Boostability and Protection Against Emerging VOCs Only)

- SARS-CoV-2 reference strain NTs.
- SARS-CoV-2 SA NTs.

In order to allow direct comparability with the reference strain, the anti-SA NTs may be adjusted to account for intrinsic variant or assay characteristics.

Titers (and IgG concentrations, secondary and exploratory endpoints) above the LLOQ are considered accurate and their quantitated values will be reported. Values below the LLOQ, denoted as BLQ, will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. LLOQ results will be included in the analysis specification once they are available.

3.1.3. Vaccine Efficacy Endpoints (for Phase 2/3 Only)

- COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants with no serological or virological evidence (prior to 7 days after receipt of the second dose) of past SARS-CoV-2 infection (counting cases from 7 days after the second dose).
- COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT (counting cases from 7 days after the second dose).

3.2. Secondary Endpoints

3.2.1. Immunogenicity Endpoints

Phase 1

In participants complying with the key protocol criteria (evaluable participants) at the following time points after receipt of study intervention:

- 7 and 21 days after Dose 1; 7 and 14 days and 1, 6, 12, and 24 months after Dose 2.

Below are the secondary immunogenicity endpoints for Phase 1:

- SARS-CoV-2 neutralizing titers.
- S1-binding IgG levels.
- RBD-binding IgG levels.

Phase 2/3

Participants 12 to 15 years of age and 16 to 25 years of age:

- SARS-CoV-2 neutralizing titers.

Participants in the subset for evaluation of boostability and protection against emerging VOCs:

- SARS-CoV-2 reference strain NTs.
- SARS-CoV-2 SA NTs.

In order to allow direct comparability with the reference strain, the anti-SA NTs may be adjusted to account for intrinsic variant or assay characteristics.

3.2.2. Vaccine Efficacy Endpoints (for Phase 2/3 Only)

- COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants with no serological or virological evidence (prior to 14 days after receipt of the second dose) of past SARS-CoV-2 infection (counting cases from 14 days after the second dose).
- COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT (counting cases from 14 days after the second dose).
- Confirmed severe COVID-19 incidence per 1000 person-years of follow-up in participants with no serological or virological evidence (prior to 7 days and prior to 14 days after receipt of the second dose) of past SARS-CoV-2 infection (counting cases from 7 days and 14 days after the second dose).

- Confirmed severe COVID-19 incidence per 1000 person-years of follow-up (counting cases from 7 days and 14 days after the second dose).

- According to the CDC-defined symptoms, COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants with no serological or virological evidence (prior to 7 days and prior to 14 days after receipt of the second dose) of past SARS-CoV-2 infection (counting cases from 7 days and 14 days after the second dose).

- According to the CDC-defined symptoms, COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT (counting cases from 7 days and 14 days after the second dose).

- Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on N-binding antibody seroconversion in participants with no serological or virological evidence of past SARS-CoV-2 infection or confirmed COVID-19.

- Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on central laboratory–confirmed NAAT in participants with no serological or virological evidence (up to the start of the asymptomatic surveillance period) of past SARS-CoV-2 infection.

3.3. Exploratory Endpoints

3.3.1. Safety Endpoints (for Phase 1 Boostability Assessment Only)

- Local reactions (pain at the injection site, redness, and swelling) for up to 7 days after Dose 3.

- Systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain) for up to 7 days after Dose 3.

- AEs from Dose 3 to 1 month after Dose 3.

- SAEs from Dose 3 to 1 month after Dose 3.

3.3.2. Vaccine Efficacy Endpoints (for Phase 2/3 Only)

- COVID-19 incidence per 1000 person-years of blinded follow-up based on central laboratory or locally confirmed NAAT in participants without, and with and without, evidence of infection (counting cases from 7 days after the second dose).

- COVID-19 incidence per 1000 person-years of follow-up based on central laboratory or locally confirmed NAAT in participants who received BNT162b2 at initial randomization or subsequently (counting cases from 7 days after the second BNT162b2 vaccination).

- Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on N-binding antibody seroconversion in participants who received BNT162b2 and who have no serological or virological evidence of past SARS-CoV-2 infection or confirmed COVID-19.

- Incidence of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on central laboratory–confirmed NAAT in participants with serological or virological evidence (up to the start of the asymptomatic surveillance period) of past SARS-CoV-2 infection.

3.3.3. Immunogenicity Endpoints

In Phase 1 participants participating in boostability assessment at the following time points after receipt of a third dose of BNT162b2:

- At the time of Dose 3 and 7 days and 1 month after Dose 3.

Below are the exploratory immunogenicity endpoints for Phase 1:

- SARS-CoV-2 reference-strain neutralizing titers.

- SARS-CoV-2 SA-variant neutralizing titers.

- Full-length S-binding or S1-binding IgG levels.

In Phase 2/3 participants at the following time points after receipt of study intervention:

- Baseline and 1, 6, 12, and 24 months after completion of vaccination.

Below are the exploratory immunogenicity endpoints for Phase 2/3:

- SARS-CoV-2 neutralizing titers.

- Full-length S-binding or S1-binding IgG levels.

3.3.4. Additional Endpoints (for Phase 2/3 Only)

- All safety, immunogenicity, and efficacy endpoints described above will be summarized separately for participants with confirmed stable HIV.

- AEs, SAEs, and SARS-CoV-2 neutralizing titers will be summarized separately for participants 16 to 55 of age vaccinated with study intervention produced by manufacturing “Process 1” and each lot of “Process 2.” All participants who received “Process 2” vaccine and a random sample of 250 participants 16 to 55 years of age selected from those who received “Process 1” vaccine will be included for the side-by-side descriptive summary of “Process 1” and each lot of “Process 2.”

- Identification of SARS-CoV-2 variant(s).

- SARS-CoV-2 NTs for any VOCs not already specified.
- SARS-CoV-2 NTs for a third dose of BNT162b2 (at 30 µg or a lower dose of 5 or 10 µg) or a third or fourth dose of BNT162b2$_{SA}$.
- Cell-mediated immune response endpoints.

3.4. Baseline and Other Variables

Measurements or samples collected prior to Dose 1 are considered the baseline data for the assessments.

3.4.1. Demographics, Medical History, and Physical Examination

The demographic variables are age at Dose 1 (in years), sex (male or female), race (black/African American, American Indian or Alaskan native, Asian, Native Hawaiian or other Pacific Islander, white), and ethnicity (Hispanic/Latino, non-Hispanic/non-Latino, not reported). In cases where more than 1 category is selected for race, the participant would be counted under the category "multiracial" for analysis. For Phase 2/3, BMI will also be included in the demographic variables.

Age at the time of vaccination (in years) will be derived based on the participant's birthday. For example, if the vaccination day is 1 day before the participant's 19th birthday, the participant is considered to be 18 years old. For participants who were randomized but not vaccinated, the randomization date will be used in place of the date of vaccination at Dose 1 for the age calculation. If the randomization date is also missing, then the informed consent date will be used for the age calculation.

Medical history will be categorized according to MedDRA. Comorbidities that increase the risk for severe COVID-19 illness will be categorized based on medical history terms.

For Phase 1, a physical examination will be performed. It will evaluate any clinically significant abnormalities within the following body systems: general appearance; skin; head, eyes, ears, nose, and throat; heart; lungs; abdomen; musculoskeletal; extremities; neurological; and lymph nodes. Clinically significant abnormal results will be recorded in the CRF.

For Phase 2/3, If the clinical assessment indicates that a physical examination is necessary to comprehensively evaluate the participant, physical examination will be performed and recorded any findings in the source documents and, if clinically significant, it will be recorded on the medical history CRF.

3.4.2. E-Diary Completion

For all participants in Phase 1, a subset of at least 6000 in Phase 2/3, and participants in the subset for evaluation of boostability and protection against emerging VOCs, an e-diary will be considered transmitted if any data for local reactions, systemic events, or use of antipyretic medication are present for any day. If all data are missing for all items on the e-diary for all 7 days after vaccination, then the e-diary will be considered not transmitted.

An e-diary will be considered completed if all expected data for all 7 days are available (ie, not missing). Otherwise, the e-diary will be considered incomplete. For any given day, an e-diary will be considered complete if all expected data are available.

3.4.3. Prior/Concomitant Vaccines and Concomitant Medications

The following concomitant medications and vaccinations will be recorded in the CRF:

- All vaccinations received from 28 days prior to study enrollment until the 6-month follow-up visit (Visit 8 for Phase 1 participants, and Visit 4 for Phase 2/3 participants). In addition, for Phase 1 participants who go on to receive a third dose of BNT162, concomitant vaccinations will be collected from the time the participant provides informed consent (for receipt of Vaccination 3) through and including Visit 8c (1 month after the third dose). For BNT162-experienced participants in the subset for evaluation of boostability and protection against emerging VOCs, all vaccinations received will be recorded from 28 days prior to the time the participant provides informed consent (for participation in the subset) through and including Visit 306. For BNT162b2-naïve participants in the subset for evaluation of protection against emerging VOCs, all vaccinations received will be recorded from 28 days prior to study enrollment through and including Visit 405.

- Prohibited medications listed in the protocol, Section 6.5.1, will be recorded, to include start and stop dates, name of the medication, dose, unit, route, and frequency.

- In addition, for participants enrolled in Phase 1, all current medication at baseline will be recorded, to include start date, name of the medication, dose, unit, route, and frequency.

3.5. Safety Endpoints

Local reactions, systemic events, AEs, and SAEs have been described above in the primary safety endpoints.

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

Data for all participants will be assessed to determine if participants meet the criteria for inclusion in each analysis population prior to unblinding and releasing the database and classifications will be documented per SOPs.

Population	Description
Enrolled	All participants who have a signed ICD.
Randomized	All participants who are assigned a randomization number in the IWR system.

Population	Description
Dose 1 evaluable immunogenicity	For Phase 1 only, all eligible randomized participants who receive the vaccine to which they are randomly assigned at the first dose, have at least 1 valid and determinate immunogenicity result from the blood collection within an appropriate window after Dose 1 (same as visit window, ie, within 19-23 days after Dose 1), and have no other important protocol deviations as determined by the clinician.
Dose 2 evaluable immunogenicity	All eligible randomized participants who receive 2 doses of the vaccine to which they are randomly assigned, with Dose 2 received within the predefined window (within 19-42 days after Dose 1), have at least 1 valid and determinate immunogenicity result after Dose 2 from the blood collection within an appropriate window after Dose 2 (within 6-8 days after Dose 2 for Phase 1 and within 28-42 days after Dose 2 for Phase 2/3), and have no other important protocol deviations as determined by the clinician.
Dose 3 booster evaluable immunogenicity	All eligible randomized participants who receive 2 doses of BNT162b2 (or BNT162b1 for Phase 1) as initially randomized, with Dose 2 received within the predefined window (within 19-42 days after Dose 1), receive a third dose of BNT162b2 or $BNT162b2_{SA}$ as rerandomized (or receive a third dose of BNT162b2 for Phase 1), have at least 1 valid and determinate immunogenicity result after Dose 3 from a blood collection within an appropriate window (within 28-42 days after Dose 3), and have no other important protocol deviations as determined by the clinician.
Dose 4 booster evaluable immunogenicity	All eligible randomized participants who receive 2 doses of BNT162b2 as initially randomized, with Dose 2 received within the predefined window (within 19-42 days after Dose 1), receive 2 booster doses of $BNT162b2_{SA}$ as rerandomized, have at least 1 valid and determinate immunogenicity result after Dose 4 from a blood collection within an appropriate window (within 28-42 days after Dose 4), and have no other important protocol deviations as determined by the clinician.
Dose 1 all-available immunogenicity	For Phase 1 only: all randomized participants who receive at least 1 dose of the study intervention with at least 1 valid and determinate immunogenicity result after Dose 1 but before Dose 2.
Dose 2 all-available immunogenicity	All randomized participants who receive at least 1 dose of the study intervention with at least 1 valid and determinate immunogenicity result after Dose 2.

Population	Description
Dose 3 booster all-available immunogenicity	All randomized participants who receive 2 doses of BNT162b2 (or BNT162b1 for Phase 1) at initial randomization, receive a third dose of BNT162b2 or BNT162b2$_{SA}$ at rerandomization (or receive a third dose of BNT162b2 for Phase 1), and have at least 1 valid and determinate immunogenicity result after Dose 3.
Dose 4 booster all-available immunogenicity	All randomized participants who receive 2 doses of BNT162b2 at initial randomization, receive 2 booster doses of BNT162b2$_{SA}$ at rerandomization, and have at least 1 valid and determinate immunogenicity result after Dose 4.
Evaluable efficacy (7 days)	All eligible randomized participants who receive all vaccination(s) as randomized, with Dose 2 received within the predefined window (within 19-42 days after Dose 1) and have no other important protocol deviations as determined by the clinician on or before 7 days after Dose 2.
Evaluable efficacy (14 days)	All eligible randomized participants who receive all vaccination(s) as randomized, with Dose 2 received within the predefined window (within 19-42 days after Dose 1) and have no other important protocol deviations as determined by the clinician on or before 14 days after Dose 2.
Evaluable efficacy (seroconversion)	All eligible randomized participants who receive all vaccination(s) as randomized, with Dose 2 received within the predefined window (within 19-42 days after Dose 1), have at least 1 N-binding antibody test result available at a post–Dose 2 visit, and have no other important protocol deviations as determined by the clinician prior to the first post–Dose 2 N-binding antibody test.
Evaluable efficacy (asymptomatic surveillance)	All eligible randomized participants who receive all vaccination(s) as randomized, with Dose 2 received within the predefined window (within 19-42 days after Dose 1), consented to participate in the asymptomatic surveillance, and have no other important protocol deviations as determined by the clinician on or before the start of the asymptomatic surveillance period.
All-available efficacy	Dose 1 all-available efficacy: All randomized participants who receive at least 1 vaccination. Dose 2 all-available efficacy: All randomized participants who complete 2 vaccination doses.
Safety	All randomized participants who receive 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.

Population	Description
Booster safety	All participants who receive at least 1 booster dose of the study intervention.

The important protocol deviations will be determined by the medical monitor. An important protocol deviation is a protocol deviation that, in the opinion of the sponsor's clinician, would materially affect assessment of immunogenicity/efficacy, eg, participant receipt of a prohibited vaccine or medication that might affect immune response or a medication error with suspected decrease in potency of the vaccine. The sponsor's clinician will identify those participants with important protocol deviations that result in exclusion from analysis populations before any unblinded analysis in Phase 2/3 is carried out.

5. GENERAL METHODOLOGY AND CONVENTIONS

To facilitate rapid review of data in real time, sponsor staff will be unblinded to study intervention allocation for the participants in Phase 1. The majority of sponsor staff will be blinded to study intervention allocation in Phase 2/3. All laboratory testing personnel performing serology assays will remain blinded to study intervention assigned/received throughout the study. Further details can be found in the protocol, Section 6.3. The timing for statistical analyses is specified in Section 7.

5.1. Hypotheses and Decision Rules

5.1.1. Vaccine Efficacy Hypothesis

Phase 2/3 of the study has 2 primary efficacy endpoints evaluating VE, which is defined as VE = 100 × (1 – IRR). IRR is calculated as the ratio of first confirmed COVID-19 illness rate in the active vaccine group to the corresponding illness rate in the placebo group (see Appendix 3 for details on the calculation of IRR and VE). The assessment of VE will be based on posterior probabilities of VE_1 >30% and VE_2 >30% using beta-binomial models. VE_1 represents VE for prophylactic BNT162b2 against confirmed COVID-19 in participants without evidence of infection before vaccination, and VE_2 represents VE for prophylactic BNT162b2 against confirmed COVID-19 in all participants after vaccination.

For participants with multiple confirmed cases, only the first case will contribute to the VE calculation for each hypothesis. VE_1 and VE_2 will be evaluated sequentially to control the overall type I error to the desired level of 2.5%. VE is demonstrated if there is sufficient evidence (high posterior probability) that either VE_1 >30% or both VE_1 and VE_2 are >30%. The assessment for the primary analysis will be based on posterior probability using a beta-binomial model (see Appendix 2 for details).

The secondary objectives regarding VE against asymptomatic SARS-CoV-2 infection (determined by asymptomatic seroconversion of N-binding antibody and/or asymptomatic SARS-CoV-2 infection based on central laboratory–confirmed NAAT) will be evaluated based on the lower bound of the 95% CI calculated using the Clopper-Pearson method. VE will be demonstrated if the lower bound of the 2-sided 95% CI for VE is >20%.

