22 April 2022
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Human Medicines Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

COMIRNATY

COVID-19 mRNA vaccine (nucleoside-modified)

Procedure no: EMEA/H/C/005735/P46/046

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

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List of abbrevations

Abbreviation	Term
AE	adverse event
AESI	adverse event of special interest
CHMP	Committee for Medicinal Products for Human Use
COVID-19	Coronavirus Disease 2019
CSR	clinical study report
DART	developmental and reproductive toxicity
EMA	European Medicines Agency
EU	European Union
FIH	first-in-human
GLP	Good Laboratory Practice
GMC	geometric mean concentration
GMFR	geometric mean fold rise
GMR	geometric mean ratio
IgG	immunoglobulin G
IM	intramuscular(ly)
LNP	lipid nanoparticle
LPLV	last participant last visit
MAA	Marketing authorisation application
MAH	marketing-authorisation holder
mRNA	messenger RNA
NAAT	nucleic acid amplification test
NHP	non-human primate
PBS	phosphate-buffered saline
PDCO	Paediatric Committee
PIP	Paediatric Investigational Plan
PT	preferred term
RNA	ribonucleic acid
S	spike glycoprotein
SAP	statistical analysis plan
SARS-CoV-2	SARS Coronavirus-2; virus causing the disease COVID-19
sCSR	supplemental CSR
SOC	system organ class
US	United States
VOC	variant of concern

1. Introduction

On 2022-01-21, the MAH submitted a completed paediatric study for Comirnaty, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended. Study C4591017 is part of a clinical development program, as per the line listing included in the submission (Annex to this report). The submission is performed 6 months after completion of study on 22 July 2021.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

C4591017: A phase 3, randomized, observer-blind study to evaluate the safety, tolerability, and immunogenicity of multiple production lots and dose levels of the vaccine candidate BNT162b2 against COVID-19 in healthy participants 12 through 50 years of age and the safety, tolerability, and immunogenicity of BNT162b2 RNA-based COVID-19 vaccine candidates as a booster dose in healthy participants 18 through 50 years of age.

Study C4591017 is a Phase 3 study with 2 parts.

- Evaluations of multiple production lots and doses of BNT162b2 in the primary study were performed for healthy participants 12-50 years of age.
- Evaluations of BNT162b2 RNA-based COVID-19 vaccine candidates in the booster study were performed for healthy participants 18-50 years of age.

The last patients last visit (LPLV) occurred on 22 July 2022 and the final CSR approved on 06 January 2022.

The current EU-approved indication for the use of Comirnaty 30 µg is

- *Active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 12 years of age and older*

In the clinical development program of the mRNA vaccine that targets SARS-CoV-2, BNT162b2 30 µg, paediatric participants ≥12 years of age were granted conditional marketing approval by the EMA on 28 May 2021. The Line Extension (EMEA/H/C/005735/X/0077) to introduce a further presentation (10 µg) and extend the indication to paediatric individuals from 5 to <12 years of age was approved by the EC on 26 November 2021.

Assessors' comments: The FDA guidelines require companies to demonstrate a lot-to- lot consistency to ensure similar immunogenicity of the different vaccine batches. For this reason, study C4591017 was conducted. The main aim of this study is to demonstrate that a similar immune response is induced by 4 lots of BNT162b2 and describe the safety and tolerability of these different vaccine lots in healthy participants, thereby supporting both US and EU manufacturing processes at commercial scale.

2.2. Information on the pharmaceutical formulation used in the study

BNT162b2 (Comirnaty), an RNA-based vaccine for immunization against COVID-19. All 4 production lots were administered at a 30-µg dose and 1 of the lots was also administered at a 20-µg dose, with the group names Arms 1, 2, 3,4, and 5, respectively.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- C4591017: A phase 3, randomized, observer-blind study to evaluate the safety, tolerability, and immunogenicity of multiple production lots and dose levels of the vaccine candidate BNT162b2 against COVID-19 in healthy participants 12 through 50 years of age and the safety, tolerability, and immunogenicity of BNT162b2 RNA-based COVID-19 vaccine candidates as a booster dose in healthy participants 18 through 50 years of age.

2.3.2. Clinical study C4591017

Description

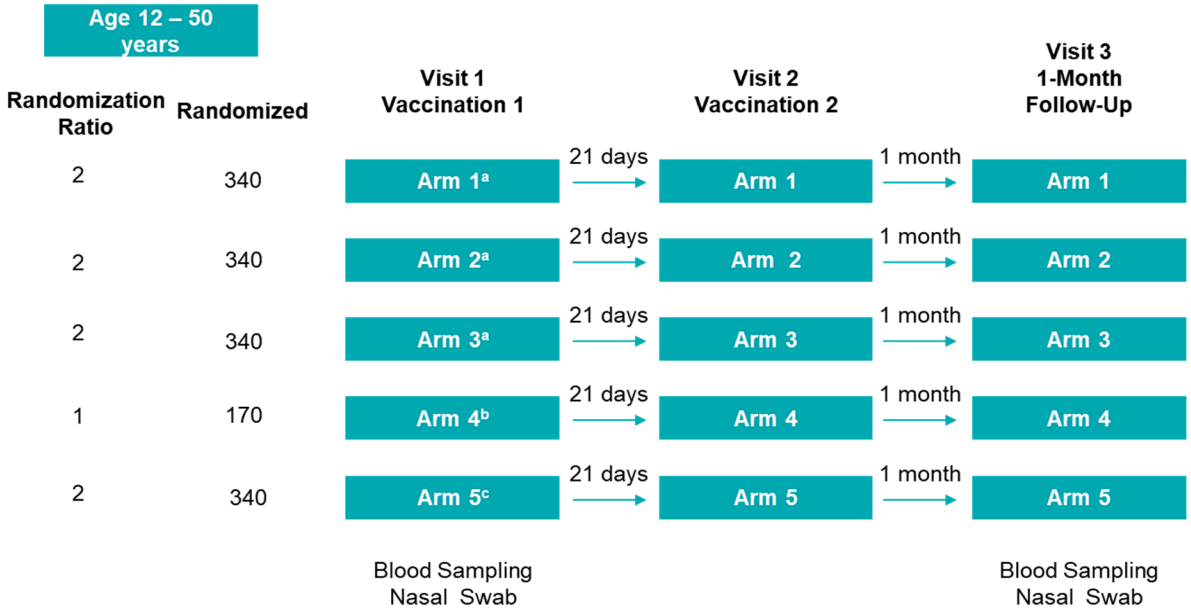
Study C4591017 is a Phase 3, randomized, observer-blind study that includes both a primary and booster study. The focus of this report is the primary study to evaluate the safety, tolerability, and immunogenicity of multiple production lots and dose levels of BNT162b2 against COVID-19 in healthy participants 12-50 years of age. There were no paediatric participants in the booster study to evaluate the safety, tolerability, and immunogenicity of BNT162b2 RNA-based COVID-19 vaccine candidates as a booster dose in healthy participants 18-50 years of age and therefore this part of the study will not be presented and discussed in the current assessment report (AR).

In the primary study, participants were randomized to 1 of 5 arms in a 2:2:2:1:2 ratio (Arm 1: Arm 2: Arm 3: Arm 4: Arm 5), where Arms 1, 2, and 3 used US-manufactured drug substance for 30-µg dosing; Arm 4 used EU-manufactured drug substance for 30-µg dosing; and Arm 5 contained US-manufactured drug substance for 20-µg dosing (US Lot 1). To allow for balanced age representation across all arms, the randomization was stratified by age groups: 12-17, 18-30, and 31-50 years of age. BNT162b2 was administered as a 2-dose schedule, separated by 21 days.

One aim of this study is to demonstrate that a similar immune response is induced by 4 lots of BNT162b2 (3 containing drug substance manufactured in the US, referred to as the "US lots" [Arms 1 through 3] and 1 containing drug substance manufactured in Europe [Arm 4],referred to as the "EU lot"), and describe the safety and tolerability of these different vaccine lots in healthy participants, thereby supporting both US and EU manufacturing processes at commercial scale. One of the US lots was administered at a 20-µg dose (Arm 5) and compared with the standard 30-µg dose from the same US lot in a noninferiority analysis. This objective would support the potential use of a lower vaccine dose in the defined study population, which will be of value, given the demand to

vaccinate the general population. The results of 20-µg dose comparison with 30-µg dose will be presented at later time point as sCSR.

Figure 1 Primary Study Schema



a. Arms 1 through 3 were administered a 30-µg dose level of lots 1 through 3, respectively, containing US-manufactured drug substance.
b. Arm 4 was administered a 30-µg dose level of Lot 4, containing EU-manufactured drug substance.
c. Arm 5 was administered a 20-µg dose level from the corresponding US lot (Arm 1, 2, or 3).

Methods

Study participants

Inclusion criteria

Age and Sex:

- Primary study: Male or female participants between the ages of 12 and 50 years,inclusive, at Visit 1 (Day 1).

Type of Participant and Disease Characteristics:

- Participants who were willing and able to comply with all scheduled visits, treatment plan, laboratory tests, lifestyle considerations, and other study procedures.
- 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 pre-existing stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease duringthe 6 weeks before enrolment were included.

Informed Consent:

- Capable of giving personal signed informed consent/have parent(s)/legal guardiancapable of giving signed informed consent.

Exclusion Criteria

Medical Conditions:

- Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, made the participant inappropriate for the study.
- Known infection with HIV, HCV, or HBV.
- History of severe adverse reactions associated with a vaccine and/or severe allergicreactions (eg, anaphylaxis) to any component of the study intervention(s).
- Previous clinical (based on COVID-19 symptoms/signs alone, if a SARS-CoV-2 NAATresult was not available) or microbiological (based on COVID-19 symptoms/signs and apositive SARS-CoV-2 NAAT result) diagnosis of COVID-19.
- Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.
- Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection.
- Women who were pregnant or breastfeeding.

Prior/Concomitant Therapy:

- Primary study: Previous vaccination with any coronavirus vaccine.
- Receipt of medications intended to prevent COVID-19.
- Individuals who received treatment with radiotherapy or immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids (if systemic corticosteroids are administered for ≥14 days at a dose of ≥20 mg/day of prednisone or equivalent), eg, forcancer or an autoimmune disease, or planned receipt throughout the study. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin or eyes) corticosteroids were permitted.
- 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:

- Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation.

