23 April 2026
EMADOC-1700519818-3039666
Committee for Medicinal Products for Human Use (CHMP)

Assessment report on group of variations including an extension of indication

Invented name: COMIRNATY

Common name: COVID-19 mRNA vaccine

Procedure No. EMA/VR/0000320534

Marketing Authorisation Holder (MAH): BioNTech Manufacturing GmbH

Note

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

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Table of contents

List of abbreviations

Abbreviation	Definition
AE	adverse event
AESI	adverse event of special interest
BMI	body mass index
CDC	Centers for Disease Control and Prevention (United States)
CI	confidence interval
CIOMS	Council for International Organizations of Medical Sciences
COVID-19	coronavirus disease 2019
CRF	case report form
CSR	clinical study report
DCT	data collection tool
e-diary	electronic diary
ECG	electrocardiogram
ED	emergency department
EMA	European Medicines Agency
EMS	emergency medical services
EUA	emergency use authorization
FDA	Food and Drug Administration
FPFV	first participant first visit
GCP	Good Clinical Practice
GMFR	geometric mean fold rise
GMR	geometric mean ratio
GMT	geometric mean titre
ICD	informed consent document
ICH	International Council of Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	independent ethics committee
IM	Intramuscular
IRB	institutional review board
IRT	interactive response technology
LLOQ	lower limit of quantitation
LPLV	last participant last visit
MedDRA	Medical Dictionary for Regulatory Activities

MIS-C	multisystem inflammatory syndrome in children
MMWR	morbidity and mortality weekly report
modRNA	nucleoside-modified messenger ribonucleic acid
MRI	magnetic resonance imaging
mRNA	messenger ribonucleic acid

1. Background information on the procedure

1.1. Type II group of variations

Pursuant to Article 7.2 of Commission Regulation (EC) No 1234/2008, BioNTech Manufacturing GmbH submitted to the European Medicines Agency on 19 December 2025 an application for a group of variations.

The following changes were proposed:

Variation(s) requested		**Type**
C.I.6.a	C.I.6.a Addition of a new therapeutic indication or modification of an approved one	Variation type II
C.I.7.b	C.I.7.b a strength	Variation type IB

A grouped application consisting of:

C.I.6.a. To modify the approved therapeutic indication by extending from Comirnaty concentrate for dispersion for injection formulation to Comirnaty dispersion for injection formulation as well as the overall change of posology from 3mcg to 10mcg and dosing regimen simplification (i.e. from 3-dose to a 2-dose primary course for 6 months to <2 years of age and to a single dose for 2 years to <5 years of age) for the active immunization to prevent COVID-19 caused by SARS-CoV-2 in infants and children from 6 months to <5 years without history of completion of COVID-19 primary series based on sub-study A (SSA) phase 2/3 Groups 1-5 of study C4591048 as well as to support the approved 10mcg single dose simplified posology in vaccine-naïve children from 5 to 11 years of age based on substudy E (SSE) of study C4591048, listed as a category 3 study in the RMP. As consequence, sections 1, 2, 3, 4.1, 4.2, 4.8, 5.1, 6.5, 6.6 and 8 of the SmPC and sections 1, 2, 3, 4 and 6 of the PL are updated accordingly. Study C4591048 is a master phase 1/2/3 protocol to investigate the safety, tolerability, and immunogenicity of variant adapted BNT162b2 RNA – based vaccine candidate(s) in healthy children. The updated RMP version 15.2 has also been submitted. In addition, the MAH took the opportunity to implement minor editorial changes in the PI.

C.I.7.b. To delete the 3mcg strength from the Comirnaty Marketing authorisation (EU/1/20/1528/035-036, EU/1/20/1528/042, EU/1/20/1528/050).

The variation requested amendments to the Summary of Product Characteristics, Package Leaflet and to the Risk Management Plan (RMP).

Information on paediatric requirements

Pursuant to Article 8 of Regulation (EC) No 1901/2006, the application included an EMA Decision P/0105/2024 on the agreement of a paediatric investigation plan (PIP).

At the time of submission of the application, the PIP P/0105/2024 was not yet completed as some measures were deferred.

Information relating to orphan market exclusivity

Similarity

Pursuant to Article 8 of Regulation (EC) No. 141/2000 and Article 3 of Commission Regulation (EC) No 847/2000, the MAH did not submit a critical report addressing the possible similarity with authorised orphan medicinal products because there is no authorised orphan medicinal product for a condition related to the proposed indication.