5.1.2. Immunogenicity Hypothesis

5.1.2.1. Hypothesis for Immunogenicity Bridging of 12 to 15 Years to 16 to 25 Years

One of the secondary objectives in the Phase 3 part of the study is to evaluate noninferiority of the immune response to prophylactic BNT162b2 in participants 12 to 15 years of age compared to the response in participants 16 to 25 years of age at 1 month after Dose 2. The (Dose 2) evaluable immunogenicity population will be used for the following hypothesis testing:

H_0: $\ln(\mu_2) - \ln(\mu_1) \leq \ln(0.67)$

where ln (0.67) corresponds to a 1.5-fold margin for noninferiority, ln(μ2) and ln(μ1) are the natural log of the geometric mean of SARS-CoV-2 neutralizing titers from BNT162b2 recipients 12 to 15 years of age and 16 to 25 years of age, respectively, measured 1 month after Dose 2. If the lower limit of the 95% CI for the GMR (12-15 years of age to 16-25 years of age) is >0.67, the noninferiority objective is met.

5.1.2.2. Hypothesis for Boostability and Protection Against Emerging SARS-CoV-2 VOCs

The primary and secondary objectives for boostability and protection against emerging VOCs for BNT162b2-experienced participants and BNT162b2-naïve participants will be assessed based on:

- GMRs of SARS-CoV-2 SA and/or reference strain neutralizing titers using a 1.5-fold noninferiority margin. Noninferiority is met if the lower limit of the alpha-adjusted CI for the GMR is >0.67 and the point estimate of the GMR is ≥0.8.

- The difference in percentages of participants with seroresponse to the SA strain and/or the reference strain using a 10% noninferiority margin. Noninferiority is met if the lower limit of the alpha-adjusted CI for the difference in percentages of participants with seroresponse is >-10%.

Seroresponse is defined as achieving ≥4-fold rise from baseline (before Dose 1). If the baseline measurement is below LLOQ, the postvaccination measure of ≥4 × LLOQ is considered seroresponse.

5.1.3. Sample Size

5.1.3.1. Phase 1

Phase 1 comprises 15 participants (randomization ratio of 4:1 so that 12 receive active vaccine and 3 receive placebo) per group; 13 vaccine groups are studied, corresponding to a total of 195 participants.

5.1.3.2. Efficacy Against COVID-19

For Phase 2/3, with assumptions of a true VE of 60% after the second dose of study intervention, a total of approximately 164 first confirmed COVID-19 illness cases will provide approximately 90% power. This would be achieved with 17,600 evaluable participants per group or 21,999 vaccine recipients randomized in a 1:1 ratio with placebo, for a total sample size of 43,998, based on the assumption of a 1.3% illness rate per year in the placebo group, accrual of 164 first primary-endpoint cases within 6 months, and 20% of the participants being nonevaluable or having serological evidence of prior infection with SARS-CoV-2, potentially making them immune to further infection. Dependent upon the evolution of the pandemic, it is possible that the COVID-19 attack rate may be much higher, in which case accrual would be expected to be more rapid, enabling the study's primary endpoint to be evaluated much sooner. The total number of participants enrolled in Phase 2/3 may vary depending on the incidence of COVID-19 at the time of the enrollment, the true underlying VE, and a potential early stop for efficacy or futility.

5.1.3.3. Efficacy Against Asymptomatic Infection

The secondary objectives regarding VE against asymptomatic SARS-CoV-2 infection will be assessed in Phase 2/3 participants (determined by asymptomatic seroconversion of N-binding antibody and/or asymptomatic SARS-CoV-2 infection based on central laboratory–confirmed NAAT). Assuming a true VE of 70%, a total of 53 asymptomatic cases will provide approximately 90% power to conclude true VE>20%. A total of 206 cases is needed to have 90% power if the true VE is 50%. The hypothesis for asymptomatic seroconversion of N-binding antibody will be tested if at least 206 cases are accrued. The hypothesis for asymptomatic infection based on central laboratory–confirmed NAAT in participants who are consented to participate in the intensive surveillance phase will be tested if at least 53 cases are accrued.

5.1.3.4. Immunogenicity Bridging of 12 to 15 Years to 16 to 25 Years

In Phase 3, approximately 2000 participants are anticipated to be 12 to 15 years of age. A random sample of 280 participants will be selected for each of the 2 age groups (12 to 15 years and 16 to 25 years) as an immunogenicity subset for the noninferiority assessment. With the standard deviation and observed GMT difference assumed in the power analysis below, a sample size of 225 evaluable participants (or 280 vaccine recipients) per age group will provide a power of 90.4% to declare the noninferiority of adolescents to 16- to 25-year-olds in terms of neutralizing antibody GMR, 1 month after the second dose (see Table 9).

Table 9. Power Analysis for Noninferiority Assessment

Criteria	Standard Deviation (Log Value)[a]	Assumed Observed GMT Difference (Log Scale)	Number of Evaluable Participants per Age Group	Power[b]
Lower limit of 95% CI for GMR (12-15/16-25) >0.67	0.65	-0.2	225	90.4%

Abbreviation: GMR = geometric mean ratio; GMT = geometric mean titer.
a. Reference: 1 month after Dose 2, BNT162b2 (30 µg), 18- to 55-year age group (C4591001 Phase 2).
b. At 0.05 alpha level (2-sided).

5.1.3.5. Boostability and Protection Against Emerging SARS-CoV-2 VOCs

To assess boostability and protection against emerging SARS-CoV-2 VOCs, approximately 300 participants will be enrolled in each of the 3 groups (BNT162b2-experienced participants to receive either a third dose of BNT162b2 at 30 µg [Group 1] or a third dose of $BNT162b2_{SA}$ [Group 2], BNT162b2-naïve participants to receive 2 doses of $BNT162b2_{SA}$ [Group 3]) to provide an acceptable safety database.

Assuming a 20% nonevaluable rate, approximately 240 evaluable participants in each group will contribute to immunogenicity evaluation. This will provide sufficient power for noninferiority evaluations with appropriate multiplicity adjustment for type I error control.

For comparisons based on GMR, the assay standard deviation in log scale is assumed to be 0.74 based on results from Phase 2 of the study and adjusted for assay variability. A GMR of 1 is assumed for each comparison.

For comparisons based on seroresponse, a 90% response rate is assumed for each comparative group or at each comparative time point.

Within-Group Comparison for BNT162b2-Experienced Participants

For each randomized group of BNT162b2-experienced participants (Group 1: received a third dose of BNT162b2 at 30 µg, and Group 2: received a third dose of $BNT162b2_{SA}$), with 240 evaluable participants and the stated assumptions for the GMR and standard deviation, the study has >99.9% power to demonstrate noninferiority based on GMR for the objectives in vaccine-experienced individuals using a 1.5-fold margin.

Assuming a true response rate of 90% at each time point and 10% of the participants having a different response status at 2 comparative time points, the study has 99% power to show noninferiority based on seroresponse rate for the objectives in vaccine-experienced individuals using a 10% margin. The study will have 89% power to show noninferiority if 20% of the participants have a different response status at 2 comparative time points.

Between-Group Comparison of BNT162b2-Naïve Participants to Selected Existing Phase 3 Participants Who Received 2 Doses of BNT162b2

Approximately 300 participants will be selected from the existing Phase 3 participants who received 2 doses of BNT162b2 to form the control group for the BNT162b2-naïve participants. A propensity score and Mahalanobis-metric matching approach will be used to select the matching control group participants to ensure comparable distribution of age, sex, and other demographic factors in the control group and BNT162b2-naïve group. The propensity score (ie, the probability of being in the BNT162b2-naïve group rather than in the control group) based on a logistic regression, including age, sex, and state/region as matching factors, will be calculated. For each BNT162b2-naïve participant, the 5 existing Phase 3 participants with the closest propensity score as the preliminary matching participants will be identified and then the 1 with the closest Mahalanobis distance will be chosen as the final match.

With 240 evaluable BNT162b2-naïve participants and 240 evaluable participants in the control group and the above-stated assumptions for the GMR, standard deviation, and seroresponse rate, the study has >99.9% power to declare noninferiority based on GMR for the objectives in vaccine-naïve individuals using a 1.5-fold margin and 89.7% power to declare noninferiority based on seroresponse rate using a 10% margin.

5.1.3.6. Safety

For safety outcomes, Table 10 shows the probability of observing at least 1 AE for a given true event rate of a particular AE, for various sample sizes. For example, if the true AE rate is 10%, with 12 participants in a vaccine group, there is 72% probability of observing at least 1 AE.

Table 10. Probability of Observing at Least 1 AE by Assumed True Event Rates With Different Sample Sizes

Assumed True Event Rate of an AE	N=12	N=45	N=180	N=300	N=3000	N=6000	N=9000	N=15000
0.01%	0.00	0.00	0.02	0.03	0.26	0.45	0.59	0.78
0.02%	0.00	0.01	0.04	0.06	0.45	0.70	0.83	0.95
0.04%	0.00	0.02	0.07	0.11	0.70	0.91	0.97	>0.99
0.06%	0.01	0.03	0.10	0.16	0.83	0.97	0.99	>0.99
0.08%	0.01	0.04	0.13	0.21	0.91	0.99	0.99	>0.99
0.10%	0.01	0.04	0.16	0.26	0.95	0.99	0.99	>0.99
0.15%	0.02	0.07	0.24	0.36	0.99	0.99	>0.99	>0.99
0.20%	0.02	0.09	0.30	0.45	>0.99	>0.99	>0.99	>0.99
0.25%	0.03	0.11	0.36	0.53	>0.99	>0.99	>0.99	>0.99
0.30%	0.04	0.13	0.42	0.59	>0.99	>0.99	>0.99	>0.99
0.35%	0.04	0.15	0.47	0.65	>0.99	>0.99	>0.99	>0.99
0.50%	0.06	0.20	0.59	0.78	>0.99	>0.99	>0.99	>0.99
1.00%	0.11	0.36	0.84	0.95	>0.99	>0.99	>0.99	>0.99
2.00%	0.22	0.60	0.97	>0.99	>0.99	>0.99	>0.99	>0.99
3.00%	0.31	0.75	>0.99	>0.99	>0.99	>0.99	>0.99	>0.99

Table 10. Probability of Observing at Least 1 AE by Assumed True Event Rates With Different Sample Sizes

Assumed True Event Rate of an AE	N=12	N=45	N=180	N=300	N=3000	N=6000	N=9000	N=15000
5.00%	0.46	0.90	>0.99	>0.99	>0.99	>0.99	>0.99	>0.99
7.00%	0.58	0.96	>0.99	>0.99	>0.99	>0.99	>0.99	>0.99
10.00%	0.72	0.99	>0.99	>0.99	>0.99	>0.99	>0.99	>0.99

5.1.4. Multiplicity Considerations

5.1.4.1. Phase 1

For Phase 1, there is no hypothesis testing.

5.1.4.2. Phase 2/3 Vaccine Efficacy

For Phase 2/3, a Bayesian approach will be applied for the first primary efficacy endpoint at the interim and final analyses. The boundaries for declaring efficacy at interim analyses and success criteria for the final analysis are adjusted appropriately to control the type I error at 0.025 (Table 13).

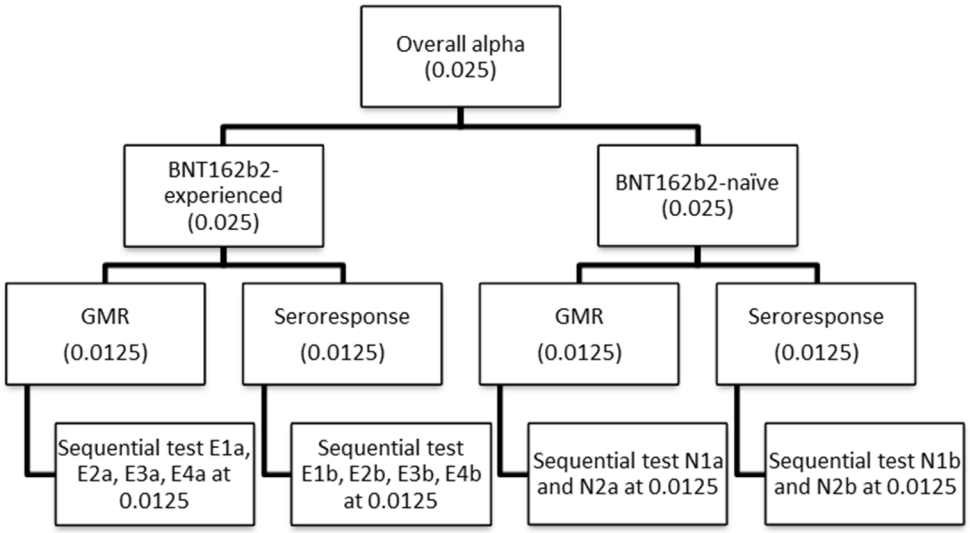
5.1.4.3. Phase 2/3 Immunogenicity

Figure 1 outlines the type I error control strategy for multiple objectives across different populations (BNT162b2-experienced or BNT162b2-naïve) and estimands (GMR or seroresponse).

The objectives for BNT162b2-experienced participants and BNT162b2-naïve participants will be evaluated independently. The vaccine-experienced and vaccine-naïve individuals are different populations with different objectives. The 2 populations are included in the same study to improve operational efficiency. Therefore, no type I error adjustments will be applied to the assessments of the 2 populations.

For each population, the objectives will be evaluated separately for each estimand. To control the overall type I error, the 1-sided alpha of 0.025 will be split and allocated equally to each estimand. Specifically, for each estimand, the hypotheses will be tested in sequential order (as listed in the objectives in Section 3) using a 1-sided alpha of 0.0125 (Figure 1, where E and N represent vaccine-experienced and vaccine-naïve, respectively, and a and b represent GMR and seroresponse estimands, respectively).

Figure 1. Multiplicity Schema



5.2. General Methods

Time points for local reactions and systemic events refer to data within 7 days after each dose. CIs for all endpoints in the statistical analysis will be presented as 2-sided at the 95% level unless specified otherwise.

5.2.1. Analyses for Binary Data

Descriptive statistics for categorical variables (eg, proportions) are the percentage (%), the numerator (n), and the denominator (N) used in the percentage calculation, and the 95% CIs where applicable.

The exact 95% CI for binary endpoints for each group will be computed using the F distribution (Clopper-Pearson).[1] The 95% CI for the between-group difference for binary endpoints will be calculated using the Miettinen and Nurminen method.[2]

For the within-group comparison of binary endpoints, eg, percentage of participants with seroresponse, the 2-sided 95% CI for the difference in proportions will be calculated using an adjusted Wald interval as described by Agresti and Min (2005).[3] This is done by adding 0.5 to each cell according to Agresti and Min's method, and thus 2 is added to the total n (see the table below). The following table gives a representation of the cells in a 2 × 2 table for matched proportions of participants achieving seroresponse.

Illustration of cells in a 2 × 2 table for matched proportions

Time Point 1	Time Point 2		
	Participants with seroresponse	Participants without seroresponse	Total
Participants with seroresponse	a	b	a + b (p1)
Participants without seroresponse	c	d	c + d
Total	a + c (p2)	b + d	n

The interest of comparison, p2 – p1 can be written as (a + c)/n – (a + b)/n = (c – b)/n. The 2-sided 95% CI for the difference in matched proportions using the adjusted Wald method is:

$$\frac{(c^* - b^*)}{n^*} \pm \frac{z_{\alpha/2}\sqrt{(b^* + c^*) - [(c^* - b^*)^2/n^*]}}{n^*}$$

with $b^* = b + 0.5,\ c^* = c + 0.5, n^* = n + 2$, α = 0.05.

For Phase 2/3 only, the 3-tier approach will be used to summarize AEs. For both Tier 1 (if any are identified during the study) and Tier 2 events, a 95% CI for the between-group difference in proportions will be calculated based on the Miettinen and Nurminen[2] method. In addition, for Tier 1 events (if any), the asymptotic p-values will also be presented for the difference in proportions, based on the same test statistic and under the assumption that the test statistic is asymptotically normally distributed. For Tier 3 events, counts and percentages for each vaccine group will be provided.

A Bayesian beta-binomial model with a minimally informative prior will be also used for VE primary endpoints (see Appendix 2).

5.2.2. Analyses for Count Data

The number of occurrences of a certain event is count data and thus could be modeled using Poisson distribution. The incidence rate is estimated as the number of events observed divided by the total person-years of follow-up.