- Previous participation in other studies involving study intervention containing LNPs.

Other Exclusions:

- Investigator site staff or Pfizer/BioNTech employees directly involved in the conduct ofthe study, site staff otherwise supervised by the investigator, and their respective familymembers.

Assessor´s comment: The inclusion and exclusion criteria are very similar to the pivotal marketing authorization trial C4591001 and are therefore acceptable.

Treatments

In the primary study, study intervention refers to BNT162b2, an RNA-based vaccine for immunization against COVID-19. All 4 production lots were administered at a 30-µg dose and 1 of the lots was also administered at a 20-µg dose, with the group names Arms 1, 2, 3,4, and 5, respectively. The study evaluated a 2-dose (separated by 21 days) schedule in healthy participants 12 through 50 years of age.

A list of the investigational products administered in this study and their respective lotnumbers is provided in ***Table 1*** below.

Table 1 Investigational Product Lot Numbers – Final

Investigational Product	Manufacturer	Vendor Lot Number (Manufacturer)	Lot Number[a] (Pfizer)
BNT162b2	BioNTech	EL8723Y	PA2092203/P221545-0009L
Lot 1 groups[b]: Arm 1 (30 µg), Arm 5 (20 µg), and booster dose (30 µg)		EL8723Y	PA2092203/P221545-01
		EL8723Z	PA2090562/P221545-01
Lot 2 group: Arm 2 (30 µg)		EL3249C	PA2090076/P221545-01
Lot 3 group: Arm 3 (30 µg)		EL3248C	PA2090069/P221545-01
Lot 4 group: Arm 4 (EU) (30 µg)		EL1491Z	PA2089539/P221545-01
Diluent (normal saline 0.9% sodium chloride solution)	Pfizer	DK2074	20-002221
		DK2074	20-002957

Abbreviation: EU = Europe.
Note: C4591017 End of Study Information and Quality Control (QC) Record for Study Drug Appendix (Section D) dated 27Oct2021 was used to create this table.
Note: Several lot numbers (vendor and Pfizer) are noted for Lot 1 to indicate differences in label applications to the vials (no label or label removed).
a. Lot number assigned to the investigational product by Pfizer Global Clinical Supply.
b. Multiple lot numbers for Lot 1 indicate differences in labeling of the bulk drug product (delabeled for lot numbers ending in "Y" and unlabeled for lot numbers ending in "Z"). Batches ending in "Y" and "Z" were separated from drug product batch EL8723.
Protocol C4591017 Investigational Product Lot Numbers Table – Final, Final, Version 2.0, 04Jan2022.

Objectives, Outcomes/endpoints

Table 2 Study C4591017 Objectives, Estimands, Endpoints, and Analyses – Primary Study – Participants 12-50 Years of Age

Objectives	Estimands	Endpoints	Paediatric Subgroup Analyses in Final CSR
Primary Immunogenicity – Lot Comparisons			
• To demonstrate that the immune responses induced by BNT162b2 are similar across the 3 US lots (Arms 1, 2, and 3) in participants without evidence of SARS-CoV-2 infection during the study.	In participants complying with the key protocol criteria (evaluable participants): • GMR from one US lot to another lot (Arm 1/Arm 2, Arm 1/Arm 3, and Arm 2/Arm 3) 1 month after Dose 2	• Full-length S-binding IgG concentrations	• No analyses for 12-17 years of age subgroup
• To demonstrate that the immune response induced by the EU lot (Arm 4) of BNT162b2 is similar to the pooled US lots (Arms 1, 2, and 3) in participants without evidence of SARS-CoV-2 infection during the study.	In participants complying with the key protocol criteria (evaluable participants): • GMR from the EU lot (Arm 4) to the pooled US lots (Arm 4/pooled Arms 1, 2, and 3) 1 month after Dose 2	• Full-length S-binding IgG concentrations	• No analyses for 12-17 years of age subgroup
Primary Immunogenicity – Dose Comparison			
• To demonstrate the noninferiority of the immune response to prophylactic BNT162b2 in participants receiving 20 µg compared to participants receiving the standard 30-µg dose (prepared from the same lot) without evidence of SARS-CoV-2 infection during the study. [a]	In participants complying with the key protocol criteria (evaluable participants): • GMR, estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in the 2 dose groups 1 month after Dose 2	• SARS-CoV-2 neutralizing titers	

Table 2 Study C4591017 Objectives, Estimands, Endpoints, and Analyses – Primary Study – Participants 12-50 Years of Age

Objectives	Estimands	Endpoints	Paediatric Subgroup Analyses in Final CSR
Primary Safety			
• To evaluate the safety of BNT162b2 when administered on a 2-dose schedule in healthy participants 12 through 50 years of age.	In participants receiving at least 1 dose of study intervention from each vaccine group (individual and pooled US lots, the EU lot, or the 20-µg dose), 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 and SAEs from Dose 1 to 1 month after Dose 2	• 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	• Local reactions by age group • Systemic events by age group • AEs by SOC and PT by age group – 12-17 years of age
Secondary Immunogenicity			
• To describe the immune responses induced by different 30-µg dose lots of BNT162b2.	In evaluable participants from each vaccine group (individual and pooled US lots, and the EU lot): • GMCs at baseline (before Dose 1) and 1 month after Dose 2 • GMFR from baseline (before Dose 1) to 1 month after Dose 2	• Full-length S-binding IgG concentrations	• GMCs of full-length S-binding IgG concentrations by subgroups
• To describe the immune responses induced by different doses of BNT162b2. [a]	In evaluable participants from each vaccine group (20 µg and 30 µg from the same US lot): • GMTs at baseline (before Dose 1) and 1 month after Dose 2 • GMFR from baseline (before Dose 1) to 1 month after Dose 2	• SARS-CoV-2 neutralizing titers	

a. To be presented in the sCSR
Note: "US lots" refers to lots of study vaccine containing drug substance manufactured in the US and the "EU lot" refers to the lot of study vaccine containing drug substance manufactured in Europe.
The results from the grey shaded objectives will be presented later.

Assessor's comment: part of the study results will be presented later as sCSR (marked with grey background in the table above). This is acceptable.

Sample size

The study sample size was based on the lot-to-lot similarity evaluation for the first and second primary immunogenicity endpoints, full-length S-binding IgG concentrations 1 month after Dose 2, using a 1.5-fold equivalence margin for each between-lot comparison across the 3 US lots (Arms 1 to 3) and the comparison of the EU Lot (Arm 4) to the US lots.

Power calculations are based on the pairwise comparison of 0 vs δ, 0 vs δ, and 0 vs 0 for the mean full-length S-binding IgG levels (on the natural log scale) between 2 US lots and 0 vs δ between the EU lot and the pooled US lots. A δ of 0.2 corresponds to an assumption that the true GMR of any lot to another lot is between 0.82 and 1.22. Common assay standard deviations from each lot are assumed to be 0.6456 based on results from Phase 1 of Study C4591001 (BNT162b2 30 µg 18- to 55-year age group). With 270 evaluable participants per US lot (Arms 1-3), and the stated assumptions on the maximum between-lot difference and the standard deviation, the study has a power of 91.7% for considering the 3 US lots to be similar. The study will also provide 92.8% power for considering the EU lot (Arm 4) similar to the US lots, with 135 evaluable participants in the EU lot (Arm 4) and 810 evaluable participants in the pooled US lots (Arms 1-3) (see Table 3).With 270 evaluable participants each in the 20-µg dose group and corresponding 30-µg dose group, and assumptions on the standard deviation and mean difference of -0.2 in SARS-CoV-2 neutralizing titers (on the natural log scale) between the 2 dose groups, the study has 94.7% power to declare noninferiority of 20 µg to 30 µg (Table 3). Assuming a non-evaluable rate of 20%, the study will randomize approximately 340 participants in each US lot (Arms 1-3), 170 participants in the EU lot (Arm 4), and 340 participants in the 20-µg dose group (Arm 5) to achieve the required evaluable participants.

Table 3. Power for Lot-Similarity and Non-Inferiority Assessments

Hypothesis	Criteria	Standard Deviation (Log Value)[a]	Assumed Observed Mean Difference (Log Scale)	Number of Evaluable Participants	Power[b]
First primary (similarity of 3 US lots)	95% CI for GMR is contained in (0.67, 1.5) for all 3 pair comparisons	0.6456	0.2, 0.2, and 0 between any 2 US lots	270 per US lot	91.7%
Second primary (similarity of EU and US lots)	95% CI for GMR is contained in (0.67, 1.5)	0.6456	0.2	135 EU lot vs 810 pooled US lots	92.8%
Third primary (noninferiority of 20 µg to 30 µg)	Lower limit of 95% CI for GMR is >0.67	0.65	-0.2	270 per dose group	94.7%

Abbreviation: GMR = geometric mean ratio.

a. Reference: BNT162b2 (30 µg), 18- to 55-year age group (C4591001 Phase 1, N=12) for S1-binding IgG levels and BNT162b2 (30 µg), 18- to 55-year age group (C4591001 Phase 2) for SARS-CoV-2 neutralizing titers. Calculation may be updated if additional information becomes available to better estimate the standard deviation.

b. At the 0.05 alpha level (2-sided).

Randomisation and blinding (masking)

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

The majority of sponsor and Pfizer staff were blinded to the study intervention allocation. The blinded study team was unblinded to the primary study randomization information at the time of database release of the primary study. These same study team members remained blinded to the randomization information for the booster study until completion of that phase.

The primary and booster studies were observer-blinded for staff at the investigative sites. The staff who received, stored, dispensed, prepared, and administered the study interventions were unblinded. All other site personnel, including the investigator, investigator staff, and participants, were blinded to study intervention assignments.

Statistical Methods

Unless stated otherwise, "vaccine group" in this section refers to participants receiving any 1 of the three 30-µg US lots, the (30-µg) EU lot, or the 20-µg dose group for the primary study and to participants receiving BNT162b2 at 30 µg or BNT162b2.B.1.351 at 30 µg.

CIs for all endpoints in the statistical analysis are presented as 2-sided at the 95% level unlessspecified otherwise.