1.2. Steps taken for the assessment of the product

The Rapporteur and Co-Rapporteur appointed by the CHMP were:

Rapporteur: Filip Josephson Co-Rapporteur: Nicolas Beix

Timetable	Actual dates
Submission date	19 December 2025
Start of procedure:	24 January 2026
CHMP Rapporteur's preliminary assessment report circulated on:	23 March 2026
PRAC Rapporteur's preliminary assessment report circulated on:	26 March 2026
Joint Rapporteur's updated assessment report circulated on:	15 April 2026
CHMP opinion:	23 April 2026

2. Scientific discussion

2.1. Introduction

This assessment report includes immunogenicity and safety data from Study C4591048 Substudy A and E, to support an updated posology for infants and children from 6 months to <5 years of age from 3 µg to 10 µg. Furthermore, an updated dosing regimen from 3-dose to 2-dose primary course for 6 months to <2 years of age; and a single dose for 2 years to <5 years of age is proposed.

An updated RMP v15.2 has also been provided.

C4591048 Substudy A is a randomised single-blinded (sponsor-unblinded) study in Phase 1 and open-label in Phase 2/3.

- Substudy A: Phase 1 is a single-blinded, dose-finding study to evaluate the safety, tolerability, and immunogenicity of a 3-dose series of bivalent BNT162b2 (original/Omi BA.4/BA.5) administered on a 0-, 3-, and 11-week schedule (at 3, 6, or 10 µg), followed by a fourth dose with BNT162b2 Monovalent (Omi XBB.1.5) ~6 months after Dose 3, administered at the same dose level as was received for the primary vaccination series.
- Substudy A (Groups 1 – 5): Phase 2/3 is an open-label study evaluating the safety, tolerability, and immunogenicity of a 2-dose series of BNT162b2 Monovalent (Omi XBB.1.5) administered on a 0- and 8-week schedule at the 10 µg dose level in COVID 19 vaccine-naïve individuals 6 months to <2 yrs of age, and a single dose of BNT162b2 Monovalent (Omi XBB.1.5) at the 10 µg dose level in COVID 19 vaccine-naïve participants 2 to <5 yrs of age.

- 2-dose regimen of BNT162b2 (Omi KP.2) 10 µg in 6 months to <2 years (Group 6) is not included in this SCS, and data will be reported later. Evaluation of this group is ongoing.

- An internal audit of Site 1163 was conducted as part of the clinical quality assurance program. The audit identified data quality concerns, including discrepancies in source documentation and protocol deviations. In response, sensitivity analyses for primary safety and immunogenicity endpoints were performed excluding data from Site 1163 in addition to the primary analyses.

Study C4591048 Substudy E is an open-label study to evaluate the safety, tolerability, and immunogenicity of an updated BNT162b2 (Omi XBB.1.5) vaccine in participants 5 to <12 years of age who were COVID-19 vaccine-naïve. Participants received a single 10 µg dose of BNT162b2 (Omi XBB.1.5). This report presents final immunogenicity and safety data from the 310 participants ≥5 to <12 years of age enrolled in Study C4591048 Substudy E.

Disease or condition

The global outbreak of COVID-19, caused by the SARS-CoV-2 virus, originating in Wuhan, China was characterised by the WHO as a pandemic in March 2020. With the constant change and accumulating mutations in the genetic code of SARS-CoV-2, multiple variants have now emerged, including the Omicron variants and subvariants that continue to circulate globally.

The majority of infections result in asymptomatic or mild disease with full recovery. Underlying health conditions such as hypertension, diabetes, cardiovascular disease, chronic respiratory disease, chronic kidney disease, immune compromised status, cancer and obesity are considered risk factors for developing severe COVID-19. Other risk factors include organ transplantation and chromosomal abnormalities. Increasing age is another risk factor for severe disease and death due to COVID-19.

COVID-19 primarily manifest respiratory symptoms, such as cough and nasal congestion, and systemic symptoms, such as fever and chills. The clinical manifestations may also include loss of taste or smell, and the spectrum of illness can range from asymptomatic infection to severe pneumonia, ARDS, respiratory failure, septic shock, multiple organ dysfunction or failure, and death. While COVID-19 is primarily a pulmonary disease, it can also lead to cardiac, dermatologic, haematologic, hepatic, neurologic, renal, and other complications, including thromboembolic events and peri- and myocarditis.

The aetiology and pathogenesis of the main acute COVID-19 disease manifestations (i.e., pneumonia, myocarditis) are well understood. COVID-19 is also associated with a heterogenous group of post-acute, persistent symptoms and sequelae (currently described as long COVID), for which aetiology and pathogenesis are less well understood.