Assuming an observed event is from Poisson distribution with parameter λT, where λ is the incidence rate and T is the total person-years of follow-up, based on the relationship between the Poisson and chi-square distribution,[4] the exact lower and upper α-percent 2-sided confidence limits for λT can be estimated by:

$Y_l = \frac{\chi^2_{2Y,\alpha/2}}{2}$ and $Y_u = \frac{\chi^2_{2(Y+1),1-\alpha/2}}{2}$, respectively, where Y is the number of events observed.

The exact lower and upper confidence limit for incidence rate λ can then be obtained as $\frac{Y_l}{T}$ and $\frac{Y_u}{T}$, respectively.

5.2.3. Analyses for Continuous Data

Unless otherwise stated, descriptive statistics for continuous variables are n, mean, median, standard deviation, minimum, and maximum.

5.2.3.1. Geometric Means

For immunogenicity results of SARS-CoV-2 neutralizing titers, the GMTs will be computed along with associated 95% CIs. The GMTs will be calculated as the mean of the assay results after making the logarithm transformation and then exponentiating the mean to express results on the original scale. Two-sided 95% CIs will be obtained by taking log transforms of titers, calculating the 95% CI with reference to Student's t-distribution, and then exponentiating the confidence limits. Similarly, GMCs and 95% CIs will be calculated for S1-binding IgG levels and RBD-binding IgG levels.

5.2.3.2. Geometric Mean Fold Rises

GMFRs will be defined as the result after vaccination divided by the result before vaccination. GMFRs are limited to participants with nonmissing values at both time points.

GMFRs will be calculated as the mean of the difference of logarithmically transformed neutralization titers or antibody levels (later result minus earlier result) and exponentiating the mean. The associated 2-sided 95% CIs are obtained by constructing CIs using Student's t-distribution for the mean difference on the natural log scale and exponentiating the confidence limits.

5.2.3.3. Geometric Mean Ratios

For SARS-CoV-2 neutralizing titers and S1-binding IgG levels and RBD-binding IgG levels, the GMRs will be provided along with associated 95% CIs. GMRs will be limited to participants with nonmissing values for both SARS-CoV-2 neutralizing titers and S1-binding IgG levels/RBD-binding IgG levels at each time point. The GMR will be calculated as the mean of the difference of logarithmically transformed assay results (eg, SARS-CoV-2 neutralizing titers minus S1-binding IgG level for each participant) and exponentiating the mean. Two-sided CIs will be obtained by calculating CIs using Student's t-distribution for the mean difference of the logarithmically transformed assay results and exponentiating the confidence limits.

For SARS-CoV-2 neutralizing titers in participants 12 to 15 years of age and 16 to 25 years of age, the GMRs will be provided along with associated 95% CI. The GMR and its 2-sided 95% CI will be derived by calculating differences in means and CIs on the natural log scale of the titers based on the Student's t-distribution and then exponentiating the results. The difference in means on the natural log scale will be 12 to 15 years minus 16 to 25 years. Noninferiority will be declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.

For assessment of boostability and protection against emerging VOCs, the comparisons of different NTs (anti-SA or anti–reference strain) or the same NTs at different time points within the same group will be limited to participants with nonmissing values at both time

points or both NT measurements. GMRs will be calculated as the mean of the difference of logarithmically transformed titers for each participant (eg, later time point minus earlier time point) and exponentiating the mean. The associated 2-sided CIs will be obtained by constructing CIs using Student's t distribution for the mean difference on the logarithm scale and exponentiating the confidence limits.

For the between-group comparison, GMRs will be calculated as the mean of the difference of logarithmically transformed assay results between 2 groups and exponentiating the mean. The associated 2-sided 97.5% CIs will be obtained by calculating CIs using Student's t-distribution for the mean difference of the logarithmically transformed titers and exponentiating the confidence limits.

5.2.3.4. Geometric Mean Fold Rise Ratios

The ratios of GMFR A to GMFR B and GMFR A to GMFR C may be explored, where GMFR A is the GM of the ratio of the SARS-CoV-2 neutralizing titer at the time point after vaccination to the corresponding titer at the time point before vaccination, GMFR B is the GM of the ratio of the S1-binding IgG level at the time point after vaccination to the corresponding antibody level at the time point before vaccination, and GMFR C is the GM of the ratio of the RBD-binding IgG level at the time point after vaccination to the corresponding antibody level at the time point before vaccination.

5.2.3.5. Reverse Cumulative Distribution Curves

Empirical RCDCs will plot proportions of participants with values equal to or exceeding a specified assay value versus the indicated assay value, for all observed assay values. Data points will be joined by a step function with data points on the left side of the step.

5.3. Methods to Manage Missing Data

For endpoints, the missing data handling rules are described in the corresponding endpoint sections.

For the missing dates, the sponsor data standard rules for imputation will be applied (eg, partial dates for AEs will be imputed according to Pfizer standard algorithms).

Missing COVID-19 test data in Phase 2/3 for computing VE will be imputed in the sensitivity analysis. Details are included in Section 6.1.3.1.2.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoint(s)

6.1.1. Safety Endpoints

The safety analyses after the first dose and after booster dose(s) are based on the safety population and booster safety population, respectively. Analyses of reactogenicity endpoints are based on a subset of the safety population that includes participants with any e-diary data reported after vaccination. Participants will be summarized by vaccine group according to

the study interventions they actually received. Missing e-diary data will not be imputed; missing AE dates will be handled according to the Pfizer safety rules.

6.1.1.1. Local Reactions

6.1.1.1.1. Main Analysis

- Estimand: The percentage of participants reporting local reactions (redness, swelling, and pain at the injection site) within 7 days after each dose (Section 2.1).
- Analysis set: Safety or booster safety populations (Section 4).
- Analysis time point: Within 7 days after each dose.
- Analysis methodology: Descriptive statistics (Section 5.2.1).
- Intercurrent events and missing data: The participants without any e-diary data throughout the 7 days after vaccination will be excluded from the analysis at that particular vaccination; missing values will not be imputed.
- Reporting results: Descriptive statistics for each and any local reaction after each dose in each vaccine group will be presented by maximum severity and cumulatively across severity levels. Confirmed e-diary errors will be excluded from the analysis. Descriptive summary statistics will include counts and percentages of participants with the indicated endpoint and the associated 2-sided Clopper-Pearson 95% CIs.

6.1.1.1.2. Supplementary Analyses

To support the assessment of local reactions, the following endpoints (as defined in Section 3.1.1.1) will be summarized with the same analysis time point and analysis population, analysis methodology, and appropriate reporting results. Confirmed e-diary errors will be excluded from these analyses.

- Duration (days) of each local reaction after each dose.
- Onset day of each local reaction after each dose.

These continuous endpoints will be summarized by displaying n, mean, median, standard deviation, minimum, and maximum for each vaccine group.

Figures:

Bar charts with the proportions of participants for each local reaction throughout 7 days will be plotted for each vaccine group. The bars will be divided into severity categories to highlight the proportions of participants by maximum severity.

6.1.1.2. Systemic Events

6.1.1.2.1. Main Analysis

- Estimand: The percentage of participants reporting systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain) within 7 days after each dose (Section 2.1).
- Analysis set: Safety or booster safety populations (Section 4).
- Analysis time point: Within 7 days after each dose.
- Analysis methodology: Descriptive statistics (Section 5.2.1).
- Intercurrent events and missing data: The participants without any e-diary data throughout the 7 days after vaccination will be excluded from the analysis at that particular vaccination; missing values will not be imputed.
- Reporting results: Descriptive statistics for each systemic event after each dose in each vaccine group will be presented by maximum severity and cumulatively across severity levels. Descriptive summary statistics will include counts and percentages of participants with the indicated endpoint and the associated 2-sided Clopper-Pearson 95% CIs.

6.1.1.2.2. Supplementary Analyses

The following endpoints for assessment of systemic events will be summarized similarly to the assessment of local reactions:

- Duration of each systemic event after each dose.
- Onset day of each systemic event after each dose.

These continuous endpoints will be summarized by displaying n, mean, median, standard deviation, minimum, and maximum for each vaccine group.

The use of antipyretic medication (see Section 3.1.1.3) will be summarized similarly to systemic events, except that there is no severity level associated with the use of antipyretic medication.

Figures:

Bar charts with the proportions of participants reporting each systemic event throughout 7 days after each dose will be plotted for each vaccine group. The bars will be divided into severity categories to highlight the proportions of participants by severity.

6.1.1.3. Adverse Events

6.1.1.3.1. Main Analysis

- Estimand: The percentage of participants reporting AEs from Dose 1 to 1 month after the second dose for all phases, from Dose 1 to 7 days after the second dose for the first 360 participants randomized in Phase 2, from Dose 1 (of booster BNT162b2 or BNT162b2$_{SA}$) to 1 month after the last dose for participants in the Phase 3 subset for evaluation of boostability and protection against emerging VOCs, and from Dose 3 to 1 month after Dose 3 for participants receiving BNT162b2 as a third dose as part of protocol amendment 18 (Section 2.1).

- Analysis set: Safety or booster safety populations (Section 4).

- Analysis time point: Dose 1 to 1 month after the second dose for all phases, Dose 1 to 7 days after the second dose for the first 360 participants randomized in Phase 2, Dose 1 (of booster BNT162b2 or BNT162b2$_{SA}$) to 1 month after the last dose for participants in the Phase 3 subset for evaluation of boostability and protection against emerging VOCs, and from Dose 3 to 1 month after Dose 3 for participants receiving BNT162b2 as a third dose as part of protocol amendment 18.

- Analysis methodology: Descriptive statistics (Section 5.2.1) for all phases and additional 3-tiered approach for Phase 2/3 (Section 3.1.1.4).

- Intercurrent events and missing data: Partial AE dates will be imputed using the Pfizer standard algorithm.

- Reporting results: AEs will be categorized according to MedDRA terms. A 3-tier approach will be used to summarize AEs for Phase 2/3 only. Under this approach AEs are classified into 1 of 3 tiers (Section 3.1.1.4). For both Tier 1 and Tier 2 events, 2-sided 95% CIs for the difference between the active vaccine and placebo groups in the percentage of participants reporting the events based on the Miettinen and Nurminen[2] method will be provided. In addition, for Tier 1 events, the asymptotic p-values will also be presented for the difference between groups in the percentage of participants reporting the events, based on the same test statistic and under the assumption that the test statistic is asymptotically normally distributed. AE displays will be sorted in descending order of point estimates of risk difference within SOC. Descriptive summary statistics (counts, percentages, and associated Clopper-Pearson 95% CIs) will be provided for any AEs for each vaccine group.

6.1.1.3.2. Supplementary Analyses

Immediate AEs (within the first 30 minutes after each dose) will also be summarized for each vaccine group. All AEs after informed consent and prior to the first vaccination will not be included in the analyses but will be listed.

6.1.1.4. Serious Adverse Events

6.1.1.4.1. Main Analyses

- Estimand: The percentage of participants reporting SAEs from Dose 1 to 6 months after the second dose for all phases, from Dose 1 to 7 days after the second dose for the first 360 participants randomized in Phase 2, from Dose 1 (of booster BNT162b2 or $BNT162b2_{SA}$) to 5 or 6 months after the last dose for participants in the Phase 3 subset for evaluation of boostability and protection against emerging VOCs, and from Dose 3 to 6 months after Dose 3 for participants receiving BNT162b2 as a third dose as part of protocol amendment 18 (Section 2.1).

- Analysis set: Safety or booster safety populations (Section 4).

- Analysis time point: Dose 1 to 6 months after the second dose for all phases, Dose 1 to 7 days after the second dose for the first 360 participants randomized in Phase 2, Dose 1 (of booster BNT162b2 or $BNT162b2_{SA}$) to 5 or 6 months after the last dose for participants in the Phase 3 subset for evaluation of boostability and protection against emerging VOCs, and from Dose 3 to 6 months after Dose 3 for participants receiving BNT162b2 as a third dose as part of protocol amendment 18.

- Analysis methodology: Descriptive statistics (Section 5.2.1).

- Intercurrent events and missing data: Partial SAE dates will be imputed using the Pfizer standard algorithm.

- Reporting results: SAEs will be categorized according to MedDRA terms. Counts, percentages, and the associated Clopper-Pearson 95% CIs of SAEs will be provided for each vaccine group.

6.1.1.5. Hematology and Chemistry Parameters (for Phase 1 Only)

6.1.1.5.1. Main Analyses

- Estimands: The percentage of participants with abnormal hematology and chemistry laboratory values 1 and 7 days after Dose 1; and 7 days after Dose 2 (Section 2.1).

- The percentage of participants with grading shifts in hematology and chemistry laboratory assessments between baseline and 1 and 7 days after Dose 1; and before Dose 2 and 7 days after Dose 2 (Section 2.1).

- Analysis set: Safety population (Section 4).

- Analysis time point: 1 and 7 days after Dose 1; and 7 days after Dose 2.

- Analysis methodology: Descriptive statistics including counts and percentage (Section 5.2.1).

- Intercurrent events and missing data: Missing values will not be imputed.

- Reporting results: Descriptive summary statistics will be provided including counts and percentages of participants with the indicated endpoint and the associated Clopper-Pearson 2-sided 95% CIs.

6.1.2. Immunogenicity Endpoints (for the Phase 3 Subset for Evaluation of Boostability and Protection Against Emerging VOCs Only)

6.1.2.1. SARS-CoV-2 Reference Strain NT and SA NT at 1 Month After Dose 3 vs Reference Strain NT at 1 Month After Dose 2 in BNT162b2-Experienced Participants

6.1.2.1.1. Main Analyses

- Estimands:
  - E1a: GMR of reference strain NT 1 month after the third dose of BNT162b2 at 30 µg to 1 month after the second dose of BNT162b2 in the same individuals (Section 2.1).
  - E2a: GMR of SA NT 1 month after 1 dose of BNT162b2$_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 in the same individuals (Section 2.1).
- Analysis set: Dose 3 booster evaluable and all-available immunogenicity populations (Section 4).
- Analysis time points: 1 month after the second dose of BNT162b2, 1 month after the third dose of BNT162b2 at 30 µg, and 1 month after 1 dose of BNT162b2$_{SA}$.
- Analysis methodology: The comparisons of different NTs (anti-SA or anti–reference strain) or the same NTs at different time points within the same group will be limited to participants with nonmissing values at both time points or both NT measurements. GMRs will be calculated as the mean of the difference of logarithmically transformed titers for each participant (eg, later time point minus earlier time point) and exponentiating the mean (Section 5.2.3.3). The associated 2-sided 97.5% CIs will be obtained by constructing CIs using Student's t-distribution for the mean difference on the logarithm scale and exponentiating the confidence limits. Noninferiority of E1a and E2a will be assessed sequentially. Noninferiority will be declared if the lower bound of the 2-sided 97.5% CI for the GMR is >0.67 and the point estimate of the GMR is ≥0.8.
- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.
- Reporting results: The GMTs at each time point, GMRs, and the associated 2-sided 97.5% CIs will be provided.

Figures:

Empirical RCDCs will be provided for SARS-CoV-2 SA and reference strain NTs at each time point.

6.1.2.2. Seroresponse to the Reference Strain and SA Strain at 1 Month After Dose 3 vs Seroresponse to the Reference Strain at 1 Month After Dose 2 in BNT162b2-Experienced Participants

6.1.2.2.1. Main Analyses

- Estimands:
  - E1b: The difference in percentages of participants with seroresponse to the reference strain at 1 month after the third dose of BNT162b2 at 30 µg and 1 month after the second dose of BNT162b2 in the same individuals (Section 2.1).
  - E2b: The difference in percentages of participants with seroresponse to the SA strain at 1 month after 1 dose of $BNT162b2_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2 in the same individuals (Section 2.1).
- Analysis set: Dose 3 booster evaluable and all-available immunogenicity populations (Section 4).
- Analysis time points: 1 month after the second dose of BNT162b2, 1 month after the third dose of BNT162b2 at 30 µg, and 1 month after 1 dose of $BNT162b2_{SA}$.
- Analysis methodology: Similar to E1a and E2a, the within-group comparisons of seroresponse to different NTs (anti-SA or anti–reference strain) or the same NTs at different time points within the same group will be limited to participants with nonmissing values at both time points or both NT measurements. The percentages of participants with seroresponse at each time point and the difference in percentages will be provided. The 2-sided 97.5% CIs for the difference in percentages of participants with seroresponse will be calculated using the adjusted Wald interval as described by Agresti and Min (2005)[3] for comparing matched proportions (Section 5.2.1). Noninferiority of E1b and E2b will be assessed sequentially. Noninferiority will be declared if the lower bound of the 2-sided 97.5% CI for the difference in percentages of participants with seroresponse is greater than -10%.
- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.
- Reporting results: The counts, percentages of participants with seroresponse at each time point, the difference in percentages, and the associated 2-sided 97.5% CIs will be provided.