For all the immunogenicity endpoints, the analysis was based on the evaluable immunogenicity population. An additional analysis was performed based on the all-available immunogenicity population if there was a 10% difference in sample size between the all-available immunogenicity population and the evaluable immunogenicity population.Participants were summarized according to the vaccine group to which they were randomized.

Table 4. Study C4591017 Safety and Immunogenicity Analysis Populations – Primary Study – Participants 12-50 Years of Age

Population	Description
Safety	All randomized participants who received at least 1 dose of the study intervention.
All-available immunogenicity	All randomized participants who received at least 1 dose of the study intervention with at least 1 valid and determinate immunogenicity result after vaccination.
Evaluable immunogenicity	All participants who 1. were eligible and randomized; 2. received 2 doses of vaccine to which they were randomized, with Dose 2 received within the predefined window (19-42 days, inclusive, after Dose 1); 3. had at least 1 valid immunogenicity result within an appropriate window 1 month after Dose 2 (28-42 days, inclusive, after Dose 2); 4. negative for both SARS-CoV-2 tests (RT-PCR and N-binding antibody assay) at both the Day 1 and 1-month post–Dose 2 visits; and 5. had no other important protocol deviations as determined by the clinician.

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).

Analyses for Continuous Data
Unless otherwise stated, descriptive statistics for continuous variables are n, mean, median, standard deviation, minimum, and maximum.

Geometric Mean Ratios
Model-Based
As the primary approach, the GMR and associated 95% CI will be calculated by exponentiating the difference in LS means and the corresponding CIs based on analysis of logarithmically transformed assay results using a linear regression model.
Unadjusted
The GMRs will be calculated as the mean of the difference of logarithmically transformed assay results between 2 vaccine groups 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.

Geometric Means
The geometric means 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 assay results, calculating the 95% CI with reference to Student's t-distribution, and then exponentiating the confidence limits.

Geometric Mean Fold Rises
GMFRs are defined as ratios of the results at a later time point to the results at an earlier time point. GMFRs are limited to participants with non-missing values at both time point. GMFRs will be calculated as the mean of the difference of logarithmically transformed assay results (later time point minus earlier time point) and exponentiating the mean. The associated 2-sided 95% 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.

Immunogenicity evaluations
Serum samples were obtained for testing via the full-length S-binding IgG-concentration assay. SARS-CoV-2 neutralizing titers for the primary study and all immunogenicity test results in the booster study are not included in the submitted CSR and will be presented in the sCSR.

Nasal (midturbinate) swabs were obtained in order to detect SARS-CoV-2 via RT-PCR (NAAT) as one of the determinations for participants to be included in the evaluable immunogenicity analysis.

Additional details on the collection and analysis of biological samples, including long-term storage and usage, are provided in Appendix 16.1.1, Protocol Section 8.1 of the submitted CSR.

Immunogenicity analysis

The 3 primary immunogenicity objectives are to be assessed sequentially in the following order to control study wise type I error: 1) similarity across the 3 US lots, 2) noninferiority of the 20-µg dose level to the 30-µg dose level, and 3) similarity between the EU Lot and the pooled US lots. The primary immunogenicity objective of similarity between the EU Lot and the pooled US lots is to be assessed only if the other 2 primary objectives are met. The second objective of noninferiority of the 20-µg dose level to the 30-µg dose level will be analysed in the sCSR, so the third objective of similarity between the EU Lot and the pooledUS lots cannot be formally assessed in this CSR.

Model-Based: As the main approach in the primary study, the GMR and associated 95% CIwere calculated by exponentiating the difference in LS means and the corresponding CIs based on analysis of logarithmically transformed assay results using a linear regression model with terms of age and vaccine group.

Unadjusted: The GMRs in the primary study were calculated as the mean of the difference of logarithmically transformed assay results between 2 vaccine groups 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.

The analysis of S-binding IgG in the primary study presented in this CSR is summarizedbelow.

GMRs of full-length S-binding IgG concentrations between the US lots

- For full-length S-binding levels, the GMRs for each between-lot comparison (Arm 1/Arm 2, Arm 1/Arm 3, and Arm 2/Arm 3) at 1 month after Dose 2 wereprovided along with associated 2-sided 95% CIs.
- Using a 1.5-fold equivalence margin, 2 lots will be considered similar if the 2-sided95% CI for each GMR is contained in the interval (0.67, 1.5). The 3 US lots will beconsidered similar if the 1.5-fold equivalence criterion is met for all 3 between-lot comparisons (Arm 1 to Arm 2, Arm 1 to Arm 3, and Arm 2 to Arm 3).

GMR of full-length S-binding IgG concentrations between the EU Lot and the 3 US lots

- The GMR of the EU Lot (Arm 4) to the pooled US lots (Arm 4/pooled Arms 1, 2, and3) at 1 month after Dose 2 will be provided along with associated 2-sided 95% CIs.
- Using a 1.5-fold equivalence margin, the EU Lot (Arm 4) and the pooled US lots (Arms 1 to 3) will be considered similar if the 2-sided 95% CI for the GMR is contained in the interval (0.67, 1.5) and primary objectives on the US lot similarityand dose comparison are both met.

GMCs of full-length S-binding IgG concentrations

- The GMCs and 2-sided 95% CIs were provided for each vaccine group (individual US lots, the pooled US lots, and the EU Lot) at baseline (before Dose 1) and at 1 month after Dose 2.

GMFRs of full-length S-binding IgG concentrations

- The GMFRs and 2-sided 95% CIs were provided for each vaccine group (individual US lots, the pooled US lots, and the EU Lot) from baseline (before Dose 1) to 1 month after Dose 2.

Assessor´s comment: the design and methods of the study are acceptable.

Safety evaluations

Electronic Diary

Participants used a reactogenicity e-diary and recorded local reactions, systemic events, and antipyretic/analgesic medication usage for 7 days from the day of administration of the studyintervention.

Adverse Events and Serious Adverse Events

During the primary study, AEs and SAEs were collected during the study from the signing ofthe ICD through and including Visit 3 (1-month follow-up). In addition, any AEs occurring up to 48 hours after the blood draw and nasal swab collection at Visit 3 reported by the participant were collected.

Safety analysis

The safety analyses were based on the safety population. Participants were summarized byvaccine group according to the investigational products they received.

Descriptive statistics are provided for each reactogenicity endpoint for each dose and vaccinegroup. Local reactions and systemic events from Day 1 through Day 7 after each vaccinationare presented by severity and cumulatively across severity levels. Descriptive summary statistics included counts and percentages of participants with the indicated endpoint and the associated Clopper-Pearson 95% CIs.

AEs and SAEs are categorized according to MedDRA terms. Counts, percentages, and the associated Clopper-Pearson 95% CIs of AEs and SAEs from Dose 1 to 1 month after Dose 2are provided for each vaccine group.

Assessor´s comment: the design and methods of the study safety evaluations are acceptable.

Results

Participant flow

In the primary study, 1574 participants 12-50 years of age were randomised and 1573 (99.9%) vaccinated with at least 1 dose that were included in the safety population. A total of 1557 (98.9%) of participants completed the study; of the 2 participants who discontinued from the investigational product for safety-related reasons (both discontinued from receiving Dose 2 but continued in the study for safety follow-up), neither were paediatric participants 12-17 years of age.

Table 5 Disposition of All Randomized Participants – Primary Study

	Vaccine Group (as Randomized)						
	Arm 1 (US Lot 1) (N[a]=351) n[b] (%)	**Arm 2 (US Lot 2) (N[a]=352) n[b] (%)**	**Arm 3 (US Lot 3) (N[a]=347) n[b] (%)**	**Pooled US Lots (N[a]=1050) n[b] (%)**	**Arm 4 (EU Lot) (N[a]=173) n[b] (%)**	**Arm 5 (20 µg) (N[a]=351) n[b] (%)**	**Total (N[a]=1574) n[b] (%)**
Randomized	351 (100.0)	352 (100.0)	347 (100.0)	1050 (100.0)	173 (100.0)	351 (100.0)	1574 (100.0)
Not vaccinated	0	0	1 (0.3)	1 (0.1)	0	0	1 (0.1)
Vaccinated							
Dose 1	351 (100.0)	352 (100.0)	346 (99.7)	1049 (99.9)	173 (100.0)	351 (100.0)	1573 (99.9)
Dose 2	351 (100.0)	352 (100.0)	344 (99.1)	1047 (99.7)	173 (100.0)	350 (99.7)	1570 (99.7)
Completed the study	347 (98.9)	346 (98.3)	344 (99.1)	1037 (98.8)	171 (98.8)	349 (99.4)	1557 (98.9)
Discontinued from receiving Dose 2 but continued in the study for safety follow-up	0	0	1 (0.3)	1 (0.1)	0	1 (0.3)	2 (0.1)
Reason for discontinuation							
Adverse event	0	0	0	0	0	1 (0.3)	1 (0.1)
Pregnancy	0	0	1 (0.3)	1 (0.1)	0	0	1 (0.1)
Withdrawn from the study	4 (1.1)	6 (1.7)	2 (0.6)	12 (1.1)	2 (1.2)	2 (0.6)	16 (1.0)
Withdrawn after Dose 1 and before Dose 2	0	0	1 (0.3)	1 (0.1)	0	0	1 (0.1)
Withdrawn after Dose 2	4 (1.1)	6 (1.7)	1 (0.3)	11 (1.0)	2 (1.2)	2 (0.6)	15 (1.0)
Reason for withdrawal							
Lost to follow-up	1 (0.3)	1 (0.3)	2 (0.6)	4 (0.4)	1 (0.6)	0	5 (0.3)
Other	1 (0.3)	2 (0.6)	0	3 (0.3)	0	1 (0.3)	4 (0.3)
Withdrawal by subject	2 (0.6)	3 (0.9)	0	5 (0.5)	0	1 (0.3)	6 (0.4)
Withdrawal by parent/guardian	0	0	0	0	1 (0.6)	0	1 (0.1)

Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4, and a 20-µg dose of BNT162b2 was administered in Arm 5. Arm 5 study vaccine was from US Lot1.
Note: One participant was randomized to Arm 5 (Lot 1 [20 µg]). At Vaccination 2 the participant received a 20-µg dose of the investigational product butmay have received the dose from a different arm/lot to which the participant was randomized.

a. N = number of participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.