2.2. Quality aspects

Deletion of 3 µg strength of JN.1 (EU/1/20/1528/035-036), KP.2 (EU/1/20/1528/042) and LP.8.1 (EU/1/20/1528/050) variant-adapted presentations from the Comirnaty Marketing Authorisation. This is a consequential change to the change of posology from 3 µg to 10 µg and dosing regimen simplification for infants and children from 6 months to <5 years of age. The module 3 and product information is updated accordingly.

The deletion of the 3 µgstrength is endorsed, since the other available strengths may be considered sufficient for the paediatric population indicated in the Marketing Authorisation of Comirnaty (refer to clinical aspects below).

2.3. Clinical aspects

2.3.1. Introduction

GCP

The clinical trial was performed in accordance with GCP as claimed by the MAH.

The MAH has provided a statement to the effect that the clinical trial conducted outside the community was carried out in accordance with the ethical standards of Directive 2001/20/EC.

2.4. Clinical efficacy

Study C4591048 is a Phase 1/2/3 master study designed to investigate the safety, tolerability, and immunogenicity of variant-adapted BNT162b2 RNA-based vaccine candidate(s) in healthy children. The data in this report pertain to information from Substudy A. Substudy A Phase 2/3 was an open-label study, conducted during a period when multiple variant-adapted COVID-19 vaccines, including BNT162b2 (original/Omi BA.4/BA.5, Omi XBB.1.5, and Omi KP.2), were being evaluated globally.

2.4.1. Dose response study

Methods

Study participants

Substudy A recruited children ≥6 months to <5 years.

Eligible study participants in Phase 1 were COVID-19 vaccine-naïve healthy male or female participants ≥6 months through <4 years 3 months of age at time of randomisation.

Treatments

Phase 1 (dose-finding): Randomised, single-blinded evaluation of 3 doses of bivalent BNT162b2 (Original/Omi BA.4/BA.5) at 3, 6, or 10 µg, followed by a fourth dose of BNT162b2 (Omi XBB.1.5) at the same dose level. Data from this study informed dose selection for Phase 2/3.

Objectives and outcomes/endpoints

Table 1: Phase 1 immunogenicity objectives and endpoints

Objectives	Estimands	Endpoints
	Secondary	
To describe the immune responses elicited by prophylactic variant-adapted BNT162b2 at each dose level and variant-adapted vaccine type (if applicable) in COVID-19 vaccine–naïve participants ≥6 months to <5 years of age.	In participants complying with the key protocol criteria (evaluable participants) in each vaccine group and each age group: • GMTs at each time point for each strain-specific neutralising titre • GMFR from before the study vaccination to each subsequent time point prior to Dose 4 • Percentage of participants with seroresponse at each time point following vaccination prior to	• SARS-CoV-2 reference-strain–neutralising titres • SARS-CoV-2 Omicron BA.4/BA.5–neutralising titres • SARS-CoV-2 Omicron XBB.1.5–neutralising titres (for 1-month post–Dose 3 and 1-month post–Dose 4 time points only)

	Dose 4	

Randomisation and blinding

All participants were centrally assigned to study intervention using an IRT. This was a randomised study that was single-blinded (sponsor-unblinded) in Phase 1.

Statistical methods

For all the immunogenicity endpoints, the analysis will be based on the evaluable immunogenicity population. Analyses of the all-available immunogenicity population were also performed to confirm robustness of analysis results. Participants were summarised according to the vaccine group to which they were randomised.

Phase 1

Phase 1 immunogenicity analyses evaluated SARS-CoV-2 neutralising antibody responses in COVID-19 vaccine–naïve participants ≥6 months to <2 years of age and 2 to <5 years of age following a 3-dose regimen (3, 6, or 10 µg) of bivalent BNT162b2 (Original/Omi BA.4/BA.5), with a fourth dose of BNT162b2 (Omi XBB.1.5) at the same dose level.

Responses were assessed against reference, Omicron BA.4/BA.5, and Omicron XBB.1.5 strains at key time points. Results were benchmarked against a historical cohort from Study C4591007 who received three doses of BNT162b2 3 µg (original, monovalent).

The validated SARS-CoV-2 authentic virus neutralisation assay was used to determine the neutralising titres.

GMTs, GMFRs, and Seroresponse Rates:

GMTs and GMFRs with 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titres and fold rises, respectively, and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

Seroresponse was defined as achieving a ≥4-fold rise from baseline (before the study vaccination). If the baseline measurement was below the LLOQ, a postvaccination measure of ≥4 × LLOQ was considered seroresponse. The exact 2-sided 95% CIs for percentages of participants with seroresponse was calculated using the Clopper-Pearson method.