6.1.2.3. SARS-CoV-2 SA NT at 1 Month After Dose 2 vs Reference Strain NT at 1 Month After Dose 2 in BNT162b2-Naïve Participants

6.1.2.3.1. Main Analyses

- Estimands:

- N1a: GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 (Section 2.1).

- Analysis set: Dose 2 evaluable and all-available immunogenicity populations (Section 4).

- Analysis time points: 1 month after the second dose of BNT162b2 and 1 month after the second dose of BNT162b2$_{SA}$.

- Analysis methodology: For the between-group comparison, GMRs will be calculated as the mean of the difference of logarithmically transformed assay results between 2 groups and exponentiating the mean (Section 5.2.3.3). The associated 2-sided 97.5% CIs will be obtained by calculating CIs using Student's t-distribution for the mean difference of the logarithmically transformed titers and exponentiating the confidence limits. Noninferiority will be declared if the lower bound of the 2-sided 97.5% CI for the GMR is >0.67 and the point estimate of the GMR is ≥0.8.

- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.

- Reporting results: The GMTs at each time point, GMRs, and the associated 2-sided 97.5% CIs will be provided.

Figures:

Empirical RCDCs will be provided for SARS-CoV-2 SA and reference strain NTs at each time point for each vaccine group.

6.1.2.4. Seroresponse to the SA Strain at 1 Month After Dose 2 vs Seroresponse to the Reference Strain at 1 Month After Dose 2 in BNT162b2-Naïve Participants

6.1.2.4.1. Main Analyses

- Estimands:

  - N1b: The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2 (Section 2.1).

- Analysis set: Dose 2 evaluable and all-available immunogenicity populations (Section 4).

- Analysis time points: 1 month after the second dose of BNT162b2 and 1 month after the second dose of BNT162b2$_{SA}$.

- Analysis methodology: The difference in percentages of participants with seroresponse and associated 2-sided 97.5% CIs will be calculated using the Miettinen and Nurminen method[2] (Section 5.2.1). Noninferiority will be declared if the lower bound of the

2-sided 97.5% CI for the difference in percentages of participants with seroresponse is greater than -10%.

- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.

- Reporting results: The counts, percentages of participants with seroresponse at each time point, the difference in percentages, and the associated 2-sided 97.5% CIs will be provided.

6.1.3. Vaccine Efficacy Endpoints (for Phase 2/3 Only)

6.1.3.1. COVID-19 Incidence per 1000 Person-Years of Follow-up

6.1.3.1.1. Main Analyses

- Estimands:
  - 100 × (1 – IRR) [ratio of confirmed COVID-19 illness from 7 days after the second dose per 1000 person-years of follow-up in participants without evidence of infection (prior to 7 days after receipt of the second dose) for the active vaccine group to the placebo group (Section 2.1)].
  - 100 × (1 – IRR) [ratio of confirmed COVID-19 illness from 7 days after the second dose per 1000 person-years of follow-up in participants with and without evidence of infection (prior to 7 days after receipt of the second dose) for the active vaccine group to the placebo group (Section 2.1)].

- Analysis set: Evaluable efficacy (7 days) and all-available efficacy populations (Section 4).

- Analysis time point: At interim analyses and final analysis when the surveillance period ends.

- Analysis methodology: Assessment of VE will be performed for confirmed COVID-19 from 7 days after the receipt of the second dose of study intervention onwards, and will be estimated by 100 × (1 – IRR), where IRR is the calculated ratio of COVID-19 illness rate per 1000 person-years of follow-up in the active vaccine group to the corresponding illness rate in the placebo group after the second dose (see Appendix 3 for details on the derivation of IRR and VE). The posterior probability (ie, P[VE >30%|data]) at each interim analysis and final analysis will be computed using a beta-binomial model and a specified minimally informative beta distribution as prior (details can be found in Appendix 2).

- Intercurrent events and missing data: Missing efficacy data (symptom is present without laboratory testing data) will not be imputed in the main analyses.

- Reporting results: The point estimate of VE, 95% credible intervals using the 2.5th percentile and the 97.5th percentile, and Bayesian posterior probability of VE greater than 30% will be provided (details can be found in Appendix 2).

6.1.3.1.2. Sensitivity and Supplemental Analyses

With MAR assumption, a missing efficacy endpoint (laboratory-confirmed COVID-19 results) may be imputed based on predicted probability using the fully conditional specification method.[5] The imputation will run multiple times (up to 1000) and summary statistics similar to those used in the main analysis will be tabulated across the imputations. Other imputation methods without the MAR assumption may be explored, eg, a tipping point analysis.

All COVID-19 cases after Dose 1 may be analyzed using the Dose 1 all-available efficacy population. COVID-19 disease-related information may be summarized or listed.

After the final efficacy analyses at 164 first primary cases, updated efficacy analyses will be performed with additional data accrued. The point estimate of VE in the blinded follow-up period and associated 2-sided 95% CI will be derived using the Clopper Pearson method adjusted for surveillance time, and the posterior probability (ie, P[VE >30%|data]) will be provided. VE at different follow-up time intervals and against different variant strains may be assessed.

Efficacy could also be assessed over a longer time period using time-to-event data analysis methods to account for censoring (participants censored when they receive other vaccines or withdraw) as well as potentially confounding factors. A Kaplan-Meier curve showing the cumulative incidence of COVID-19 cases over time may also be informative to understand the sustainability of VE.

For the assessment of efficacy in the presence of potential crossover, the established adjusting methods may be considered. For example, a rank-preserving structural failure time model may be appropriate to attempt to reconstruct data for the control arm as if crossover had not occurred, with the aim of reducing bias and allowing the vaccine effect to be assessed more accurately.

6.2. Secondary Endpoints

6.2.1. Immunogenicity Endpoints

Phase 1

The statistical analysis of immunogenicity results for Phase 1 will be primarily based on the Dose 1 and Dose 2 evaluable immunogenicity populations. Serology data after a postbaseline positive SARS-CoV-2 test result will not be included in the analysis based on the evaluable immunogenicity populations. An additional analysis will be performed based on the all-available populations if there is a large enough difference in sample size between the all-available immunogenicity population and the evaluable immunogenicity population. Participants will be summarized according to the vaccine group to which they were randomized. Missing serology data will not be imputed.

Phase 2/3

The statistical analysis of immunogenicity results for Phase 2/3 will be based on Dose 2 evaluable immunogenicity population. Serology data after a postbaseline positive SARS-CoV-2 test result will not be included in the analysis based on the evaluable immunogenicity population. An additional analysis may be performed based on the Dose 2 all-available immunogenicity population if needed. Participants will be summarized according to the vaccine group to which they were randomized. Missing serology data will not be imputed.

6.2.1.1. SARS-CoV-2 Neutralizing Titers (Phase 1)

6.2.1.1.1. Main Analyses

- Estimands:
  - GMTs (Section 2.1).
  - GMFR from before vaccination to each subsequent time point after vaccination (Section 2.1).
  - Proportion of participants achieving ≥4-fold rise from before vaccination to each subsequent time point after vaccination (Section 2.1).
- Analysis set: Dose 1 and Dose 2 evaluable and all-available immunogenicity populations (Section 4).
- Analysis time points: 7 and 21 days after Dose 1; 7 and 14 days and 1, 6, 12 and 24 months after Dose 2.
- Analysis methodology: GMs and the associated 2-sided CIs will be derived by calculating means and CIs on the natural log scale based on Student's t-distribution, and then exponentiating the results (Section 5.2.3.1). GMFRs will be limited to participants with nonmissing values prior to the first dose and at the postvaccination time point. The GMFR will be calculated as the mean of the difference of logarithmically transformed assay results (later time point – earlier time point) and exponentiated to transform results back to the original scale. Two-sided CIs will be obtained by calculating CIs using Student's t-distribution for the mean difference of the logarithmically transformed assay results and exponentiating the confidence limits (Section 5.2.3.2). Percentages of participants with ≥4-fold rise will be calculated with the associated 2-sided 95% CIs (Clopper-Pearson method).
- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.

- Reporting results: The GMTs at each time point, GMFRs from before vaccination to each subsequent time point after vaccination, and the percentages of participants achieving ≥4-fold rise and the associated 2-sided 95% CIs from before vaccination to each time point after vaccination.

Figures:

Empirical RCDCs will be provided for SARS-CoV-2 neutralizing titers after Dose 1 and after Dose 2 (Section 5.2.3.5).

6.2.1.2. S1-Binding IgG Levels and RBD-Binding IgG Levels (Phase 1)

6.2.1.2.1. Main Analyses

- Estimands:
  - GMCs (Section 2.1).
  - GMFR from before vaccination to each subsequent time point after vaccination (Section 2.1).
  - Proportion of participants achieving ≥4-fold rise from before vaccination to each subsequent time point after vaccination (Section 2.1).
- Analysis set: Dose 1 and Dose 2 evaluable and all-available immunogenicity populations (Section 4).
- Analysis time points: 7 and 21 days after Dose 1; 7 and 14 days and 1, 6, 12, and 24 months after Dose 2.
- Analysis methodology: GMs and the associated 2-sided CIs will be derived by calculating means and CIs on the natural log scale based on Student's t-distribution, and then exponentiating the results (Section 5.2.3.1). GMFRs will be limited to participants with nonmissing values prior to the first dose and at the postvaccination time point. The GMFR will be calculated by exponentiating the mean of the difference of logarithmically transformed assay results (later time point – earlier time point). Two-sided CIs will be obtained by calculating CIs using Student's t-distribution for the mean difference of the logarithmically transformed assay results and exponentiating the confidence limits (Section 5.2.3.2). Percentages of participants with ≥4-fold rise will be calculated with the associated 2-sided 95% CIs (Clopper-Pearson method).
- Intercurrent events and missing data: Concentrations below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.
- Reporting results: The GMCs, GMFRs, and percentages of participants with ≥4-fold rise and the associated 2-sided 95% CIs will be provided for each study intervention (active/placebo) within each group before vaccination and at each time point.

Figures:

Empirical RCDCs will be provided for S1-binding IgG levels and RBD-binding IgG levels after Dose 1 and after Dose 2 (Section 5.2.3.5).

6.2.1.3. SARS-CoV-2 Neutralizing Titers vs SARS-CoV-2 S1-Binding IgG Levels and RBD-Binding IgG Levels (Phase 1)

6.2.1.3.1. Main Analyses

- Estimands:
  - GMR of SARS-CoV-2 neutralizing titers to S1-binding IgG levels (Section 2.1).
  - GMR of SARS-CoV-2 neutralizing titers to RBD-binding IgG levels (Section 2.1).
- Analysis set: Dose 1 and Dose 2 evaluable and all-available immunogenicity populations (Section 4).
- Analysis time points: 7 and 21 days after Dose 1; 7 and 14 days and 1, 6, 12, and 24 months after Dose 2.
- Analysis methodology: GMRs will be limited to participants with nonmissing values for both SARS-CoV-2 neutralizing titers and S1-binding IgG level or RBD-binding IgG level at each time point. The GMR will be calculated as the mean of the difference of logarithmically transformed assay results (eg, SARS-CoV-2 neutralizing titers minus S1-binding IgG levels for each participant) and exponentiating the mean (Section 5.2.3.3). Two-sided CIs will be obtained by calculating CIs using Student's t-distribution for the mean difference of the logarithmically transformed assay results and exponentiating the confidence limits (Section 5.2.3.3).
- Intercurrent events and missing data: Concentrations below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.
- Reporting results: The GMRs and the associated 2-sided 95% CIs will be provided for each study intervention within each group before vaccination and at each time point.

6.2.1.4. SARS-CoV-2 Neutralizing Titers in Participants 12 to 15 Years of Age vs Those 16 to 25 Years of Age (Phase 2/3)

6.2.1.4.1. Main Analyses

- Estimands: GMR, estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in the 2 age groups (12-15 years of age to 16-25 years of age) 1 month after completion of vaccination (Section 2.1).
- Analysis set: Dose 2 evaluable and all-available immunogenicity populations (Section 4).

- Analysis time points: 1 month after Dose 2.

- Analysis methodology: The GMR and its 2-sided 95% CI will be derived by calculating differences in means and CIs on the natural log scale of the titers based on the Student's t-distribution and then exponentiating the results. The difference in means on the natural log scale will be 12 to 15 years minus 16 to 25 years. Noninferiority will be declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67 (Section 5.2.3.3).

- Intercurrent events and missing data: Concentrations below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.

- Reporting results: The GMRs and the associated 2-sided 95% CIs will be provided.

6.2.1.4.2. Supplemental Analyses

The counts, percentages of participants with seroresponse (achieving ≥4-fold rise from baseline, as defined in Section 5.1.2.2), the difference in percentages between the 2 age groups (12-15 years of age minus 16-25 years of age), and the associated 2-sided 95% CIs will be provided.

6.2.1.5. SARS-CoV-2 SA NT and Reference Strain NT at 1 Month After Dose 3 vs Reference Strain NT at 1 Month After Dose 2 in BNT162b2-Experienced Participants

6.2.1.5.1. Main Analyses

- Estimands:

  - E3a: GMR of SA NT 1 month after the third dose of BNT162b2 at 30 µg to the reference strain NT 1 month after the second dose of BNT162b2 in the same individuals (Section 2.1).

  - E4a: GMR of reference strain NT 1 month after 1 dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 in the same individuals (Section 2.1).

- Analysis set: Dose 3 booster evaluable and all-available immunogenicity populations (Section 4).

- Analysis time points: 1 month after the second dose of BNT162b2, 1 month after the third dose of BNT162b2 at 30 µg, and 1 month after 1 dose of BNT162b2$_{SA}$.

- Analysis methodology: GMRs and the associated 2-sided 97.5% CIs will be calculated in the same way as for the primary endpoints E1a and E2a (Section 6.1.2.1.1). If noninferiority is established for both E1a and E2a, E3a and E4a will be assessed sequentially using the same criterion (lower bound of the 2-sided 97.5% CI for the GMR is >0.67 and the point estimate of the GMR is ≥0.8).

- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.

- Reporting results: The GMTs at each time point, GMRs, and the associated 2-sided 97.5% CIs will be provided.

Figures:

Empirical RCDCs will be provided for SARS-CoV-2 SA and reference strain NTs at each time point.

6.2.1.6. Seroresponse to the SA Strain and Reference Strain at 1 Month After Dose 3 vs Seroresponse to the Reference Strain at 1 Month After Dose 2 in BNT162b2-Experienced Participants

6.2.1.6.1. Main Analyses

- Estimands:

  - E3b: The difference in percentages of participants with seroresponse to the SA strain at 1 month after the third dose of BNT162b2 at 30 µg and seroresponse to the reference strain at 1 month after the second dose of BNT162b2 in the same individuals (Section 2.1).

  - E4b: The difference in percentages of participants with seroresponse to the reference strain at 1 month after 1 dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2 in the same individuals (Section 2.1).

- Analysis set: Dose 3 booster evaluable and all-available immunogenicity populations (Section 4).

- Analysis time points: 1 month after the second dose of BNT162b2, 1 month after the third dose of BNT162b2 at 30 µg, and 1 month after 1 dose of BNT162b2$_{SA}$.

- Analysis methodology: The difference in percentages of participants with seroresponse and the associated 2-sided 97.5% CIs will be calculated in the same way as for the primary endpoints E1b and E2b (Section 6.1.2.2.1). If noninferiority is established for both E1b and E2b, E3b and E4b will be assessed sequentially using the same criterion (lower bound of the 2-sided 97.5% CI for the difference in percentages is greater than -10%).

- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.

- Reporting results: The counts, percentages of participants with seroresponse at each time point, the difference in percentages, and the associated 2-sided 97.5% CIs will be provided.

6.2.1.7. SARS-CoV-2 SA NT After Dose 3 (BNT162b2-Experienced Participants)

6.2.1.7.1. Main Analyses

- Estimands:
  - GMR of SA NT 1 month after 1 dose of BNT162b2$_{SA}$ to 1 month after the third dose of BNT162b2 at 30 µg (Section 2.1).
  - The difference in percentages of participants with seroresponse to the SA strain at 1 month after 1 dose of BNT162b2$_{SA}$ and 1 month after the third dose of BNT162b2 at 30 µg (Section 2.1).
- Analysis set: Dose 3 booster evaluable and all-available immunogenicity populations (Section 4).
- Analysis time points: 1 month after the third dose of BNT162b2 at 30 µg and 1 month after 1 dose of BNT162b2$_{SA}$.
- Analysis methodology: GMR and the associated 2-sided 95% CI will be calculated in the same way as for the primary endpoint N1a (Section 6.1.2.3.1). The difference in percentages of participants with seroresponse and the associated 2-sided 95% CIs will be calculated in the same way as for the primary endpoints N1b (Section 6.1.2.4.1).
- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.
- Reporting results: The GMTs at each time point, GMRs, and the associated 2-sided 95% CIs will be provided. The counts, percentages of participants with seroresponse at each time point, the difference in percentages, and the associated 2-sided 95% CIs will be provided.