PFIZER CONFIDENTIAL SDTM Creation: 29OCT2021 (00:07) Source Data: adds Table Generation: 15NOV2021 (20:17) (Database Snapshot Date : 26OCT2021) Output File: ./C4591017_SEC/C4591017_CSR/adds_s002_rand

Recruitment

The study was conducted in the USA, 16 sites participated. Each site recruited around 100 subjects. First subject first visit took place on 15 February 2021 and last subject last visit on 22 July 2021.

Baseline data

Almost all participants (99.9%) in each vaccine group received Dose 1 in the primary studyand overall, 98.0% of participants received Dose 2 within the protocol-specified time frame(Table 6). One participant randomized to receive US Lot 1 received US Lot 3 at Dose 2 andwas excluded from the evaluable immunogenicity population.

Table 6. Vaccine Administration Timing – Primary Study – All RandomizedParticipants

	Vaccine Group (as Randomized)						
	Arm 1 (US Lot 1) (N[a]=351) n[b] (%)	**Arm 2 (US Lot 2) (N[a]=352) n[b] (%)**	**Arm 3 (US Lot 3) (N[a]=347) n[b] (%)**	**Pooled US Lots (N[a]=1050) n[b] (%)**	**Arm 4 (EU Lot) (N[a]=173) n[b] (%)**	**Arm 5 (20 µg) (N[a]=351) n[b] (%)**	**Total (N[a]=1574) n[b] (%)**
Randomized	351 (100.0)	352 (100.0)	347 (100.0)	1050 (100.0)	173 (100.0)	351 (100.0)	1574 (100.0)
Not vaccinated	0	0	1 (0.3)	1 (0.1)	0	0	1 (0.1)
Dose 1	351 (100.0)	352 (100.0)	346 (99.7)	1049 (99.9)	173 (100.0)	351 (100.0)	1573 (99.9)
Dose 2[c]	351 (100.0)	352 (100.0)	344 (99.1)	1047 (99.7)	173 (100.0)	350 (99.7)	1570 (99.7)
<19 Days	0	0	1 (0.3)	1 (0.1)	0	0	1 (0.1)
19 to 23 Days[d]	344 (98.0)	341 (96.9)	338 (97.4)	1023 (97.4)	171 (98.8)	349 (99.4)	1543 (98.0)
>23 Days	7 (2.0)	11 (3.1)	5 (1.4)	23 (2.2)	2 (1.2)	1 (0.3)	26 (1.7)

Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4, and a 20-µg dose of BNT162b2 was administered in Arm 5. Arm 5 study vaccine was from US Lot 1.
a. N = number of participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
c. Days calculated since Dose 1.
d. Protocol-specified time frame.
PFIZER CONFIDENTIAL SDTM Creation: 31OCT2021 (22:52) Source Data: adsl Table Generation: 03NOV2021 (22:47)
(Database Snapshot Date: 26OCT2021) Output File: ./C4591017_SEC/C4591017_CSR/adsl_vax_time_rand

The safety population (N=1573) in the primary study was similarly distributed between male and female participants, and the majority of participants were White and non-Hispanic/non-Latino. Participants were similarly distributed across age groups and included a total of 445 (28.3%; range: 27.3-29.2%) paediatric participants 12-17 years of age.

The evaluable immunogenicity population (N=1423) demographic characteristics were similar to those in the safety population and consisted of 406 (28.5%; range: 25.0-29.9%) paediatric participants 12-17 years of age.

Table 7. Demographic Characteristics – Primary Study – Safety Population

	Vaccine Group (as Administered)						
	Arm 1 (US Lot 1) (N[a]=351) n[b] (%)	Arm 2 (US Lot 2) (N[a]=352) n[b] (%)	Arm 3 (US Lot 3) (N[a]=346) n[b] (%)	Pooled US Lots (N[a]=1049) n[b] (%)	Arm 4 (EU Lot) (N[a]=173) n[b] (%)	Arm 5 (20 µg) (N[a]=351) n[b] (%)	Total (N[a]=1573) n[b] (%)
Sex							
Male	174 (49.6)	176 (50.0)	187 (54.0)	537 (51.2)	90 (52.0)	188 (53.6)	815 (51.8)
Female	177 (50.4)	176 (50.0)	159 (46.0)	512 (48.8)	83 (48.0)	163 (46.4)	758 (48.2)
Race							
White	286 (81.5)	280 (79.5)	283 (81.8)	849 (80.9)	142 (82.1)	283 (80.6)	1274 (81.0)
Asian	36 (10.3)	48 (13.6)	40 (11.6)	124 (11.8)	24 (13.9)	44 (12.5)	192 (12.2)
Black or African American	21 (6.0)	16 (4.5)	15 (4.3)	52 (5.0)	2 (1.2)	14 (4.0)	68 (4.3)
Multiracial	6 (1.7)	5 (1.4)	5 (1.4)	16 (1.5)	4 (2.3)	5 (1.4)	25 (1.6)
American Indian or Alaska Native	0	1 (0.3)	1 (0.3)	2 (0.2)	0	3 (0.9)	5 (0.3)
Native Hawaiian or other Pacific Islander	1 (0.3)	1 (0.3)	1 (0.3)	3 (0.3)	0	2 (0.6)	5 (0.3)
Not reported	1 (0.3)	1 (0.3)	1 (0.3)	3 (0.3)	1 (0.6)	0	4 (0.3)
Ethnicity							
Hispanic/Latino	44 (12.5)	32 (9.1)	55 (15.9)	131 (12.5)	22 (12.7)	42 (12.0)	195 (12.4)
Non-Hispanic/non-Latino	306 (87.2)	319 (90.6)	291 (84.1)	916 (87.3)	151 (87.3)	309 (88.0)	1376 (87.5)
Not reported	1 (0.3)	1 (0.3)	0	2 (0.2)	0	0	2 (0.1)
Age group (at vaccination)							
12-17 Years	99 (28.2)	96 (27.3)	101 (29.2)	296 (28.2)	48 (27.7)	101 (28.8)	445 (28.3)
18-30 Years	121 (34.5)	125 (35.5)	114 (32.9)	360 (34.3)	61 (35.3)	122 (34.8)	543 (34.5)
31-50 Years	131 (37.3)	131 (37.2)	131 (37.9)	393 (37.5)	64 (37.0)	128 (36.5)	585 (37.2)
Age at vaccination (years)							
Mean (SD)	28.0 (11.66)	27.8 (11.76)	27.5 (11.54)	27.8 (11.64)	27.7 (11.40)	27.5 (11.71)	27.7 (11.63)
Median	27.0	26.0	26.0	26.0	26.0	27.0	26.0
Min, max	(12, 50)	(12, 50)	(12, 50)	(12, 50)	(12, 49)	(12, 50)	(12, 50)

Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4, and a 20-µg dose of BNT162b2 was administered in Arm 5. Arm 5 study vaccine was from US Lot 1.

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

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

Number analysed

Evaluable immunogenicity population contained 1423 participants:

Table 8. Evaluable immunogenicity population

	Arm 1	Arm 2	Arm 3	Pooled US	Arm 4	Arm 5	Total
N=	324	311	310	945	160	318	1423

Efficacy results

For the primary study, all immunogenicity analyses reported in the final CSR were for the 30-µg dose level of BNT162b2 (Arms 1, 2, 3 and 4).

Overall, there was a total of 151 (9.6%) participants excluded from the evaluable immunogenicity population in the primary study (Table 9). The most common reasons for exclusion were: had a non-negative result for either of the SARS-CoV-2 tests (RT-PCR or N-binding antibody assay) during the primary study (100 [6.4%]) and did not have at least 1 valid and determinate immunogenicity result within 28 to 42 days after Dose 2 (65 [4.1%]participants).

Overall, there was a total of 20 (1.3%) participants excluded from the all-available immunogenicity population in the primary study (Table 9). The main reason for exclusion was: did not have at least 1 valid and determinate immunogenicity result after vaccination (20 [1.3%] participants).

Table 9. Immunogenicity Populations – Primary Study

	Vaccine Group (as Randomized)						
	Arm 1 (US Lot 1) n[a] (%)	Arm 2 (US Lot 2) n[a] (%)	Arm 3 (US Lot 3) n[a] (%)	Pooled US Lots n[a] (%)	Arm 4 (EU Lot) n[a] (%)	Arm 5 (20 µg) n[a] (%)	Total n[a] (%)
Randomized[b]	351 (100.0)	352 (100.0)	347 (100.0)	1050 (100.0)	173 (100.0)	351 (100.0)	1574 (100.0)
All-available immunogenicity population	347 (98.9)	345 (98.0)	343 (98.8)	1035 (98.6)	170 (98.3)	349 (99.4)	1554 (98.7)
Participants excluded from all-available immunogenicity population	4 (1.1)	7 (2.0)	4 (1.2)	15 (1.4)	3 (1.7)	2 (0.6)	20 (1.3)
Reason for exclusion[c]							
Did not receive at least 1 dose of the study intervention	0	0	1 (0.3)	1 (0.1)	0	0	1 (0.1)
Did not have at least 1 valid and determinate immunogenicity result after vaccination	4 (1.1)	7 (2.0)	4 (1.2)	15 (1.4)	3 (1.7)	2 (0.6)	20 (1.3)
Evaluable immunogenicity population	324 (92.3)	311 (88.4)	310 (89.3)	945 (90.0)	160 (92.5)	318 (90.6)	1423 (90.4)
Participants excluded from evaluable immunogenicity population	27 (7.7)	41 (11.6)	37 (10.7)	105 (10.0)	13 (7.5)	33 (9.4)	151 (9.6)
Reason for exclusion[c]							
Not eligible or not randomized	0	0	1 (0.3)	1 (0.1)	0	0	1 (0.1)
Did not receive 2 doses of the vaccine to which they were randomized	1 (0.3)	0	3 (0.9)	4 (0.4)	0	1 (0.3)	5 (0.3)
Did not receive Dose 2 within 19-42 days after Dose 1	1 (0.3)	2 (0.6)	4 (1.2)	7 (0.7)	0	1 (0.3)	8 (0.5)
Did not have at least 1 valid and determinate immunogenicity result within 28-42 days after Dose 2	8 (2.3)	19 (5.4)	18 (5.2)	45 (4.3)	7 (4.0)	13 (3.7)	65 (4.1)
Had non-negative result for either SARS-CoV-2 test (RT-PCR or N-binding antibody assay) during the primary study	23 (6.6)	26 (7.4)	21 (6.1)	70 (6.7)	8 (4.6)	22 (6.3)	100 (6.4)
Had important protocol deviation(s) as determined by the clinician	0	4 (1.1)	5 (1.4)	9 (0.9)	2 (1.2)	1 (0.3)	12 (0.8)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; RT-PCR = reverse transcription–polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4, and a 20-µg dose of BNT162b2 was administered in Arm 5. Arm 5 study vaccine was from US Lot 1.
a. n = Number of participants with the specified characteristic, or the total sample.
b. These values are the denominators for the percentage calculations.
c. Participants may have been excluded for more than 1 reason.