Results

Participants flow

Most participants (99.0%) in 6 months-<2 years age group received at least 1 dose of study vaccine. The majority completed the first three doses, with 94.8% receiving Dose 2 and 91.7% receiving Dose 3.

In total, 81.3% of participants received Dose 4. All of these participants received BNT162b2 (Omi XBB.1.5) except 2 participants in the 3 µg group who received bivalent BNT162b2 (original/Omi BA.4/BA.5).

Twenty participants (20.8%) withdrew from the study, with most withdrawals due to withdrawal by parent/guardian (12.5%) or being lost to follow-up (6.3%). Protocol deviations accounted for 2.1% of withdrawals. Most participants (78.1%) completed the study (Table below).

Table 2. Disposition of All Randomised Participants - Substudy A - Phase 1 - 6 Months to <2 Years of Age.

	Vaccine Group (as Randomised)			
	Bivalent BNT162b2 (Original/Omi			
	BA.4/BA.5) 3 µg n[a] (%)	n[a] (%)	6 µg 10 µg n[a] (%)	Total n[a] (%)
Randomised[b]	32 (100.0)	31 (100.0)	33 (100.0)	96 (100.0)
Not vaccinated	0	1 (3.2)	0	1 (1.0)
Vaccinated	32 (100.0)	30 (96.8)	33 (100.0)	95 (99.0)
Dose 1	32 (100.0)	30 (96.8)	33 (100.0)	95 (99.0)
Dose 2	31 (96.9)	29 (93.5)	31 (93.9)	91 (94.8)
Dose 3	30 (93.8)	27 (87.1)	31 (93.9)	88 (91.7)
Dose 4[c]	26 (81.3)	24 (77.4)	28 (84.8)	78 (81.3)
Completed 1-month post-Dose 2 visit	31 (96.9)	27 (87.1)	31 (93.9)	89 (92.7)
Completed 1-month post-Dose 3 visit	30 (93.8)	26 (83.9)	31 (93.9)	87 (90.6)
Completed 1-month post-Dose 4 visit	25 (78.1)	24 (77.4)	28 (84.8)	77 (80.2)
Completed the study	24 (75.0)	24 (77.4)	27 (81.8)	75 (78.1)
Withdrawn from study	8 (25.0)	6 (19.4)	6 (18.2)	20 (20.8)
Reason for withdrawal from study				
Lost to follow-up	2 (6.3)	2 (6.5)	2 (6.1)	6 (6.3)
Protocol deviation	1 (3.1)	0	1 (3.0)	2 (2.1)
Withdrawal by parent/guardian	5 (15.6)	4 (12.9)	3 (9.1)	12 (12.5)

a. n = Number of participants with the specified characteristic.
b. These values are the denominators for the percentage calculations.
c. All participants received BNT162b2 (Omi XBB.1.5) at the specified dose level at dose 4 except 2 participants who received Bivalent BNT162b2 (Original/Omi BA.4/BA.5) 3 µg.
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All participants (100%) in age group 2-<5 years received at least 1 dose of study vaccine. The majority completed the first three doses, with 95.8% receiving Dose 2 and 90.1% receiving Dose 3 (table below). Most participants (78.9%) received Dose 4 and all received BNT162b2 (Omi XBB.1.5).

- Seventeen participants (23.9%) withdrew from the study, with most withdrawals due to withdrawal by parent/guardian (15.5%) or being lost to follow-up (7.0%).
- Approximately 76% of participants (76.1%) completed the study.

Table 3. Disposition of All Randomised Participants - Substudy A - Phase 1 - 2 to<5 Years of Age.

	Vaccine Group (as Randomised)			
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)			
	3 µg n[a] (%)	6 µg n[a] (%)	10 µg n[a] (%)	Total n[a] (%)
Randomised[b]	23 (100.0)	24 (100.0)	24 (100.0)	71 (100.0)
Not vaccinated	0	0	0	0
Vaccinated	23 (100.0)	24 (100.0)	24 (100.0)	71 (100.0)