Figures:

Empirical RCDCs will be provided for SARS-CoV-2 SA NTs at each time point for each vaccine group.

6.2.1.8. SARS-CoV-2 SA NT at 1 Month After Dose 4 vs Reference Strain NT at 1 Month After Dose 2 in BNT162b2-Experienced Participants

6.2.1.8.1. Main Analyses

- Estimands:

- GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to the reference strain NT 1 month after the second dose of BNT162b2 in the same individuals (Section 2.1).

- The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and seroresponse to the reference strain at 1 month after the second dose of BNT162b2 in the same individuals (Section 2.1).

- Analysis set: Dose 4 booster evaluable and all-available immunogenicity populations (Section 4).

- Analysis time points: 1 month after the second dose of BNT162b2 and 1 month after the second dose of BNT162b2$_{SA}$.

- Analysis methodology: GMR and the associated 2-sided 95% CI will be calculated in the same way as for the primary endpoints E1a and E2a (Section 6.1.2.1). The difference in percentages of participants with seroresponse and the associated 2-sided 95% CIs will be calculated in the same way as for the primary endpoints E1b and E2b (Section 6.1.2.2.1).

- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.

- Reporting results: The GMTs at each time point, GMRs, and the associated 2-sided 95% CIs will be provided. The counts, percentages of participants with seroresponse at each time point, the difference in percentages, and the associated 2-sided 95% CIs will be provided.

Figures:

Empirical RCDCs will be provided for SARS-CoV-2 SA and reference strain NTs at each time point.

6.2.1.9. SARS-CoV-2 SA NT at 1 Month After Dose 2 (BNT162b2-Naïve Participants)

6.2.1.9.1. Main Analyses

- Estimands:

  - N2a: GMR of SA NT 1 month after the second dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 (Section 2.1).

- Analysis set: Dose 2 evaluable and all-available immunogenicity populations (Section 4).

- Analysis time points: 1 month after the second dose of BNT162b2 and 1 month after the second dose of BNT162b2$_{SA}$.

- Analysis methodology: GMR and the associated 2-sided 97.5% CI will be calculated in the same way as for the primary endpoint N1a (Section 6.1.2.3.1). Statistical superiority of N2a will be assessed if noninferiority of N1a is established. Superiority of N2a will be declared if the lower bound of the 2-sided 97.5% CI for the GMR is greater than 1.

- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.

- Reporting results: The GMTs at each time point, GMRs, and the associated 2-sided 97.5% CIs will be provided.

Figures:

Empirical RCDCs will be provided for SARS-CoV-2 SA at each time point for each vaccine group.

6.2.1.10. Seroresponse to the SA Strain at 1 Month After Dose 2 (BNT162b2-Naïve Participants)

6.2.1.10.1. Main Analyses

- Estimands:

  - N2b: The difference in percentages of participants with seroresponse to the SA strain at 1 month after the second dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2 (Section 2.1).

- Analysis set: Dose 2 evaluable and all-available immunogenicity populations (Section 4).

- Analysis time points: 1 month after the second dose of BNT162b2 and 1 month after the second dose of BNT162b2$_{SA}$.

- Analysis methodology: The difference in percentages of participants with seroresponse and the associated 2-sided 97.5% CIs will be calculated in the same way as for the primary endpoint N1b (Section 6.1.2.4.1). Statistical superiority of N2b will be assessed if noninferiority of N1b is established. Superiority of N2b will be declared if the lower bound of the 2-sided 97.5% CI for the difference in percentages of participants with seroresponse is greater than 0%.

- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.

- Reporting results: The counts, percentages of participants with seroresponse at each time point, the difference in percentages, and the associated 2-sided 97.5% CIs will be provided.

6.2.1.11. Reference Strain NT at 1 Month After Dose 2 (BNT162b2-Naïve Participants)

6.2.1.11.1. Main Analyses

- Estimands:
  - GMR of reference strain NT 1 month after the second dose of BNT162b2$_{SA}$ to 1 month after the second dose of BNT162b2 (Section 2.1).
  - The difference in percentages of participants with seroresponse to the reference strain at 1 month after the second dose of BNT162b2$_{SA}$ and 1 month after the second dose of BNT162b2 (Section 2.1).
- Analysis set: Dose 2 evaluable and all-available immunogenicity populations (Section 4).
- Analysis time points: 1 month after the second dose of BNT162b2 and 1 month after the second dose of BNT162b2$_{SA}$.
- Analysis methodology: GMR and the associated 2-sided 95% CI will be calculated in the same way as for the primary endpoint N1a (Section 6.1.2.3.1). The difference in percentages of participants with seroresponse and the associated 2-sided 95% CIs will be calculated in the same way as for the primary endpoints N1b (Section 6.1.2.4.1).
- Intercurrent events and missing data: Titers below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.
- Reporting results: The GMTs at each time point, GMRs, and the associated 2-sided 95% CIs will be provided. The counts, percentages of participants with seroresponse at each time point, the difference in percentages, and the associated 2-sided 95% CIs will be provided.

Figures:

Empirical RCDCs will be provided for SARS-CoV-2 reference strain NTs at each time point for each vaccine group.

6.2.2. Vaccine Efficacy Endpoints (for Phase 2/3 Only)

6.2.2.1. COVID-19 Incidence per 1000 Person-Years of Follow-up

6.2.2.1.1. Main Analyses

- Estimands:
  - 100 × (1 – IRR) [ratio of confirmed COVID-19 illness from 14 days after the second dose per 1000 person-years of follow-up in participants without evidence of infection (prior to 14 days after receipt of the second dose) for the active vaccine group to the placebo group (Section 2.1)].

- 100 × (1 – IRR) [ratio of confirmed COVID-19 illness from 14 days after the second dose per 1000 person-years of follow-up in participants with and without evidence of infection (prior to 14 days after receipt of the second dose) for the active vaccine group to the placebo group (Section 2.1)].

- Analysis set: Evaluable efficacy (14 days) and all-available efficacy populations (Section 4).

- Analysis time point: End of the surveillance period or at IAs if requested.

- Analysis methodology: The same method used for primary VE endpoints will be applied (Section 6.1.3.1.1).

- Intercurrent events and missing data: Missing efficacy data will not be imputed in the main analyses.

- Reporting results: The same output generated for primary VE endpoints will be provided (Section 6.1.3.1.1).

6.2.2.2. Confirmed Severe COVID-19 Incidence per 1000 Person-Years of Follow-up

6.2.2.2.1. Main Analyses

- Estimands:

  - 100 × (1 – IRR) [ratio of confirmed severe COVID-19 illness from 7 days and from 14 days after the second dose per 1000 person-years of follow-up in participants without evidence of infection (prior to 7 days and 14 days after receipt of the second dose) for the active vaccine group to the placebo group (Section 2.1)].

  - 100 × (1 – IRR) [ratio of confirmed severe COVID-19 illness from 7 days and from 14 days after the second dose per 1000 person-years of follow-up in participants with and without evidence of infection (prior to 7 days and 14 days after receipt of the second dose) for the active vaccine group to the placebo group (Section 2.1)].

- Analysis set: Evaluable efficacy (7 days and 14 days) and all-available efficacy populations (Section 4).

- Analysis time point: End of the surveillance period or at IAs if requested.

- Analysis methodology: The same method used for primary VE endpoints will be applied (Section 6.1.3.1.1).

- Intercurrent events and missing data: Missing efficacy data will not be imputed in the main analyses.

- Reporting results: The same output generated for primary VE endpoints will be provided (Section 6.1.3.1.1).

6.2.2.2.2. Supplemental Analyses

All severe COVID-19 cases occurring after Dose 1 will be summarized descriptively.

After the final efficacy analyses at 164 first primary cases, updated efficacy analyses will be performed for severe COVID-19 incidence from 7 days after the second dose with additional data accrued. The point estimate of VE in the blinded follow-up period and associated 2-sided 95% CI will be derived using the Clopper Pearson method adjusted for surveillance time, and the posterior probability (ie, P[VE >30%|data]) will be provided.

In addition to the protocol definition of severe COVID-19, supportive analyses using the CDC definition of severe COVID-19 will be performed.

6.2.2.3. Confirmed COVID-19 Incidence per 1000 Person-Years of Follow-up (According to the CDC-Defined Symptoms)

6.2.2.3.1. Main Analyses

- Estimands:
  - 100 × (1 – IRR) [ratio of confirmed COVID-19 illness according to the CDC-defined symptoms from 7 days and from 14 days after the second dose per 1000 person-years of follow-up in participants without evidence of infection (prior to 7 days and 14 days after receipt of the second dose) for the active vaccine group to the placebo group (Section 2.1)].
  - 100 × (1 – IRR) [ratio of confirmed COVID-19 illness according to the CDC-defined symptoms from 7 days and from 14 days after the second dose per 1000 person-years of follow-up in participants with and without evidence of infection (prior to 7 days and 14 days after receipt of the second dose) for the active vaccine group to the placebo group (Section 2.1)].
- Analysis set: Evaluable efficacy (7 days and 14 days) and all-available efficacy populations (Section 4).
- Analysis time point: End of the surveillance period.
- Analysis methodology: Assessment of VE will be performed for centrally confirmed COVID-19 according to the CDC-defined symptoms from 7 days and from 14 days after the receipt of the second dose of study intervention onwards, and will be estimated by 100 × (1 – IRR), where IRR is the calculated ratio of COVID-19 illness rate according to the CDC-defined symptoms per 1000 person-years of follow-up in the active vaccine group to the corresponding illness rate in the placebo group after the second dose. The 2-sided 95% CI for VE will be derived using the Clopper-Pearson method adjusted for surveillance time.
- Intercurrent events and missing data: Missing efficacy data will not be imputed in the main analyses.

- Reporting results: VE and the associated 2-sided 95% CIs derived using the Clopper-Pearson method adjusted for surveillance time will be provided.

6.2.2.4. Incidence of Asymptomatic SARS-CoV-2 Infection per 1000 Person-Years of Follow-up (According to the N-Binding Antibody Seroconversion)

6.2.2.4.1. Main Analyses

- Estimands:
  - 100 × (1 – IRR) [ratio of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on N-binding antibody seroconversion in participants with no serological or virological evidence of past SARS-CoV-2 infection or confirmed COVID-19 for the active vaccine group to the placebo group (Section 2.1)].
- Analysis set: Evaluable efficacy (seroconversion) and all-available efficacy populations (Section 4).
- Analysis time point: End of the surveillance period.
- Analysis methodology: An asymptomatic case (Appendix 4) is defined as positive N-binding antibody at a post–Dose 2 visit in participants without serological evidence of infection (determined by negative N-binding antibody) at Visit 1 or virological evidence of infection (determined by negative NAAT at Visit 1 and Visit 2 and at the time of a potential COVID-19 illness). A secondary definition will be applied without the requirement for a negative NAAT at Visit 2. VE will be estimated by 100 × (1 - IRR), where IRR is the calculated ratio of asymptomatic infection per 1000 person-years of follow-up in the active vaccine group to the corresponding infection in the placebo group. The 2-sided 95% CI for VE will be derived using the Clopper-Pearson method adjusted for surveillance time. The VE is demonstrated if the lower bound of the 2-sided 95% CI for VE is greater than 20%. The analysis of the primary definition of asymptomatic cases will be based on the evaluable efficacy (seroconversion) population and the Dose 2 all-available efficacy population. The analysis of the secondary definition of asymptomatic cases will be based on the Dose 1 all-available efficacy population.
- Intercurrent events and missing data: Missing efficacy data will not be imputed in the main analyses.
- Reporting results: VE and the associated 2-sided 95% CIs derived using the Clopper-Pearson method adjusted for surveillance time will be provided.

6.2.2.4.2. Supplemental Analyses

Descriptive summary of VE against asymptomatic infection over different time intervals (ie, prior to 1 month after Dose 2, from 1 month after Dose 2 onward), along with the associated 2-sided 95% CI, will be calculated using the same method as above.

6.2.2.5. Incidence of Asymptomatic SARS-CoV-2 Infection per 1000 Person-Years of Follow-up (According to the Central Laboratory–Confirmed NAAT)

6.2.2.5.1. Main Analyses

- Estimands:
  - 100 × (1 – IRR) [ratio of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on central laboratory–confirmed NAAT in participants without serological or virological evidence of infection (up to the start of the asymptomatic surveillance period) for the active vaccine group to the placebo group (Section 2.1)].
- Analysis set: Evaluable efficacy (asymptomatic surveillance) and all-available efficacy populations (Section 4) and only participants who consented to participate in the asymptomatic surveillance.
- Analysis time point: End of the surveillance period.
- Analysis methodology: An asymptomatic case definition based on central laboratory–confirmed NAAT can be found in Appendix 5. VE will be estimated by 100 × (1 - IRR), where IRR is the calculated ratio of asymptomatic infection per 1000 person-years of follow-up in the active vaccine group to the corresponding infection in the placebo group. The 2-sided 95% CI for VE will be derived using the Clopper-Pearson method adjusted for surveillance time. The success criterion is met if lower bound of the 2-sided 95% CI for VE is greater than 20%.
- Intercurrent events and missing data: Missing efficacy data will not be imputed in the main analyses.
- Reporting results: VE and the associated 2-sided 95% CIs derived using the Clopper-Pearson method adjusted for surveillance time will be provided.

6.3. Exploratory Endpoints

6.3.1. Safety Endpoints (for Phase 1 Boostability Assessment Only)

6.3.1.1. Local Reactions

6.3.1.1.1. Main Analysis

- Estimand: The percentage of participants reporting local reactions (redness, swelling, and pain at the injection site) within 7 days after Dose 3 (Section 2.1).
- Analysis set: Phase 1 participants who received a third dose of BNT162b2 6 to 12 months after the second dose of either BNT162b1 or BNT162b2.
- Analysis time point: Within 7 days after Dose 3.
- Analysis methodology: Descriptive statistics (Section 5.2.1).

- Intercurrent events and missing data: The participants without any e-diary data throughout the 7 days after vaccination will be excluded from the analysis at that particular vaccination; missing values will not be imputed.

- Reporting results: Descriptive statistics for each and any local reaction after Dose 3 by initial vaccine and age group will be presented by maximum severity and cumulatively across severity levels. Confirmed e-diary errors will be excluded from the analysis. Descriptive summary statistics will include counts and percentages of participants with the indicated endpoint and the associated 2-sided Clopper-Pearson 95% CIs.

6.3.1.1.2. Supplementary Analyses

To support the assessment of local reactions, the following endpoints (as defined in Section 3.1.1.1) will be summarized with the same analysis time point and analysis population, analysis methodology, and appropriate reporting results. Confirmed e-diary errors will be excluded from these analyses.

- Duration (days) of each local reaction after each dose.

- Onset day of each local reaction after each dose.

These continuous endpoints will be summarized by displaying n, mean, median, standard deviation, minimum, and maximum for each initial vaccine and age group.

Figures:

Bar charts with the proportions of participants for each local reaction throughout 7 days will be plotted for each initial vaccine and age group. The bars will be divided into severity categories to highlight the proportions of participants by maximum severity.

6.3.1.2. Systemic Events

6.3.1.2.1. Main Analysis

- Estimand: The percentage of participants reporting systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain) within 7 days after Dose 3 (Section 2.1).

- Analysis set: Phase 1 participants who received a third dose of BNT162b2 6 to 12 months after the second dose of either BNT162b1 or BNT162b2.

- Analysis time point: Within 7 days after Dose 3.

- Analysis methodology: Descriptive statistics (Section 5.2.1).

- Intercurrent events and missing data: The participants without any e-diary data throughout the 7 days after vaccination will be excluded from the analysis at that particular vaccination; missing values will not be imputed.

- Reporting results: Descriptive statistics for each systemic event after Dose 3 in each initial vaccine and age group will be presented by maximum severity and cumulatively across severity levels. Descriptive summary statistics will include counts and percentages of participants with the indicated endpoint and the associated 2-sided Clopper-Pearson 95% CIs.

6.3.1.2.2. Supplementary Analyses

The following endpoints for assessment of systemic events will be summarized similarly to the assessment of local reactions:

- Duration of each systemic event after each dose.
- Onset day of each systemic event after each dose.