Assessor´s comment: the study had high adherence as around 90 % of the randomized population became the evaluable immunogenicity population.

Primary Immunogenicity

The 3 primary immunogenicity objectives in the primary study are to be assessed sequentially in the following order to control study wise type I error: 1) similarity across the3 US lots, 2) noninferiority of the 20-µg dose level to the 30-µg dose level, and 3) similarity between the EU lot and the pooled US lots.

For the primary immunogenicity (GMR) analyses in participants 12-50 years of age, there were no analyses specific to paediatric participants 12-17 years of age.

The 3 US lots (Arms 1, 2, and 3) met the 1.5-fold equivalence criteria for all 3 between-lot full length S-binding IgG model-based GMR (95% CI) comparisons and were considered similar.

Table 10. Geometric Mean Ratios of Full-Length S-Binding IgG Concentrations (U/mL) Between Individual US Lots – 1 Month After Dose 2 – Linear Regression – Primary Study – Evaluable Immunogenicity Population

Vaccine Group (as Randomized)								
Arm 1 (US Lot 1)		Arm 2 (US Lot 2)		Arm 3 (US Lot 3)		Comparison GMR[a] (95% CI[a])		
n[b]	GMC[c] (95% CI[c])	n[b]	GMC[c] (95% CI[c])	n[b]	GMC[c] (95% CI[c])	Arm 1 (US Lot 1) /Arm 2 (US Lot 2)	Arm 1 (US Lot 1) /Arm 3 (US Lot 3)	Arm 2 (US Lot 2) /Arm 3 (US Lot 3)
324	6299.5 (5835.4, 6800.5)	311	6231.9 (5763.7, 6738.2)	310	6774.8 (6264.9, 7326.1)	1.01 (0.91, 1.13)	0.93 (0.83, 1.04)	0.92 (0.82, 1.03)

Abbreviations: GMC = geometric mean concentration; GMR = geometric mean ratio; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; LS=least squares; S = spike protein.
Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3.
a. GMRs and the corresponding 2-sided 95% CIs were calculated by exponentiating the difference in LS means and corresponding CIs based on analysis of logarithmically transformed assay results using a linear regression model with terms of age and vaccine group.
b. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.
c. GMCs and 2-sided 95% CIs were calculated by exponentiating the LS mean of the concentrations and corresponding CIs based on the same linear regression model as above. Assay results below the LLOQ were set to 0.5 × LLOQ.

Assessor´s comment: similar immunogenicity of 3 different vaccine lots manufactured in the USA was demonstrated.

The similarity of the EU lot (Arm 4) to the pooled US lots cannot be formally declared until the dose comparison analysis is conducted in the sCSR however, the full-length S-binding IgG GMR (95% CI) of the EU lot to the pooled US lots was contained in the interval (0.67, 1.5) defined by the 1.5-fold equivalence margin.

Table 11. Geometric Mean Ratio of Full-Length S-Binding lgG Concentrations (U/mL) Between EU Lot and Pooled US Lots – 1 Month After Dose 2 – Linear Regression – Primary Study – Evaluable Immunogenicity Population

Vaccine Group (as Randomized)				
Arm 4 (EU Lot)		Pooled US Lots		Comparison GMR[a] (95% CI[a])
n[b]	GMC[c] (95% CI[c])	n[b]	GMC[c] (95% CI[c])	Arm 4 (EU Lot) /Pooled US Lots
160	6098.6 (5474.7, 6793.7)	945	6428.8 (6149.5, 6720.7)	0.95 (0.84, 1.07)

Abbreviations: GMC = geometric mean concentration; GMR = geometric mean ratio; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; LS=least squares; S = spike protein.
Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4.
a. GMR and the corresponding 2-sided 95% CI were calculated by exponentiating the difference in LS means and corresponding CIs based on analysis of logarithmically transformed assay results using a linear regression model with terms of age and vaccine group.
b. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.
c. GMCs and 2-sided 95% CIs were calculated by exponentiating the LS mean of the concentrations and corresponding CIs based on the same linear regression model as above. Assay results below the LLOQ were set to 0.5 × LLOQ.

Assessor´s comment: similar immunogenicity of pooled vaccine lots manufactured in the USA and one vaccine lot from the EU was demonstrated. Non-inferiority analysis is expected to be shown in coming sCSR.

Secondary Immunogenicity

For the secondary immunogenicity (GMFR, GMC) analyses in participants 12-50 years of age, data specific to paediatric participants 12-17 years of age was included for the GMC analyses only.

Full-length S-binding IgG GMFRs (95% CI) from baseline to 1 month after Dose 2 were similar for all the US lots. Full-length S-binding IgG GMFRs (95% CI) from baseline to 1 month after Dose 2 were similar for the EU lot and the pooled US lots.

Table 12. Geometric Mean Fold Rise in Full-Length S-Binding IgG Concentrations (U/mL) From Baseline to 1 Month After Dose 2 – Primary Study – Evaluable Immunogenicity Population

	Vaccine Group (as Randomized)									
	Arm 1 (US Lot 1)		Arm 2 (US Lot 2)		Arm 3 (US Lot 3)		Pooled US Lots		Arm 4 (EU Lot)	
Sampling Time Point[a]	n[b]	GMFR[c] (95% CI[c])	n[b]	GMFR[c] (95% CI[c])	n[b]	GMFR[c] (95% CI[c])	n[b]	GMFR[c] (95% CI[c])	n[b]	GMFR[c] (95% CI[c])
1 Month after Dose 2	323	2036.6 (1744.5, 2377.7)	311	2367.1 (2028.6, 2762.2)	310	2645.2 (2271.2, 3080.8)	944	2331.9 (2133.7, 2548.5)	160	2373.8 (1901.2, 2963.9)

Abbreviations: GMFR = geometric mean fold rise; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; S = spike protein.
Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4.
a. Protocol-specified timing for blood sample collection.
b. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.
c. GMFRs and the corresponding 2-sided 95% CIs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

Full-length S-binding IgG GMCs 1 month after Dose 2 across all vaccine groups were lower in older age subgroups (12-17 years of age ranged from 9582.2 to 11857.6, 18-30 years of age ranged from 5653.1 to 6929.1, and 31-50 years of age ranged from 4182.9 to 4743.3).

Assessor´s comment: As for the primary immunogenicity endpoint (GMC) also the secondary endpoint (GMFR) demonstrated similarity between USA vaccine lots.

MAH Immunogenicity conclusions:

- The 3 US lots met the 1.5-fold equivalence criteria for all 3 between-lot full-length S-binding IgG comparisons and were considered similar (model-based GMR [95% CI] estimates were contained in the interval [0.67, 1.5]: US Lot 1 to US Lot 2: 1.01 [0.91,1.13]; US Lot 1 to US Lot 3: 0.93 [0.83, 1.04]; and US Lot 2 to US Lot 3: 0.92 [0.82, 1.03]). Similar results were observed in the all-available population for model-based GMRs and in the evaluable immunogenicity and all-available immunogenicity population for unadjusted GMRs.
- The similarity of the EU lot to the pooled US lots cannot be formally declared until the dose comparison analysis is conducted in the sCSR, however the full-length S-binding IgG GMR (95% CI) of the EU lot to the pooled US lots was contained in the interval (0.67, 1.5) defined by the 1.5-fold equivalence margin.

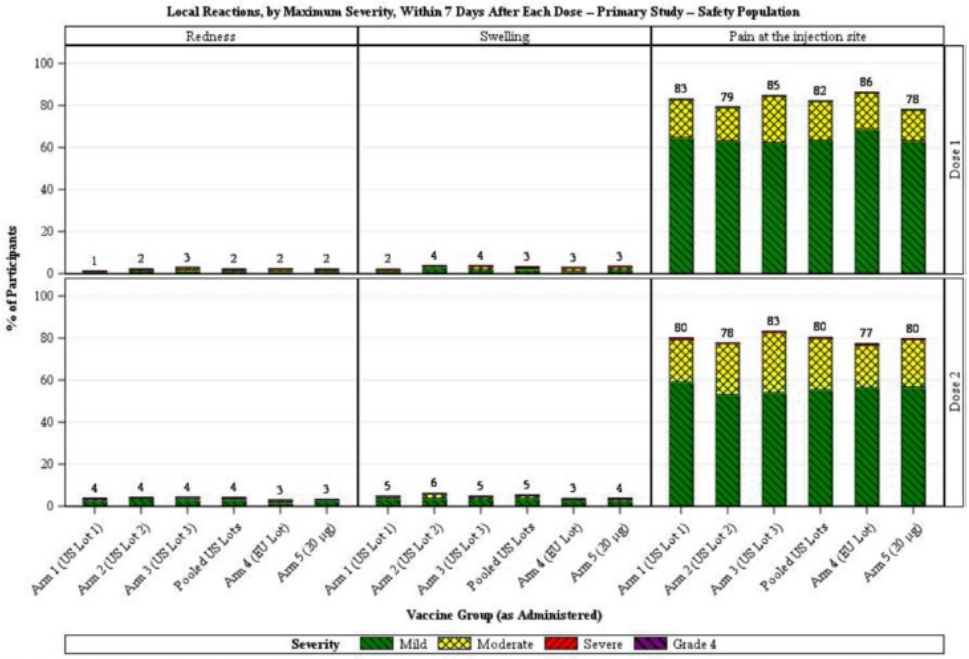
- Full-length S-binding IgG GMFRs (95% CI) from baseline to 1 month after Dose 2 were similar for all the US lots. Full-length S-binding IgG GMFRs (95% CI) from baseline to 1 month after Dose 2 were similar for the EU lot and the pooled US lots.

- ***Safety results***

- There were no paediatric participants in the booster study to evaluate the safety, tolerability, and immunogenicity of BNT162b2 RNA-based COVID-19 vaccine candidates as a booster dose in healthy participants 18-50 years of age and thereby only results from the primary study are discussed below.

- **Local reactions**
  The proportion of participants reporting local reactions in the primary study was similar across all vaccine groups (Fig 2). The proportion of participants reporting local reactions, in general, were similar after Dose 1 and Dose 2. The most common local reaction reported after Dose 1 or Dose 2 was pain at the injection site (range: 78.1% to 86.1% of participants after Dose 1 and 77.3% to 83.1% of participants after Dose 2). Most local reactions after Dose 1 or Dose 2 were mild to moderate with no Grade 4 local reactions reported. The proportions of participants reporting local reactions by maximum severity by subgroup (age group, race, and sex) were similar. Median duration of local reactions was 1 to 4 days after Dose 1 and 1 to 2 days after Dose 2. Median onset day of any local reactions after Dose 1 or Dose 2 was Day 1.

Figure 2. Participants Reporting Local Reactions, by Maximum Severity, Within 7 Days on Any Day After Each Dose – Primary Study – Safety Population



Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4, and a 20-µg dose of BNT162b2 was administered in Arm 5. Arm 5 study vaccine was from US Lot 1.
Note: Number above each bar denotes percentage of participants reporting the reaction with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 29OCT2021 (01:01) Source Data: adfacevd
Table Generation: 12NOV2021 (01:19) (Database Snapshot Date: 26OCT2021) Output File: /C4591017_SEC/C4591017_CSR/adce_f001_lr_maxsev_any

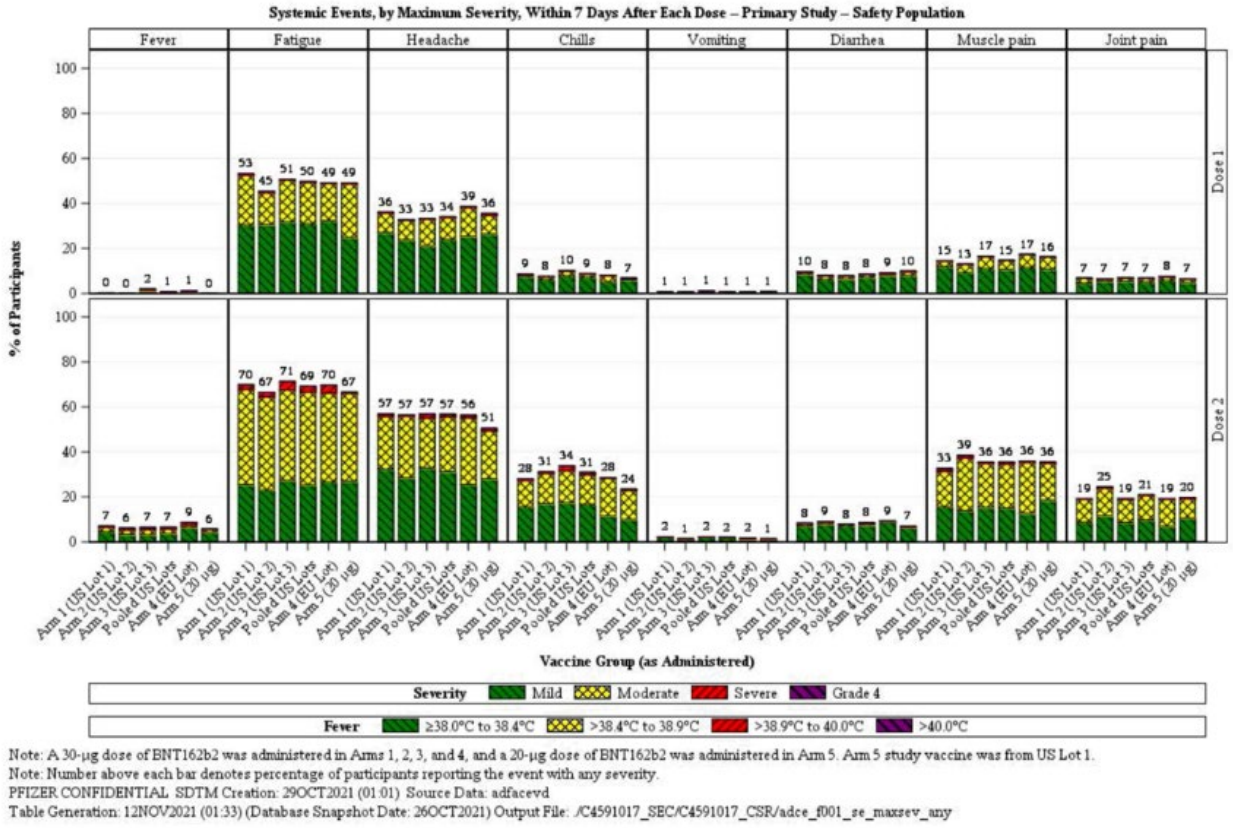
Assessor´s comment: The proportion of participants reporting local reactions was similar across all vaccine groups. The most common local reaction was pain at the injection site. Most local reaction events were mild or moderate with no Grade 4 events reported.

The safety results evaluating local reactions are in agreement with previously reported studies.

Systemic Events

The proportion of participants reporting systemic events in the primary study was similar across all vaccine groups (Fig 3). In general, a higher proportion of participants reported systemic events after Dose 2 than after Dose 1. The most common systemic events reported after Dose 1 or Dose 2 were fatigue (range: 45.5% to 53.3% and 66.6% to 71.4% participants, respectively), headache (range: 32.7% to 38.7% and 50.6% to 57.0% participants, respectively), and new or worsened muscle pain (range: 13.1% to 17.3% and 32.7% to 38.6% participants, respectively). Most systemic events after Dose 1 and Dose 2 were mild to moderate with no Grade 4 systemic events reported. The use of antipyretic/analgesic medication ranged from 14.5% to 22.0% after Dose 1 and 35.2% to 41.9% after Dose 2 for all vaccine groups. The proportions of participants reporting systemic events by maximum severity by subgroup (age group, race, and sex) were similar. Median duration of systemic events was 1 to 2 days after Dose 1 and Dose 2. Median onset day of any systemic events after Dose 1 was Day 1 and after Dose 2 was Day 2.

Figure 3. Participants Reporting Systemic Events, by Maximum Severity, Within 7 Days on Any Day After Each Dose – Safety Population



Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4, and a 20-µg dose of BNT162b2 was administered in Arm 5. Arm 5 study vaccine was from US Lot 1.
Note: Number above each bar denotes percentage of participants reporting the event with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 29OCT2021 (01:01) Source Data: adfacevd
Table Generation: 12NOV2021 (01:33) (Database Snapshot Date: 26OCT2021) Output File: /C4591017_SEC/C4591017_CSR/adce_f001_se_maxsev_any

Assessor´s comment: The proportion of participants reporting systemic events was similar across all vaccine groups. The most common systemic events were fatigue, headache, and new or worsened muscle pain. Most systemic events were mild or moderate with no Grade 4 events reported.

The safety results evaluating systemic events are in agreement with previously reported studies.

Adverse Events

The incidence of any AE from Dose 1 to 1 month after Dose 2 in the primary study ranged from 5.2% (US Lot 3) to 10.4% (EU Lot) (Table 13). There was a total of 2 SAEs, both of which were severe, but neither were related.

There was a total of 2 participants who were withdrawn for safety-related reasons: 1 participant was withdrawn because of pregnancy, and 1 participant reported AEs of dermatitis and angioedema which were assessed by the investigator as related to the investigational product (1 participant who received 20 µg of US Lot 1[Arm 5]).

AEs from Dose 1 to 1 month after Dose 2 were most commonly reported in the SOCs of infections and infestations (0.3% to 2.9% of participants) and skin and subcutaneous tissue disorders (0 to 2.9% of participants).

Related AEs from Dose 1 to 1 month after Dose 2 were most commonly reported in the SOCs of gastrointestinal disorders and nervous system disorders (both 0 to 1.2% of participants), general disorders and administration site conditions (0 to 1.1% of participants), and blood and lymphatic system disorders (0 to 0.9% of participants). There were no life-threatening AEs (Table 13).
Severe AEs by PT from Dose 1 to 1 month after Dose 2 were reported by single participants in each vaccine group.

Immediate AEs reported after Dose 1 were lymphadenopathy (1 participant who received US Lot 2) and injection site pain (1 participant who received 20 µg of US Lot 1[Arm 5]). Immediate AEs reported after Dose 2 were hypoaesthesia (1 participant who received the EU Lot) and injection site pain (1 participant who received 20 µg of US Lot 1[Arm 5]).