These continuous endpoints will be summarized by displaying n, mean, median, standard deviation, minimum, and maximum for each initial vaccine and age group.

The use of antipyretic medication (see Section 3.1.1.3) will be summarized similarly to systemic events, except that there is no severity level associated with the use of antipyretic medication.

Figures:

Bar charts with the proportions of participants reporting each systemic event throughout 7 days after Dose 3 will be plotted for each initial vaccine and age group. The bars will be divided into severity categories to highlight the proportions of participants by severity.

6.3.1.3. Adverse Events

6.3.1.3.1. Main Analysis

- Estimand: The percentage of participants reporting AEs from Dose 3 to 1 month after Dose 3 (Section 2.1).
- Analysis set: Phase 1 participants who received a third dose of BNT162b2 6 to 12 months after the second dose of either BNT162b1 or BNT162b2.
- Analysis time point: Dose 3 to 1 month after Dose 3.
- Analysis methodology: Descriptive statistics (Section 5.2.1).
- Intercurrent events and missing data: Partial AE dates will be imputed using the Pfizer standard algorithm.
- Reporting results: AEs will be categorized according to MedDRA terms. Descriptive summary statistics (counts, percentages, and associated Clopper-Pearson 95% CIs) will be provided for any AEs for each initial vaccine and age group.

6.3.1.3.2. Supplementary Analyses

Immediate AEs (within the first 30 minutes after Dose 3) will also be summarized for each initial vaccine and age group.

6.3.1.4. Serious Adverse Events

6.3.1.4.1. Main Analyses

- Estimand: The percentage of participants reporting SAEs from Dose 3 to 1 month after Dose 3 (Section 2.1).
- Analysis set: Phase 1 participants who received a third dose of BNT162b2 6 to 12 months after the second dose of either BNT162b1 or BNT162b2.
- Analysis time point: Dose 3 to 1 month after Dose 3.
- Analysis methodology: Descriptive statistics (Section 5.2.1).
- Intercurrent events and missing data: Partial SAE dates will be imputed using the Pfizer standard algorithm.
- Reporting results: SAEs will be categorized according to MedDRA terms. Counts, percentages, and the associated Clopper-Pearson 95% CIs of SAEs from Dose 3 to 1 month after Dose 3 will be provided for each initial vaccine and age group.

6.3.2. Vaccine Efficacy Endpoints (for Phase 2/3 Only)

6.3.2.1. COVID-19 Incidence per 1000 Person-Years of Blinded Follow-up

6.3.2.1.1. Main Analyses

- Estimands:
  - 100 × (1 – IRR) [ratio of confirmed COVID-19 illness based on central laboratory or locally confirmed NAAT from 7 days after the second dose through the blinded follow-up period per 1000 person-years of follow-up in participants without evidence of infection (prior to 7 days after receipt of the second dose) for the active vaccine group to the placebo group (Section 2.1)].
  - 100 × (1 – IRR) [ratio of confirmed COVID-19 illness based on central laboratory or locally confirmed NAAT from 7 days after the second dose through the blinded follow-up period per 1000 person-years of follow-up in participants with and without evidence of infection for the active vaccine group to the placebo group (Section 2.1)].
- Analysis set: Evaluable efficacy (7 days) and all-available efficacy populations (Section 4).
- Analysis time point: End of the surveillance period (blinded follow-up).

- Analysis methodology: After the primary objectives are met at the final analysis of at least 164 first primary cases, the study will continue with blinded follow-up until the participant is unblinded at the time of being eligible for receipt of BNT162b2 according to recommendations detailed separately, and available in the electronic study reference portal, or no later than at approximately Visit 4. A descriptive update of VE will be provided with additional follow-up data. VE = 100 × (1 – IRR) will be estimated with confirmed COVID-19 illness from 7 days after the second dose through the blinded follow-up period. The 2-sided 95% CI for VE will be derived using the Clopper-Pearson method adjusted for surveillance time.

- Intercurrent events and missing data: Missing efficacy data will not be imputed in the main analyses.

- Reporting results: VE and the associated 2-sided 95% CIs derived using the Clopper-Pearson method adjusted for surveillance time.

6.3.2.1.2. Supportive Analyses

Supportive analysis of time to confirmed COVID-19 illness will be performed using Kaplan-Meier cumulative incidence curves. Participants who were randomized to placebo will be censored at the time of receipt of BNT162b2. An RPSFT model may be explored to reconstruct data for the control arm.

VE at different follow-up time intervals and against different variant strains may be assessed.

6.3.2.2. COVID-19 Incidence per 1000 Person-Years of Follow-up

6.3.2.2.1. Main Analyses

- Estimands:

  - COVID-19 incidence based on central laboratory or locally confirmed NAAT from 7 days after the second dose through the entire study follow-up period prior to receiving the third dose of BNT162b2 per 1000 person-years of follow-up in participants without evidence of infection (prior to 7 days after receipt of the second BNT162b2 vaccination) who received BNT162b2 at initial randomization or subsequently (Section 2.1).

  - COVID-19 incidence based on central laboratory or locally confirmed NAAT from 7 days after the second dose through the entire study follow-up period prior to receiving the third dose of BNT162b2 per 1000 person-years of follow-up in participants with and without evidence of infection who received BNT162b2 at initial randomization or subsequently (Section 2.1).

- Analysis set: Evaluable efficacy (7 days) and all-available efficacy populations (Section 4). For participants who were randomized to placebo and subsequently received BNT162b2 after being eligible according to recommendations detailed separately, and available in the electronic study reference portal, or no later than at approximately Visit 4, the time of receipt of BNT162b2 will be reconsidered as baseline. All rules for determining evaluable efficacy and all-available efficacy populations will be similarly applied.

- Analysis time point: End of the surveillance period.

- Analysis methodology: Incidence rate (per 1000 person-years of follow-up) and exact 2-sided 95% CI based on Poisson distribution (Section 5.2.2) for confirmed COVID-19 illness from 7 days after the second BNT162b2 vaccination will be provided for participants who received BNT162b2 at initial randomization and subsequently. Kaplan-Meier cumulative incidence of COVID-19 cases over time will be plotted.

- Intercurrent events and missing data: Missing efficacy data will not be imputed in the main analyses.

- Reporting results: Incidence rate and the associated 2-sided 95% CIs, and Kaplan-Meier cumulative incidence curve will be provided.

6.3.2.3. COVID-19 Incidence per 1000 Person-Years of Follow-up for Participants Receiving BNT162b2 as a Third Dose as Part of Protocol Amendment 18

6.3.2.3.1. Main Analyses

- Estimands:

  - COVID-19 incidence based on central laboratory or locally confirmed NAAT from 7 days after Dose 3 per 1000 person-years of follow-up in participants without evidence of infection (prior to 7 days after receipt of Dose 3) (Section 2.1).

  - COVID-19 incidence based on central laboratory or locally confirmed NAAT from 7 days after Dose 3 per 1000 person-years of follow-up in participants with and without evidence of infection (Section 2.1).

- Analysis set: Participants who received BNT162b2 as a third dose as part of protocol amendment 18. All rules for determining all-available efficacy populations will be similarly applied.

- Analysis time point: End of the surveillance period.

- Analysis methodology: Incidence rate (per 1000 person-years of follow-up) and exact 2-sided 95% CI based on Poisson distribution (Section 5.2.2) for confirmed COVID-19 from 7 days after the third BNT162b2 vaccination will be provided. Kaplan-Meier cumulative incidence of COVID-19 cases over time will be plotted.

- Intercurrent events and missing data: Missing efficacy data will not be imputed in the main analyses.

- Reporting results: Incidence rate and the associated 2-sided 95% CIs, and Kaplan-Meier cumulative incidence curve will be provided.

6.3.2.4. Incidence of Asymptomatic SARS-CoV-2 Infection per 1000 Person-Years of Follow-up (According to the N-Binding Antibody Seroconversion)

6.3.2.4.1. Main Analyses

- Estimands:

  - Incidence of asymptomatic SARS-CoV-2 infection through the entire study of follow-up period per 1000 person-years of follow-up based on N-binding antibody seroconversion in participants who received BNT162b2 and who have no serological or virological evidence of past SARS-CoV-2 infection or confirmed COVID-19.

- Analysis set: Evaluable efficacy and all-available efficacy populations (Section 4).

- Analysis time point: End of the surveillance period.

- Analysis methodology: Incidence rate (per 1000 person-years of follow-up) and exact 2-sided 95% CI based on Poisson distribution (Section 5.2.2) for asymptomatic infection will be provided for participants who received BNT162b2.

- Intercurrent events and missing data: Missing efficacy data will not be imputed in the main analyses.

- Reporting results: Incidence rate and the associated 2-sided 95% CIs will be provided.

6.3.2.5. Incidence of Asymptomatic SARS-CoV-2 Infection per 1000 Person-Years of Follow-up (According to the Central Laboratory–Confirmed NAAT)

6.3.2.5.1. Main Analyses

- Estimands:

  - 100 × (1 – IRR) [ratio of asymptomatic SARS-CoV-2 infection per 1000 person-years of follow-up based on central laboratory–confirmed NAAT in participants with serological or virological evidence of past infection (up to the start of the asymptomatic surveillance period) for the active vaccine group to the placebo group (Section 2.1)].

- Analysis set: Evaluable efficacy (asymptomatic surveillance) and all-available efficacy populations (Section 4) and only participants who are consented to participate in the asymptomatic surveillance.

- Analysis time point: End of the surveillance period.

- Analysis methodology: VE will be estimated by 100 × (1 - IRR), where IRR is the calculated ratio of asymptomatic infection per 1000 person-years of follow-up in the active vaccine group to the corresponding infection in the placebo group. The 2-sided 95% CI for VE will be derived using the Clopper-Pearson method adjusted for surveillance time.

- Intercurrent events and missing data: Missing efficacy data will not be imputed in the main analyses.

- Reporting results: VE and the associated 2-sided 95% CIs derived using the Clopper-Pearson method adjusted for surveillance time will be provided.

6.3.3. Immunogenicity Endpoints

6.3.3.1. SARS-CoV-2 Reference-Strain Neutralizing Titers, SARS-CoV-2 SA-Variant Neutralizing Titers, and Full-Length S-Binding or S1-Binding IgG Levels (Phase 1)

6.3.3.1.1. Main Analyses

- Estimands:
  - GMTs/GMCs (Section 2.1).
  - GMFR from before Dose 3 to each subsequent time point, ie, 7 days and 1 month after Dose 3 (Section 2.1).

- Analysis set: Phase 1 participants who received a third dose of BNT162b2 6 to 12 months after the second dose of either BNT162b1 or BNT162b2.

- Analysis time points: At Dose 3 and 7 days and 1 month after Dose 3.

- Analysis methodology: GMs and the associated 2-sided CIs will be derived by calculating means and CIs on the natural log scale based on Student's t-distribution, and then exponentiating the results (Section 5.2.3.1). GMFRs will be limited to participants with nonmissing values prior to Dose 3 and the subsequent time point. The GMFR will be calculated by exponentiating the mean of the difference of logarithmically transformed assay results (later time point – earlier time point). Two-sided CIs will be obtained by calculating CIs using Student's t-distribution for the mean difference of the logarithmically transformed assay results and exponentiating the confidence limits (Section 5.2.3.2).

- Intercurrent events and missing data: Concentrations below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.

- Reporting results: The GMTs/GMCs, GMFRs, and the associated 2-sided 95% CIs will be provided at each time point by initial vaccine and age group.

6.3.3.2. SARS-CoV-2 Reference-Strain Neutralizing Titers and SARS-CoV-2 SA-Variant Neutralizing Titers at 1 Month After Dose 3 vs SARS-CoV-2 Reference-Strain Neutralizing Titers at 1 Month After Dose 2 (Phase 1)

6.3.3.2.1. Main Analyses

- Estimands:
  - GMR of SARS-CoV-2 reference-strain neutralizing titers at 1 month after Dose 3 to SARS-CoV-2 reference-strain neutralizing titers at 1 month after Dose 2 (Section 2.1).
  - GMR of SARS-CoV-2 SA-variant neutralizing titers at 1 month after Dose 3 to SARS-CoV-2 reference-strain neutralizing titers at 1 month after Dose 2 (Section 2.1).
- Analysis set: Phase 1 participants who received a third dose of BNT162b2 6 to 12 months after the second dose of either BNT162b1 or BNT162b2.
- Analysis time points: 1 month after Dose 3.
- Analysis methodology: GMRs will be limited to participants with nonmissing values at both time points and provided by initial vaccine and age group. The GMR will be calculated as the mean of the difference of logarithmically transformed assay results (eg, SARS-CoV-2 SA-variant neutralizing titers at 1 month after Dose 3 minus reference-strain titers at 1 month after Dose 2 for each participant) and exponentiating the mean (Section 5.2.3.3). Two-sided CIs will be obtained by calculating CIs using Student's t-distribution for the mean difference of the logarithmically transformed assay results and exponentiating the confidence limits (Section 5.2.3.3).
- Intercurrent events and missing data: Concentrations below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.
- Reporting results: The GMRs and the associated 2-sided 95% CIs will be provided by initial vaccine and age group.

6.3.3.3. SARS-CoV-2 Neutralizing Titers, and Full-length S-Binding or S1-Binding IgG Levels (Phase 2/3)

6.3.3.3.1. Main Analyses

- Estimands:
  - GMTs/GMCs (Section 2.1).
  - GMFR from before vaccination to each subsequent time point after vaccination (Section 2.1).

- Analysis set: Dose 2 evaluable and all-available immunogenicity populations (Section 4).
- Analysis time points: 1, 6, 12, and 24 months after completion of vaccination in participants with and without serological or virological evidence of SARS-CoV-2 infection before vaccination.
- Analysis methodology: GMs and the associated 2-sided CIs will be derived by calculating means and CIs on the natural log scale based on Student's t-distribution, and then exponentiating the results Section 5.2.3.1). GMFRs will be limited to participants with nonmissing values prior to the first dose and at the postvaccination time point. The GMFR will be calculated by exponentiating the mean of the difference of logarithmically transformed assay results (later time point – earlier time point). Two-sided CIs will be obtained by calculating CIs using Student's t-distribution for the mean difference of the logarithmically transformed assay results and exponentiating the confidence limits (Section 5.2.3.2). Empirical RCDCs will be provided for SARS-CoV-2 neutralizing titers and full-length S-binding or S1-binding IgG levels after Dose 1 and after Dose 2.
- Intercurrent events and missing data: Serology data deemed unevaluable because of noncompliance with the key protocol criteria will be excluded. Titers/concentrations below the LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. However, this calculation may be adjusted based upon additional data from the assay. Missing data will not be imputed.
- Reporting results: The GMTs/GMCs at each time point and GMFRs from before vaccination to each subsequent time point after vaccination and the associated 2-sided 95% CIs, and the empirical RCDCs after Dose 1 and after Dose 2, will be provided.

6.3.3.3.2. Additional Exploratory Analyses

The above analyses will be performed by baseline SARS-CoV-2 status (positive or negative).

6.3.3.4. SARS-CoV-2 Neutralizing Titers in Participants Receiving Booster Doses (Phase 3)

6.3.3.4.1. Main Analyses

- Estimands:
  - GMTs (Section 2.1).
  - GMFR from Dose 3 to each subsequent time point (Section 2.1).
- Analysis set: Participants receiving a third dose of BNT162b2 (at 30 µg or a lower dose of 5 or 10 µg) or a third or fourth dose of BNT162b2$_{SA}$.
- Analysis time points: Dose 3 and each subsequent time point.
- Analysis methodology: The same method as described in Section 6.3.3.3 will be applied.

- Intercurrent events and missing data: The same method as described in Section 6.3.3.3 will be applied.

- Reporting results: The GMTs at Dose 3 and each subsequent time point and the GMFRs from Dose 3 to each subsequent time point and associated 2-sided 95% CIs will be provided for each vaccine group and age group.

6.3.3.5. Serological Responses in Participants With Confirmed COVID-19, Confirmed Severe COVID-19, and SARS-CoV-2 Infection Without Confirmed COVID-19

The analyses described above for exploratory immunogenicity endpoints may be applied to the participants with confirmed COVID-19, confirmed severe COVID-19, and SARS-CoV-2 infection without confirmed COVID-19.

6.3.3.6. SARS-CoV-2 NTs for Any VOCs (Phase 3, Boostability and Protection Against Emerging VOCs)

GMs and associated 2-sided 95% CIs of any anti-VOC neutralizing titers will be provided at each time point for each group.

6.3.4. Additional Analysis

The ratios of (GMFR A to GMFR B) and (GMFR A to GMFR C) may be explored, where GMFR A is the geometric mean of the ratio of the SARS-CoV-2 neutralizing titer at the postvaccination time point to the corresponding titer at the prevaccination time point, GMFR B is the geometric mean of the ratio of the S1-binding IgG level at the postvaccination time point to the corresponding antibody level at the prevaccination time point, and GMFR C is the geometric mean of the ratio of the RBD-binding IgG level at the postvaccination time point to the corresponding antibody level at the prevaccination time point (Section 5.2.3.4).

The safety data and immunogenicity results for individuals with confirmed stable HIV disease will be summarized descriptively. Furthermore, VE may be assessed if there is a sufficient number of COVID-19 cases in this group of participants.

The safety and immunogenicity results for individuals 16 to 55 years of age vaccinated with study intervention produced by manufacturing “Process 1” and each lot of “Process 2” will be summarized descriptively.

AEs and SAEs reported during the open-label follow-up period will be summarized separately for participants who were unblinded at the time of being eligible for receipt of BNT162b2 according to recommendations detailed separately, and available in the electronic study reference portal, or no later than at approximately Visit 4. To account for different durations of follow-up time due to unblinding in the study, AEs and SAEs during the blinded follow-up period and open label follow-up period may be summarized as incidence rates adjusted by exposure time.

Exploratory analyses to investigate possible immunological correlates with efficacy, and characterization of infecting SARS-CoV-2 variants, may be conducted.

The cell-mediated immune response and additional humoral immune response parameters to the reference strain and SA will be summarized for the subset of participants with PBMC samples collected.

6.4. Subgroup Analysis

Subgroup analyses based on age, race, ethnicity, sex, country, and baseline SARS-CoV-2 status will be performed on all primary safety and efficacy endpoints (as supplemental analyses) for Phase 2/3.

6.5. Baseline and Other Summaries and Analyses

6.5.1. Baseline Summaries

6.5.1.1. Demographic Characteristics

Demographic characteristics, including age group, sex, race, ethnicity, and classification of BMI will be summarized for the safety population for each vaccine group and overall.

6.5.1.2. Medical History

Each reported medical history term will be mapped to a SOC and PT according to MedDRA. The number and percentage of vaccinated participants having at least 1 diagnosis, overall and at each SOC and PT level, will be summarized by vaccine group for the overall safety population.

The number and proportion of participants with comorbidities that increase the risk for severe COVID-19 illness will be summarized by each vaccine group.

6.5.2. Study Conduct and Participant Disposition

6.5.2.1. Participant Disposition

The number and percentage of randomized participants will be included in the participant disposition summary. In addition, the numbers and percentages of participants who received vaccinations (Doses 1 and 2), who completed the follow-up visits (1 month after the second dose), and who withdrew before each follow-up visit along with the reasons for withdrawal will be tabulated by vaccine group (according to randomized group assignment). The reasons for withdrawal will be those as specified in the database.

Participants excluded from each analysis population will also be summarized separately along with the reasons for exclusion, by vaccine group.

Participants follow-up time after completion of vaccinations will be summarized by vaccine group.

6.5.2.2. Blood Samples for Assay

The number and percentage of randomized participants providing blood samples within and outside of protocol-specified time frames will be tabulated separately for each time point.

6.5.2.3. E-Diaries

The participants who were vaccinated and completed e-diaries after each dose will be summarized according to the vaccine actually received. Besides the analysis described in Section 6.1.1.1 and Section 6.1.1.2, the summary will also include the numbers and percentages of vaccinated participants not transmitting the e-diary, and transmitting the e-diary for any day in the required reporting period, by as-received vaccine group for each dose.

The safety population will be used.

6.5.3. Study Vaccination Exposure

6.5.3.1. Vaccination Timing and Administration

For each dose, the number and percentage of participants randomized and receiving each study intervention within the protocol-specified time frame, as well as before and after the specified time frame, will be tabulated for each vaccine group and overall for all randomized participants. The denominator for the percentages is the total number of randomized participants in the given vaccine group or overall.

In addition, the relation of randomized vaccine to actual vaccine received will be presented as a cross tabulation of the actual vaccine received versus the randomized vaccine.

A listing of participants showing the randomized vaccine and the vaccine actually received at each dose will be presented.

6.5.4. Prior/Concomitant Vaccination and Concomitant Medications

Each prior/concomitant vaccine will be summarized according to the ATC 4th-level classification. All vaccines received within 28 days before Dose 1 will be listed. The number and percentage of participants receiving each concomitant vaccine after Dose 1 will be tabulated by vaccine group. A summary will be provided for the interval between Dose 1 and 1 month after the second dose. The safety population will be used. Concomitant medications will be summarized in a similar way as concomitant vaccines.

6.6. Safety Summaries and Analyses

Local reaction, systemic event, AE, and SAE summaries and analyses are described under Primary Endpoint(s) (Section 6.1).

7. ANALYSES TIMING

7.1. Introduction of Interim Analysis

As this is a sponsor open-label study during Phase 1, the sponsor may conduct unblinded reviews of the data during the course of the study for the purpose of safety assessment, facilitating dose escalation decisions, and/or supporting clinical development.

During Phase 2/3, 4 IAs were planned to be performed by an unblinded statistical team after accrual of at least 32, 62, 92, and 120 cases. However, for operational reasons, the first planned IA was not performed. Consequently, 3 IAs are now planned to be performed after accrual of at least 62, 92, and 120 cases. At these IAs, futility and VE with respect to the first primary endpoint will be assessed as follows:

- VE for the first primary objective will be evaluated. Overwhelming efficacy will be declared if the first primary study objective is met. The criteria for success at an interim analysis are based on the posterior probability (ie, P[VE >30%|data]) at the current number of cases. Overwhelming efficacy will be declared if the posterior probability is higher than the success threshold. The success threshold for each interim analysis will be calibrated to protect overall type I error at 2.5%. Additional details about the success threshold or boundary calculation at each interim analysis can be found in Appendix 2.

- The study will stop for lack of benefit (futility) if the predicted probability of success at the final analysis or study success is <5%. The posterior predictive POS will be calculated using a beta-binomial model. The futility assessment will be performed for the first primary endpoint, and the futility boundary may be subject to change to reflect subsequent program-related decisions by the sponsor.

- Efficacy and futility boundaries will be applied in a nonbinding way.

Bayesian approaches require specification of a prior distribution for the possible values of the unknown vaccine effect, thereby accounting for uncertainty in its value. A minimally informative beta prior, beta (0.700102, 1), is proposed for $\theta = (1\text{-VE})/(2\text{-VE})$. The prior is centered at $\theta = 0.4118$ (VE=30%), which can be considered pessimistic. The prior allows considerable uncertainty; the 95% interval for θ is (0.005, 0.964) and the corresponding 95% interval for VE is (-26.2, 0.995).

Table 11 illustrates the boundary for efficacy and futility if, for example, IAs are performed after accrual of 32, 62, 92, and 120 cases in participants without evidence of infection before vaccination. Note that although the first IA was not performed, the statistical criterion for demonstrating success (posterior probability threshold) at the interim (>0.995) and final (>0.986) analyses remains unchanged. Similarly, the futility boundaries are not changed.

Table 11. Interim Analysis Plan and Boundaries for Efficacy and Futility

Analysis	Number of Cases	Success Criteria[a]	Futility Boundary
		VE Point Estimate (Case Split)	VE Point Estimate (Case Split)
IA1	32	76.9% (6:26)	11.8% (15:17)
IA2	62	68.1% (15:47)	27.8% (26:36)
IA3	92	62.7% (25:67)	38.6% (35:57)
IA4	120	58.8% (35:85)	N/A
Final	164	52.3% (53:111)	

Abbreviations: IA = interim analysis; N/A = not applicable; VE = vaccine efficacy.
Note: Case split = vaccine: placebo.
a. Interim efficacy claim: P(VE >30%|data) > 0.995; success at the final analysis: P(VE >30%|data) > 0.986.

Additional design operating characteristics (the boundary based on the number of cases observed in the vaccine group; the probabilities for efficacy and futility given assumed various VEs with a 1:1 randomization ratio) are listed in Table 12 and Table 13 for IAs conducted at 32, 62, 92, and 120 cases and the final analysis at 164 cases. Although the IA at 32 cases was not performed, the overall Type I error (overall probability of success when true VE=30%) will still be strictly controlled at 0.025 with the originally proposed success/futility boundaries.

Table 12. Statistical Design Operating Characteristics: Probability of Success or Failure for Interim Analyses

Vaccine Efficacy (%)	Interim Analysis 1 (Total Cases = 32)		Interim Analysis 2 (Total Cases = 62)		Interim Analysis 3 (Total Cases = 92)		Interim Analysis 4 (Total Cases = 120)
	Probability of Success (Cases in Vaccine Group ≤6)	Probability of Failure (Cases in Vaccine Group ≥15)	Probability of Success (Cases in Vaccine Group ≤15)	Probability of Failure (Cases in Vaccine Group ≥26)	Probability of Success (Cases in Vaccine Group ≤25)	Probability of Failure (Cases in Vaccine Group ≥35)	Probability of Success (Cases Vaccine Group ≤35)
30	0.006	0.315	0.003	0.231	0.002	0.239	0.002
50	0.054	0.078	0.051	0.056	0.063	0.103	0.075
60	0.150	0.021	0.160	0.010	0.175	0.019	0.160
70	0.368	0.003	0.310	<0.001	0.195	0.001	0.085
80	0.722	<0.001	0.238	<0.001	0.037	<0.001	0.003

Table 13. Statistical Design Operating Characteristics: Probability of Success for Final Analysis and Overall

Vaccine Efficacy (%)	Final Analysis (Total Cases = 164)	Overall Probability of Success
	Probability of Success (Cases in Vaccine Group ≤53)	
30	0.007	0.021
50	0.196	0.439
60	0.220	0.866
70	0.036	>0.999
80	<0.001	>0.999

If neither success nor futility has been declared after all IAs, the final analysis will be performed and the first primary objective will have been met if there are 53 or fewer cases observed in the vaccine group out of a total of 164 first confirmed cases from 7 days after receipt of the second dose of study intervention onwards.

Only the first primary endpoint will be analyzed at an IA. If the first primary objective is met, the second primary objective will be evaluated at the final analysis. After the primary objectives are met, the first 6 secondary VE endpoints will be evaluated sequentially in the

following order by the same method used for the evaluation of primary VE endpoints: (1) confirmed COVID-19 occurring from 14 days after the second dose in participants without evidence of infection and (2) in all participants; (3) confirmed severe COVID-19 occurring from 7 days after the second dose in participants without evidence of infection and (4) in all participants; (5) confirmed severe COVID-19 occurring from 14 days after the second dose in participants without evidence of infection and (6) in all participants.

Success thresholds for secondary VE endpoints will be appropriately chosen to control overall type I error at 2.5%. The remaining secondary VE endpoints will be evaluated descriptively to calculate the observed VE with 95% CIs.

7.2. Interim Analyses and Summaries

Statistical analyses will be carried out when the following data are available:

- Complete safety and immunogenicity analysis approximately 1 month after Dose 2 for Phase 1.
- Safety data through 7 days after Dose 2 and immunogenicity data through 1 month after Dose 2 from the first 360 participants enrolled (180 to active vaccine and 180 to placebo, stratified equally between 18 to 55 years and >55 to 85 years) in Phase 2/3.
- Safety data through 1 month after Dose 2 from at least 6000 participants enrolled (3000 to active vaccine and 3000 to placebo) in Phase 2/3. Additional analyses of safety data (with longer follow-up and/or additional participants) may be conducted if required for regulatory purposes.
- IAs for efficacy after accrual of at least 62, 92, and 120 cases and futility after accrual of at least 62 and 92 cases.
- Safety data through 1 month after Dose 2 and noninferiority comparison of SARS-CoV-2 neutralizing titers in participants 12 to 15 years of age compared to those in participants 16 to 25 years of age, 1 month after Dose 2.
- Descriptive analysis of immunogenicity and safety of "Process 1" and "Process 2" material, 1 month after Dose 2.
- Safety analyses approximately 1 month after Dose 3 for Phase 3 participants included in the booster evaluation (30 µg or low-dose booster) and approximately 1 month after Dose 2 for newly enrolled Phase 3 participants included in the BNT162b2$_{SA}$ evaluation.
- Immunogenicity analyses approximately 1 month after Dose 3 for Phase 3 participants included in the booster evaluation (30 µg or low-dose booster) and approximately 1 month after Dose 2 for newly enrolled Phase 3 participants included in the BNT162b2$_{SA}$ evaluation, when serology data for the reference strain or for the SA strain are available.

- Analysis of efficacy against asymptomatic SARS-CoV-2 (determined by asymptomatic seroconversion of N-binding antibody and/or asymptomatic SARS-CoV-2 infection based on central laboratory–confirmed NAAT) when a sufficient number of cases have accrued to evaluate the objective(s).

- Complete safety and efficacy analysis approximately 6 months after Dose 2 for all participants in Phase 2/3.

- Safety and efficacy analyses approximately 6 months after the third dose of BNT162b2 for participants who received a third dose of BNT162b2 as part of protocol amendment 18.

- Complete efficacy and persistence-of-immunogenicity analysis after complete data are available or at the end of the study.

All analyses conducted on Phase 2/3 data while the study is ongoing will be performed by an unblinded statistical team.

7.2.1. Data Monitoring Committee

This study will use an IRC, a DMC, and a group of internal case reviewers. The IRC is independent of the study team and includes only internal members. The DMC is independent of the study team and includes only external members. The IRC and DMC charters describe the role of the IRC and DMC in more detail.

8. REFERENCES

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9. APPENDICES

Appendix 1. List of Abbreviations

Abbreviation	Term
Abs	absolute
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ATC	Anatomic Therapeutic Chemical
BLQ	below the level of quantitation
BMI	body mass index
BUN	blood urea nitrogen
CDC	Centers for Disease Control and Prevention
CI	confidence interval
COVID-19	coronavirus disease 2019
CRF	case report form
DBP	diastolic blood pressure
DMC	data monitoring committee
E1a, E1b, etc	identifier for vaccine-experienced participants (with a and b representing GMR and seroresponse estimands, respectively)
ECMO	extracorporeal membrane oxygenation
e-diary	electronic diary
FiO_2	fraction of inspired oxygen
GM	geometric mean
GMC	geometric mean concentration
GMFR	geometric mean fold rise
GMR	geometric mean ratio
GMT	geometric mean titer
HIV	human immunodeficiency virus
HR	heart rate
IA	interim analysis
ICD	informed consent document
ICU	intensive care unit
IgG	immunoglobulin G
IND	indeterminate
IRC	internal review committee
IRR	illness rate ratio
IWR	interactive Web-based response
LLOQ	lower limit of quantitation
MAR	missing at random
MCH	mean corpuscular hemoglobin
MCHC	mean corpuscular hemoglobin concentration
MCV	mean corpuscular volume

Abbreviation	Term
MedDRA	Medical Dictionary for Regulatory Activities
N1a, N1b, etc	identifier for vaccine-naïve participants (with a and b representing GMR and seroresponse estimands, respectively)
N/A	not applicable
NAAT	nucleic acid amplification test
non-S	nonspike protein
NT	neutralizing titer
PaO_2	partial pressure of oxygen, arterial
PBMC	peripheral blood mononuclear cell
POS	probability of success
PT	preferred term
RBC	red blood cell
RBD	receptor-binding domain
RCDC	reverse cumulative distribution curve
RNA	ribonucleic acid
RPSFT	rank-preserving structural failure time
RR	respiratory rate
RT-PCR	reverse transcription–polymerase chain reaction
S	spike protein
S1	spike protein S1 subunit
SA	South Africa
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SBP	systolic blood pressure
SoA	schedule of activities
SOC	system organ class
SOP	standard operating procedure
SpO_2	oxygen saturation as measured by pulse oximetry
VE	vaccine efficacy
VOC	variant of concern
WBC	white blood cell
WHO	World Health Organization

Appendix 2. Details for Bayesian Design

Bayesian group sequential design will be implemented in the Phase 3 for this study.

Notation

(1) Let VE be vaccine efficacy, θ be the case rate (number of cases in the active vaccine group divided by the total number of cases), T_1 be the total person-time in the active vaccine group, T_0 be the total person-time in the placebo group, and r be the ratio of T_1 and T_0, ie, $r = T_1/T_0$. Note that $\theta = \frac{r(1-VE)}{r(1-VE)+1}$ and $VE = 1 - \frac{\theta}{r(1-\theta)}$.