Table 13. Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – Primary Study – Safety Population

	Vaccine Group (as Administered)					
Adverse Event	Arm 1 (US Lot 1) (N^a=351) n^b (%)	Arm 2 (US Lot 2) (N^a=352) n^b (%)	Arm 3 (US Lot 3) (N^a=346) n^b (%)	Pooled US Lots (N^a=1049) n^b (%)	Arm 4 (EU Lot) (N^a=173) n^b (%)	Arm 5 (20 µg) (N^a=351) n^b (%)
Any adverse event	19 (5.4)	21 (6.0)	18 (5.2)	58 (5.5)	18 (10.4)	24 (6.8)
Related[c]	2 (0.6)	5 (1.4)	7 (2.0)	14 (1.3)	5 (2.9)	8 (2.3)
Severe	4 (1.1)	1 (0.3)	2 (0.6)	7 (0.7)	1 (0.6)	1 (0.3)
Life-threatening	0	0	0	0	0	0
Any serious adverse event	0	0	1 (0.3)	1 (0.1)	1 (0.6)	0
Related[c]	0	0	0	0	0	0
Severe	0	0	1 (0.3)	1 (0.1)	1 (0.6)	0
Life-threatening	0	0	0	0	0	0
Any nonserious adverse event	19 (5.4)	21 (6.0)	18 (5.2)	58 (5.5)	18 (10.4)	24 (6.8)
Related[c]	2 (0.6)	5 (1.4)	7 (2.0)	14 (1.3)	5 (2.9)	8 (2.3)
Severe	4 (1.1)	1 (0.3)	1 (0.3)	6 (0.6)	0	1 (0.3)
Life-threatening	0	0	0	0	0	0
Any adverse event leading to withdrawal	0	0	1 (0.3)	1 (0.1)	0	1 (0.3)
Related[c]	0	0	0	0	0	1 (0.3)
Severe	0	0	0	0	0	0
Life-threatening	0	0	0	0	0	0
Death	0	0	0	0	0	0

Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4, and a 20-µg dose of BNT162b2 was administered in Arm 5. Arm 5 study vaccine was from US Lot 1.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified adverse event. For "any event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 29OCT2021 (02:44) Source Data: adae Table Generation: 03NOV2021 (07:42)
(Database Snapshot Date : 26OCT2021) Output File: ./C4591017_SEC/C4591017_CSR/adae_s091_1md2_saf

Assessor´s comment: The incidence of any AE from Dose 1 to 1 month after Dose 2 ranged from 5.2% (US Lot 3) to 10.4% (EU Lot).

The MAH assessments are agreed.

The size of the study population was not large enough to detect rare AEs.

No new safety concerns are raised.

Deaths, Serious Adverse Events, Safety-Related Participant Withdrawals, and Other Significant Adverse Events

Deaths

No participants died during the study.

Serious Adverse Events

There were 2 participants who reported an SAE from Dose 1 to 1 month after Dose 2 (Table 14). One participant who received US Lot 3 at Dose 1 experienced an exposure during pregnancy on study day 1 followed by an SAE of spontaneous abortion on study day 30 that was not related to the investigational

vaccine as assessed by the investigator. The participant was withdrawn from the vaccination phase of the study because of the pregnancy. One participant who received the EU lot experienced an SAE of status migrainosus on study day 10 that was not related to the investigational vaccine as assessed by the investigator.

Serious Adverse Events Narratives (in short)

A 12-17 year old participant with a pertinent medical history of migraine , received Dose 1 (Arm 4 [EU lot]) on Day 1 and Dose 2 (Arm 4 [EU lot]) on Day 21. The participant experienced status migrainosus on Day 30, 9 days after receiving Dose 2. After receiving Dose 2, the participant reported moderate headache and fatigue. Both symptoms improved and were totally absent on Day 24. On Day 25, the participant reported headache and fatigue again and since then, reported headache every day with a variable intensity from mild to moderate. On Day 30 the headache and fatigue worsened to severe and the participant was treated as outpatient While being attended the participant presented with rash, neck pain, and headache. The participant received the diagnosis of status migrainosus, with an onset date on Day 30. On Day 32, the participant's symptoms worsened again. Post evaluation by pediatric neurology, infectious disease, rheumatology, vascular surgery, and hematology, the participant was admitted to the hospital on Day 34, with the diagnosis of status migrainosus. The participant reported debilitating fatigue, headache, and photosensitivity. The site was informed that the participant was started on a migraine medication according to a protocol. The participant was also prescribed ketorolac, ondansetron, and valproic acid. The participant's hospitalization was complicated by bilateral arm phlebitis (which later resolved post discharge) following dihydroergotamine IV treatment. On the same day, the participant underwent laboratory tests, which included protein electrophoresis, which showed albumin at 4.9 g/dL (normal range [NR]: 3.8-4.8 g/dL), and normal levels of alpha 1 globulin at, alpha 2 globulin, beta 1 globulin, beta 2 globulin, gamma globulin, total protein. Human leukocyte antigen B27 antigen result was positive, antineutrophil cytoplasmic antibodies (ANCA) screen with reflex was negative, and ANCA screen immunofluorescence assay was negative. On Day 35, the participant underwent brain magnetic resonance imaging (MRI) with and without contrast, which showed normal results. A SARS-CoV-2 test result was negative. OnDay 36, after ranitidine hydrochloride and prior to dihydroergotamine treatment, the participant developed an extrapyramidal reaction (dystonic reaction) with pulling of the head to the right and some failing movements. The participant was given diphenhydramine hydrochloride and the symptoms resolved. The participant also received prochlorperazine. Headache and fatigue improved mildly over hospitalization. The participant's pain went down to manageable 2/10 after 7 doses of dihydroergotamine. On Day 38, the participant was discharged from the hospital. On Day 56, the participant underwent a brain magnetic resonance venography to evaluate cerebral venous sinus thrombosis with negative results and on Day 57, an MRI venogram of head without contrast showed normal results. The participant continued to have daily migraines (level 1-6), photophobia, sound sensitivity, daily fatigue, dizziness (new symptom started on Day 51), and felt lightheaded/dizzy assessed by the investigator related to the ongoing migraine. On Day 63, the headache intensity had decreased but they were still present almost every day. The status migrainosus was ongoing at the time of the last available report. In the opinion of the investigator, there was no reasonable possibility that the status migrainosus was related to the study intervention, concomitant medications, or clinical trial procedure. Pfizer concurred with the investigator's causality assessment.

A 31-50 year-old female with a pertinent medical history reproductive disorder, received Dose 1 (Arm 3 [US Lot 3]) on Day 1. The participant had an exposure during pregnancy on Day 1after receiving Dose 1 and had a spontaneous abortion on Day 30. On Day 1, at the time of the first dose, the participant's pregnancy test result was negative. The participant was seen for Visit 2 on Day 24 and informed the site of possible pregnancy. On Day 24, the pregnancy test performed on site was positive. The participant was informed that the second dose would not be given. The participant did not smoke, drink alcohol, or use illicit drugs during this pregnancy. On Day 26, the participant informed the site that she received her

second dose of the COVID-19 vaccine (tozinameran; manufacturer: Pfizer) intramuscularly outside of the study and without consent of the site or the primary investigator on Day 24. The second dose was not part of the study vaccinations and was administered under emergency use authorization. On Day 30, the participant had a spontaneous abortion, which was considered medically significant. The participant was discontinued from the study intervention on Day 24 because of exposure during pregnancy and completed the follow-up visit on Day 52. In the opinion of the investigator, there was no reasonable possibility that the spontaneous abortion was related to the study intervention, concomitant medications, or clinical trial procedure, but rather it was related to the participant's medical history of reproductive disorder. Pfizer concurred with the investigator's causality assessment.

A 18-30-year-old participant with a pertinent medical history of contact dermatitis, drug hypersensitivity, and angioedema, received Dose 1 (Arm 5 [20 µg]) on Day 1. The participant developed acute dermatitis (generalized) on Day 4, and angioedema (generalized) on Day 5. On Day 7, the participant had an increased white blood cell count (11.4, normal range and units not provided) and was positive for antinuclear antibody (1:40). The participant received an unspecified treatment. The participant was discontinued from the study intervention on Day 7 because of dermatitis and angioedema. On Day 23, the dermatitis and angioedema resolved. The participant completed the follow-up visit on Day 10. The events of antinuclear antibody positive and increased white blood cell count were ongoing at the time of study completion. In the opinion of the investigator, there was a reasonable possibility that the dermatitis and angioedema were related to the study intervention.

A 31-50 year old participant with a pertinent medical history of drug hypersensitivity, seasonal allergy, and atrial fibrillation, received Dose 1 (Arm 2 [US Lot 2]) on Day 1 and Dose 2 (Arm 2 [US Lot 2]) on Day 47. The participant was diagnosed with COVID-19 based on symptoms and a positive SARS-CoV-2 NAAT result, performed on Day 21. On Day 31, the COVID-19 illness resolved. The participant was withdrawn from the study on Day 78 because of an unspecified reason. In the opinion of the investigator, there was no reasonable possibility that the COVID-19 was related to the study intervention.

A 31-50 year old participant with a pertinent medical history of seasonal allergy), received Dose 1 (Arm 2 [US Lot 2]) on Day 1 and Dose 2 (Arm 2 [US Lot 2]) on Day 23. The participant was diagnosed with COVID-19 based on symptoms and a positive SARS-CoV-2 rapid antigen test result on Day 13. On Day 17 the COVID-19 illness resolved. In the opinion of the investigator, there was no reasonable possibility that the COVID-19 was related to the study intervention.

Table 14. Number (%) of Participants Reporting at Least 1 Serious Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Primary Study – Safety Population

	Vaccine Group (as Administered)					
System Organ Class Preferred Term	Arm 1 (US Lot 1) (N[a]=351) n[b] (%) (95% CI[c])	Arm 2 (US Lot 2) (N[a]=352) n[b] (%) (95% CI[c])	Arm 3 (US Lot 3) (N[a]=346) n[b] (%) (95% CI[c])	Pooled US Lots (N[a]=1049) n[b] (%) (95% CI[c])	Arm 4 (EU Lot) (N[a]=173) n[b] (%) (95% CI[c])	Arm 5 (20 µg) (N[a]=351) n[b] (%) (95% CI[c])
Any event	0 (0.0, 1.0)	0 (0.0, 1.0)	1 (0.3) (0.0, 1.6)	1 (0.1) (0.0, 0.5)	1 (0.6) (0.0, 3.2)	0 (0.0, 1.0)
NERVOUS SYSTEM DISORDERS	0 (0.0, 1.0)	0 (0.0, 1.0)	0 (0.0, 1.1)	0 (0.0, 0.4)	1 (0.6) (0.0, 3.2)	0 (0.0, 1.0)
Status migrainosus	0 (0.0, 1.0)	0 (0.0, 1.0)	0 (0.0, 1.1)	0 (0.0, 0.4)	1 (0.6) (0.0, 3.2)	0 (0.0, 1.0)
PREGNANCY, PUERPERIUM AND PERINATAL CONDITIONS	0 (0.0, 1.0)	0 (0.0, 1.0)	1 (0.3) (0.0, 1.6)	1 (0.1) (0.0, 0.5)	0 (0.0, 2.1)	0 (0.0, 1.0)
Abortion spontaneous	0 (0.0, 1.0)	0 (0.0, 1.0)	1 (0.3) (0.0, 1.6)	1 (0.1) (0.0, 0.5)	0 (0.0, 2.1)	0 (0.0, 1.0)

Note: A 30-µg dose of BNT162b2 was administered in Arms 1, 2, 3, and 4, and a 20-µg dose of BNT162b2 was administered in Arm 5. Arm 5 study vaccine was from US Lot 1.
Note: MedDRA (v24.0) coding dictionary applied.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants reporting at least 1 occurrence of the specified adverse event. For "any event," n = number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 29OCT2021 (02:44) Source Data: adae Table Generation: 03NOV2021 (23:30)
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Safety-Related Participant Withdrawals

There were 2 participants who were withdrawn from the study for safety-related reasons.

One participant who received US Lot 3 was withdrawn because of pregnancy (Narrative described above).

One participant who received 20 µg of US Lot 1 (Arm 5) was withdrawn from the vaccination phase of the study because of related moderate AEs of dermatitis (study day 4) and angioedema (study day 5); the IP was withdrawn and these events resolved on study day 23.

Other Significant Adverse Events

There were 2 adult participants who received US Lot 2 who each reported an AE of special interest (COVID-19) from Dose 1 and 1 month after Dose 2 in the primary study. Both AEs occurred before Dose 2. One of the participants was diagnosed with moderate COVID-19 on study day 21 based on symptoms and a positive SARS-CoV-2 NAAT (described above). The other participant was diagnosed with mild COVID-19 on study day 13 based on symptoms and a positive rapid antigen test. While this diagnosis was based on signs/symptoms and an antigen test rather than a NAAT, this event was still considered an AESI by Pfizer (described above).

There were no cases of MIS-C.

Lymphadenopathy from Dose 1 to 1 month after Dose 2 was reported by 1 participant who received US Lot 1, 3 participants who received US Lot 2, 1 participant who received the EU Lot, and 2 participants who received 20 µg of US Lot 1 (Arm 5).

Assessor´s comment: There were 2 participants who reported a SAE from Dose 1 to 1 month after Dose 2.

One participant 12-17 years of age, with a pertinent medical history of migraine, received Dose 1 (Arm 4 [EU lot]) on Day 1 and Dose 2 (Arm 4 [EU lot]) on Day 21 and experienced status migrainosus on Day 30. This was assessed by the investigator as not related to the investigational vaccine.

One adult participant who received US Lot 3 at Dose 1 experienced an exposure during pregnancy on study day 1 followed by an SAE of spontaneous abortion on study day 30 that was not related to the investigational vaccine as assessed by the investigator. This participant was withdrawn from the vaccination phase of the study because of the pregnancy.

Furthermore, one adult participant who received 20 µg of US Lot 1 (Arm 5) was withdrawn from the vaccination phase of the study because of related moderate AEs of dermatitis and angioedema.

There were no cases of MIS-C, and no deaths reported.

The MAH assessments are agreed.

The size of the study population was not large enough to detect rare AEs or rare SAEs.

No new safety concerns are raised.

MAH Safety Conclusions

- The proportion of participants reporting local reactions and systemic events was similar across all vaccine groups. The most common local reaction was pain at the injection site. The most common systemic events were fatigue, headache, and new or worsened muscle pain. Most local reactions and systemic events were mild or moderate with no Grade 4 events reported.
- The proportion of participants who reported local reactions, were similar after Dose 1 and Dose 2. A higher proportion of participants reported systemic events and antipyretic/analgesic medication use after Dose 2 than Dose 1.
- The incidence of any AE from Dose 1 to 1 month after Dose 2 ranged from 5.2% (US Lot 3) to 10.4% (EU Lot).
- There was a total of 2 SAEs (1 participant who experienced an AE of exposure during pregnancy followed by an SAE of spontaneous abortion and 1 participant who experienced status migrainosus), both of which were severe, but neither were assessed by investigator or the MAH as related to the study vaccine.
- There were 2 participants who received US Lot 2 who were diagnosed with COVID-19, defined by the MAH as AEs of special interest, with onset between Dose 1 and Dose 2 (mild to moderate severities). There were no cases of MIS-C.
- Lymphadenopathy from Dose 1 to 1 month after Dose 2 was reported by 1 participant who received US Lot 1, 3 participants who received US Lot 2, 1 participant who received the EU Lot, and 2 participants who received 20 µg of US Lot 1 (Arm 5).
- Two participants were withdrawn for safety-related reasons, 1 of which had AEs assessed by the investigator as related to the investigational product (dermatitis and angioedema) and the other participant was withdrawn because of pregnancy.

- There were no deaths.

2.3.3. Discussion on clinical aspects

The main aim of the study was to demonstrate lot consistency of vaccine batches manufactured at different sites. The lot consistency of different vaccine batches was demonstrated in means of ability to induce antibody responses at similar scale. Similar antibody levels were demonstrated and therefore there is no concern of fluctuating quality between manufacturing sites. In total, 445 paediatric subjects (28% of the study population) aged 12-17 years were included in the study. For the primary immunogenicity (GMR) analyses in participants 12-50 years of age, there were no analyses specific to paediatric participants 12-17 years of age. For the secondary immunogenicity (GMC) analyses, the age specific immunological response was evaluated. The results showed that in the 12–17-year-old age group, antibody levels were twice as high than in older age groups as one may expect in light of the previous experience with Comirnaty and also with other vaccines.

The safety results are in agreement with previously reported studies. The size of the study population was not large enough to detect rare AEs and SAEs. No new safety concern is raised from this study.

3. CHMP overall conclusion and recommendation

The results of this study indicate no new efficacy or safety concern. The P46 procedure is considered fulfilled.

☒ **Fulfilled:**

No regulatory action required.

Annex. Line listing of all the studies included in the development program

The studies should be listed by chronological date of completion:

Non clinical studies

Product Name: BNT162b2/PF-07302048

Active substance: nucleoside-modified messenger RNA (modRNA)

Study title	Study number	Study completion date (end of in-life)	Date of final study report
Repeat-Dose Toxicity Study of Three Lipid Nanoparticle-Formulated RNA Platforms Encoding for Viral Proteins by Repeated Intramuscular Administration to Wistar Han Rats	38166	23 April 2020	Final report (original): 01 Jul 2020 Amendment 1: 17 September 2020
17-Day Intramuscular Toxicity Study of BNT162b2 (V9) and BNT162b3c in Wistar Han Rats With a 3-Week Recovery	20GR142	13 August 2020	Final report (original): 13 November 2020 Amendment 1: 17 December 2020
A Combined Fertility and Developmental Study (Including Teratogenicity and Postnatal Investigations) of BNT162b1, BNT162b2 and BNT162b3 by Intramuscular Administration in the Wistar Rat	20256434	12 October 2020	22 December 2020
BNT162b2 (V9) Immunogenicity and Evaluation of Protection against SARS-CoV-2 Challenge in Rhesus Macaques	VR-VTR-10671	01 November 2020	23 November 2020

Clinical studies

Product Name: BNT162b2/PF-07302048

Active substance: nucleoside-modified messenger RNA (modRNA)

Study title	Study number	Date of completion (last participant last visit)	Date of final study report
A Phase 3, randomized, observer-blind study to evaluate the safety, tolerability, and immunogenicity of multiple production lots and dose levels of the vaccine candidate BNT162b2 against COVID-19 in healthy participants 12 through 50 years of age and the safety, tolerability, and immunogenicity of BNT162b2 RNA-based COVID-19 vaccine candidates as a booster dose in healthy participants 18 through 50 years of age	BNT162-09 / C4591017	22 July 2021	07 January 2022

Study title	Study number	Date of completion (last participant last visit)	Date of final study report
A Phase 3, randomized, observer-blind study to evaluate the safety, tolerability, and immunogenicity of multiple formulations of the vaccine candidate BNT162b2 against COVID-19 in healthy adults 18 through 55 years of age	BNT162-11 / C4591020	01 December 2021	N/A
A multi-site, Phase I/II, 2-part, dose escalation trial investigating the safety and immunogenicity of four prophylactic SARS-CoV-2 RNA vaccines against COVID-19 using different dosing regimens in healthy and immunocompromised adults	BNT162-01	Ongoing	N/A
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	BNT162-02 / C4591001	Ongoing	N/A
A Phase 1/2, placebo-controlled, randomized, and observer-blind study to evaluate the safety, tolerability, and immunogenicity of a SARS-CoV-2 RNA vaccine candidate against COVID-19 in healthy Japanese adults	BNT162-05 / C4591005	Ongoing	N/A
A Phase 1, open-label, dose-finding study to evaluate safety, tolerability, and immunogenicity and Phase 2/3 placebo-controlled observer-blinded safety, tolerability, and immunogenicity study of a SARS-CoV-2 RNA vaccine candidate against COVID-19 in healthy children and young adults	BNT162-07 / C4591007	Ongoing	N/A
A Phase 2/3, placebo-controlled, randomized, observer-blind study to evaluate the safety, tolerability, and immunogenicity of a SARS-CoV-2 RNA vaccine candidate (BNT162b2) against COVID-19 in healthy pregnant women 18 years of age and older	BNT162-10 / C4591015	Ongoing	N/A
A Phase II, open-label, rollover trial to evaluate the safety and immunogenicity of one or two boosting doses of Comirnaty or one dose of BNT162b2s01 in BNT162-01 trial subjects, or two boosting doses of Comirnaty in BNT162-04 trial subjects.	BNT162-14	Ongoing	N/A
A Phase II trial to evaluate the safety and immunogenicity of a SARS-CoV-2 multivalent RNA vaccine in healthy subjects	BNT162-17	Ongoing	N/A
A Phase 2b open-label study to evaluate the safety, tolerability, and immunogenicity of vaccine candidate BNT162b2 in immunocompromised participants ≥2 years of age	C4591024	Ongoing	N/A
A Phase 3 master protocol to evaluate additional dose(s) of BNT162b2 in healthy individuals previously vaccinated with BNT162b2	C4591031	Ongoing	N/A