(2) Let p be the posterior probability of VE greater than or equal to 30% given the observed data on subset of enrolled participants, ie:

$$p = \Pr(VE > 30\% \mid \text{observed data from subset of enrolled participants})$$

$$= \Pr\left(\theta < \frac{r(1-30\%)}{r(1-30\%)+1} \mid \text{observed data from subset of enrolled participants}\right)$$

Under the assumption that the numbers of cases in both vaccine groups, s_1 and s_0 for cases in the active vaccine group and cases in the placebo group, respectively, follow a Poisson distribution with parameter λ_1 (incidence rate) for the active vaccine group and λ_0 for the placebo group, we can assume that s_1 is binomially distributed with Binomial (s, θ), conditional on s, the total number of cases, and with $\theta = T_1 \lambda_1 / (T_1 \lambda_1 + T_0 \lambda_0)$.

A minimally informative beta prior, Beta(0.700102, 1) is selected as the prior distribution of θ. The prior distribution is chosen such that the mean is equal to 0.4118 corresponding to VE = 30% which can be considered pessimistic. Meanwhile, the prior allows for considerable uncertainty, ie, 95% credible interval for θ is (0.005, 0.964) corresponding to 95% credible interval, (-26.2, 0.995), for VE.

Decision Algorithm for Efficacy

At certain interim analysis and final analysis, let n be the total number of observed cases and n_v be the number of observed cases from the vaccine group. For beta-binomial model, the posterior distribution of θ will be derived as Beta($\alpha' = 0.700102 + n_v$, $\beta' = 1 + n - n_v$). At each interim and final analysis p will be used for efficacy decision making in the following way:

(a) At interim analyses, efficacy is declared if $p > 99.50\%$.

(b) At final analysis, efficacy is declared if $p > 98.60\%$.

In participants without evidence of infection prior to 7 days after the second dose, IAs will be performed after accrual of at least 62, 92, and 120 cases, and final analysis will be performed after accrual of at least 164 cases.

Based on the criterion (b), at final analysis, efficacy will be declared if there are less than or equal to 53 cases observed in the vaccine group among the total number of 164 cases.

Bayesian 95% credible interval for θ can be calculated using the 2.5th percentile and the 97.5th percentile of posterior distribution, ie, Beta(α'=0.700102 + n_v , β'=1 + n - n_v). Thus, the 95% credible interval for VE can be obtained correspondingly due to the relationship between VE and θ, where $VE = 1 - \frac{\theta}{r(1-\theta)}$.

Decision Algorithm for Futility

Let Y be the random variable for the number of cases in the vaccine group at the final analysis. At certain interim analysis given the total number of observed cases n and the number of observed cases from the vaccine group n_v, the posterior probability of success q can be expressed as:

q = Pr (Y ≤ 53 | observed data, ie, n and n_v, from subset of enrolled participants)

q can be calculated analytically using posterior predictive distribution of Y, ie, Beta-Binomial distribution with parameters (n', α', β'). The probability mass function of the posterior predictive distribution is:

$$\Pr(Y = y | n', \alpha', \beta') = \binom{n'}{y} \frac{B(y + \alpha',\ n' - y + \beta')}{B(\alpha', \beta')}$$

Thus the posterior probability of success at the interim analysis can be calculated as:

q = Pr (Y ≤ 53 – n_v | n' = 164 – n, α'=0.700102 + n_v , β'=1 + n - n_v)

At interim analyses, futility is declared if q < 5.0%.

Appendix 3. IRR and VE Derivation

COVID-19 Case Definitions

Two definitions of SARS-CoV-2–related cases, and SARS-CoV-2–related severe cases, will be considered (for both, the onset date of the case will be the date that symptoms were first experienced by the participant; if new symptoms are reported within 4 days after resolution of all previous symptoms, they will be considered as part of a single illness):

Confirmed COVID-19: presence of at least 1 of the following symptoms and SARS-CoV-2 NAAT positive during, or within 4 days before or after, the symptomatic period, either at the central laboratory or at a local testing facility (using an acceptable test):

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

The second definition, which may be updated as more is learned about COVID-19, will include the following additional symptoms defined by the CDC (listed at https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html):

- Fatigue;
- Headache;
- Nasal congestion or runny nose;
- Nausea.

Confirmed severe COVID-19: confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (RR ≥30 breaths per minute, HR ≥125 beats per minute, SpO_2 ≤93% on room air at sea level, or PaO_2/FiO_2 <300 mm Hg);
- Respiratory failure (defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation, or ECMO);
- Evidence of shock (SBP <90 mm Hg, DBP <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction*;
- Admission to an ICU;
- Death.

The second definition, which may be updated as more is learned about COVID-19, will include the following outcomes defined by the CDC (listed at https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions):

- Hospitalization;
- Admission to the ICU;
- Intubation or mechanical ventilation;
- Death.

The DMC may recommend modification of the definition of severe disease according to emerging information.

* Three blinded case reviewers (medically qualified Pfizer staff members) will review all potential COVID-19 illness events. If a NAAT-confirmed case in Phase 2/3 may be considered severe, or not, solely on the basis of this criterion, the blinded data will be reviewed by the case reviewers to assess whether the criterion is met; the majority opinion will prevail.

In addition, a serological definition will be used for participants without clinical presentation of COVID-19:

- Confirmed seroconversion to SARS-CoV-2 without confirmed COVID-19: positive N-binding antibody result in a participant with a prior negative N-binding antibody result.

Surveillance Times

Fundamental to this VE trial is the surveillance for cases satisfying various endpoints within each participant that may occur during the trial. Endpoint and participant combinations where surveillance is applicable require identification of the start and the end of the surveillance period in order to determine the participant-level endpoint surveillance time. For all VE-related endpoints in this study, the start-of-surveillance times are summarized as follows:

Endpoint's Associated Participant-Level Population	Start-of-Surveillance Time
Evaluable efficacy (7 days)	Dose 2 + 7 days
Dose 2 all-available efficacy	Dose 2 + 7 days
Evaluable efficacy (14 days)	Dose 2 + 14 days
Dose 2 all-available efficacy	Dose 2 + 14 days
Dose 1 all-available efficacy	Dose 1

For all VE-related endpoints in this study, the end of a surveillance period for each participant is the earliest of the following events:

- When the first COVID-19 case occurs.
- When the participant's end of the study occurs due to, eg, withdrawal or death or trial completion, etc.
- When the participant has a first important protocol violation (only for analysis based on the evaluable efficacy population).
- When the participant is unblinded at the time of being eligible for receipt of BNT162b2 or other reasons.

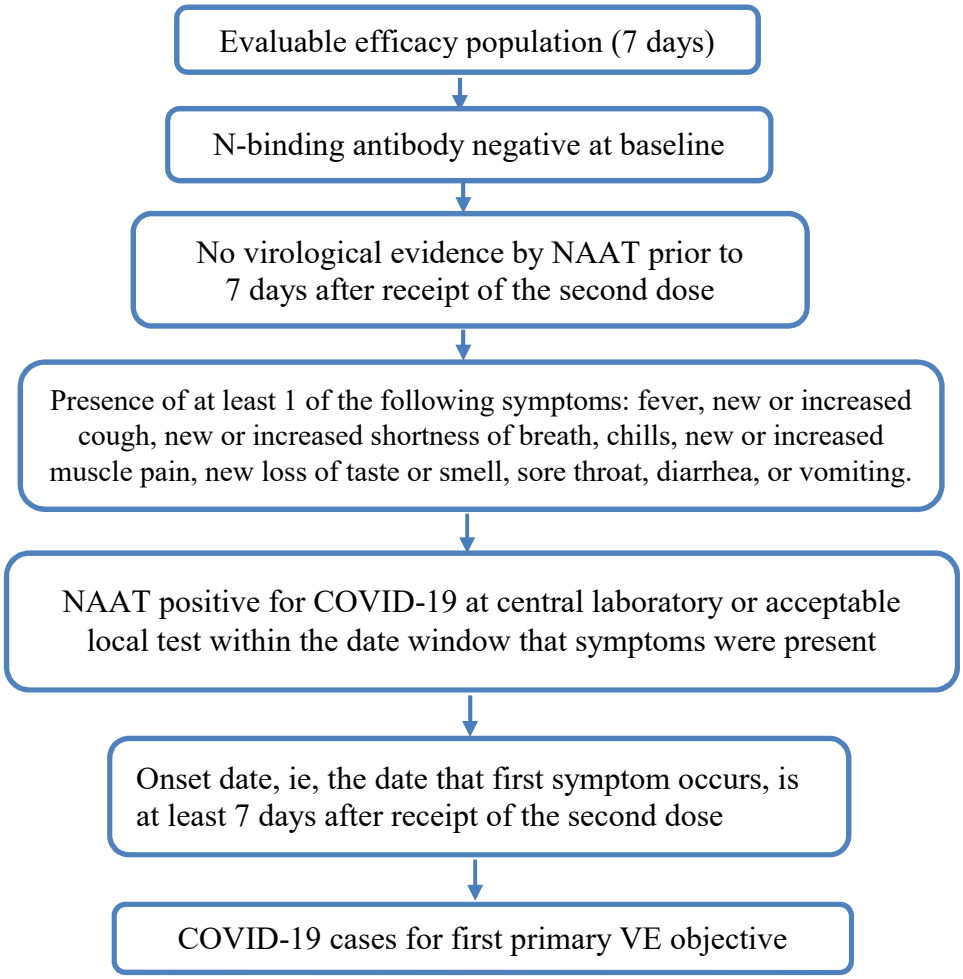
For descriptive assessment of exploratory endpoints of the COVID-19 incidence rate through the entire study follow-up period, the surveillance period is defined in the same way except that unblinding will not be considered as the end of the surveillance period.

Specific information regarding VE-related endpoint surveillance start and end times by endpoint will be provided in Analysis and Reporting Plan specification documents.

Once the COVID-19 cases and surveillance period have been identified, VE can be calculated as $100 \times (1 - IRR)$, where IRR is the ratio of confirmed COVID-19 illness per 1000 person-years of follow-up for the active vaccine group to the placebo group.

Flowchart

1. The flowchart for deriving the COVID-19 cases included below for the first primary endpoints in evaluable efficacy participants with no serological or virological evidence of past SARS-CoV-2 infection:



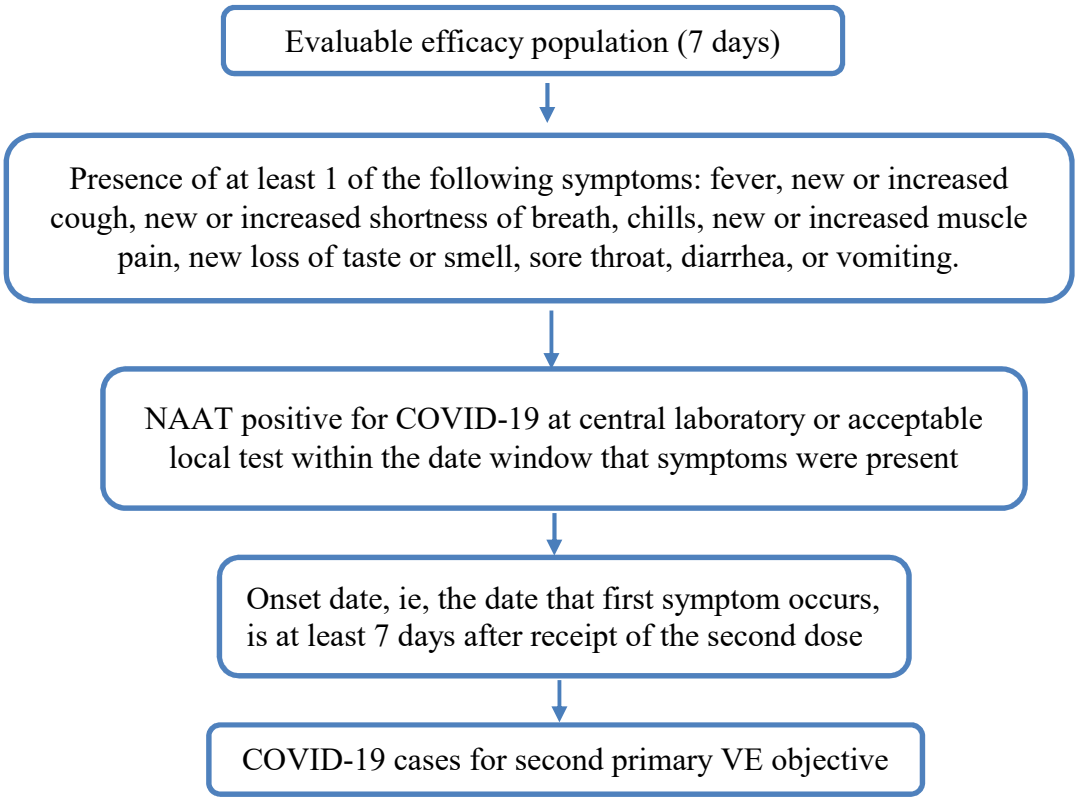
The central laboratory NAAT result will be used for the case definition, unless no result is available from the central laboratory, in which case a local NAAT result may be used if it was obtained using 1 of the following assays:

a. Cepheid Xpert Xpress SARS-CoV-2

b. Roche cobas SARS-CoV-2 real-time RT-PCR test (EUA200009/A001)

c. Abbott Molecular/RealTime SARS-CoV-2 assay (EUA200023/A001)

2. The flowchart for deriving the COVID-19 cases included below for the second primary endpoints in evaluable efficacy participants:



The flowcharts for the first 2 secondary vaccine efficacy endpoints are similar to the primary endpoints except that the case counting starts from 14 days after receipt of the second dose.

Appendix 4. Asymptomatic Case Based on N-Binding Antibody Seroconversion

Asymptomatic Case Definition

An asymptomatic case is defined as a positive N-binding antibody result at a post–Dose 2 visit in participants without serological evidence of infection (determined by negative N-binding antibody) at Visit 1 or virological evidence of infection (determined by negative NAAT results at Visit 1 and Visit 2 and at the time of a potential COVID-19 illness). A secondary definition will be applied without the requirement for a negative NAAT result at Visit 2.

Surveillance Times

For the asymptomatic case based on N-binding antibody seroconversion, the start-of-surveillance times are summarized as follows:

Endpoint's Associated Participant-Level Population	Start-of-Surveillance Time
Evaluable efficacy (seroconversion)	Dose 2
Dose 2 all-available efficacy	Dose 2
Dose 1 all-available efficacy	Dose 1

The end of a surveillance period for each participant is the earliest of the following events:

- Date of the first positive N-binding antibody test after Dose 2.
- Date of the participant's last post–Dose 2 N-binding antibody test that is prior to a COVID-19 symptom associated with a nonnegative NAAT result.
- Date of the participant's last post–Dose 2 N-binding antibody test that is on or before an important protocol violation (for analysis based on the evaluable efficacy population).

Appendix 5. Asymptomatic Case Based on Central Laboratory–Confirmed NAAT

Asymptomatic Case Definition

An asymptomatic case is defined as a positive NAAT result on a nasal swab collected during the surveillance period from participants without COVID-19 symptoms at the time the nasal swab was taken, or within 14 days after it, in participants who are consented to participate in the asymptomatic surveillance and without (or with) serological or virological evidence of past SARS-CoV-2 infection up to the start of the asymptomatic surveillance period.

Surveillance Times

The start-of-surveillance time is the start of the asymptomatic surveillance period.

The end of a surveillance period for each participant is the earliest of the following events:

- When the first positive NAAT occurs.
- When the last NAAT result is available.
- When the first COVID-19 symptom occurs.
- When the participant's asymptomatic surveillance period ends because the participant's participation in the study ended (withdrawal, death, trial completion, etc).
- When the participant has his or her first important protocol violation (only for analysis based on the evaluable efficacy population).

CLINICAL STUDY REPORT AMENDMENT
SUMMARY OF CHANGES

Protocol Number: C4591001

Study Report Title:	Interim Report – Adolescent 6-Month Update: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-CoV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals
Clinical Study Report Date:	03 December 2021
Date of Form Completion:	10 December 2021

The Clinical Study Report (CSR) was amended to make the changes noted below.

Section	Change
CSR Title Page and CSR Synopsis	CSR Title Page and CSR Synopsis Report Date and Previous Report Date were updated.
Section 11.1.1.1.1, Table 14	The data values for the comorbidities and obese subgroups were flipped with each other. Table 14 was updated to correct these values.
Section 14, Supplemental Tables 14.12 and 14.13	The data values for the comorbidities and obese subgroups were flipped with each other. Supplemental Tables 14.12 and 14.13 were updated to correct these values.