Dose 1	23 (100.0)	24 (100.0)	24 (100.0)	71 (100.0)
Dose 2	20 (87.0)	24 (100.0)	24 (100.0)	68 (95.8)
Dose 3	18 (78.3)	23 (95.8)	23 (95.8)	64 (90.1)
Dose 4[c]	13 (56.5)	23 (95.8)	20 (83.3)	56 (78.9)
Completed 1-month post-Dose 2 visit	18 (78.3)	23 (95.8)	23 (95.8)	64 (90.1)
Completed 1-month post-Dose 3 visit	15 (65.2)	23 (95.8)	22 (91.7)	60 (84.5)
Completed 1-month post-Dose 4 visit	13 (56.5)	22 (91.7)	20 (83.3)	55 (77.5)
Completed the study	13 (56.5)	21 (87.5)	20 (83.3)	54 (76.1)
Withdrawn from study	10 (43.5)	3 (12.5)	4 (16.7)	17 (23.9)
Reason for withdrawal from study				
Lost to follow-up	3 (13.0)	2 (8.3)	0	5 (7.0)
Protocol deviation	1 (4.3)	0	0	1 (1.4)
Withdrawal by parent/guardian	6 (26.1)	1 (4.2)	4 (16.7)	11 (15.5)

a. n = Number of participants with the specified characteristic.
b. These values are the denominators for the percentage calculations.
c. All participants received BNT162b2 (Omi XBB.1.5) at the specified dose level at dose 4.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adds Table Generation: 26SEP2025 (08:04) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adds_s002_disp_p1_5

Recruitment

The Phase 1 study was initiated on 24 October 2022 and the final analyses presented in this report are based on the LSLV of 16 October 2024 for Phase 1.

Conduct of the study

The Phase 1 study was conducted at 21 sites in the US.

Baseline data

Overall, 55.6% of the Phase 1 safety population 6 months through < 2 years of age were male. A total of 60.0% of participants had evidence of prior SARS-CoV-2 infection at study baseline ("baseline positive"). Most participants were White (68.9%), followed by Black or African American (17.8%); Few participants (6.7.%) had at least 1 high-risk underlying comorbidity. The median age at the first study vaccination was 9.0 months.

Table 4. Demographic Characteristics - C4591048 Substudy A Phase 1 - Evaluable Immunogenicity (4-Dose) Population - 6 Months to <2 Years of Age.

	Vaccine Group (as Administered at Dose 4)			
	BNT162b2 (Omi XBB.1.5)			
	3 µg (N[a]=12) n[b] (%)	**6 µg (N[a]=17) (N[a]=45) n[b] (%)**	**10 µg (N[a]=16) n[b] (%)**	**Total n[b] (%)**
Sex				
Male	4 (33.3)	13 (76.5)	8 (50.0)	25 (55.6)
Female	8 (66.7)	4 (23.5)	8 (50.0)	20 (44.4)
Race				
White	8 (66.7)	10 (58.8)	13 (81.3)	31 (68.9)

Black or African American	2 (16.7)	3 (17.6)	3 (18.8)	8 (17.8)
Multiracial	2 (16.7)	4 (23.5)	0	6 (13.3)
Ethnicity				
Hispanic/Latino	1 (8.3)	4 (23.5)	5 (31.3)	10 (22.2)
Non-Hispanic/non-Latino	11 (91.7)	13 (76.5)	11 (68.8)	35 (77.8)
Country				
United States	12 (100.0)	17 (100.0)	16 (100.0)	45 (100.0)
Age at Dose 1 (months)				
Mean (SD)	11.7 (4.48)	10.3 (4.52)	12.2 (5.69)	11.3 (4.92)
Median	12.5	8.0	11.5	9.0
Min, max	(6, 20)	(6, 19)	(6, 22)	(6, 22)
Baseline SARS-CoV-2 status				
Positive[c]	6 (50.0)	9 (52.9)	12 (75.0)	27 (60.0)
Negative[d]	5 (41.7)	8 (47.1)	3 (18.8)	16 (35.6)
Missing	1 (8.3)	0	1 (6.3)	2 (4.4)
Comorbidities[e]				
Yes	0	1 (5.9)	2 (12.5)	3 (6.7)
No	12 (100.0)	16 (94.1)	14 (87.5)	42 (93.3)

Overall, 58.1% of the Phase 1 safety population 2 through <5 years of age were male. A total of 97.7% of participants had evidence of prior SARS-CoV-2 infection at study baseline ("baseline positive"). Most participants were White (69.8%), followed by Black or African American (23.3%); 39.5% of participants had at least 1 high-risk underlying comorbidity. The median age at study vaccination was 2.0 years.

Table 5. Demographic Characteristics - C4591048 Substudy A Phase 1 - Evaluable Immunogenicity (4-Dose) Population - 2 to <5 Years of Age.

	Vaccine Group (as Administered at Dose 4)			
	BNT162b2 (Omi XBB.1.5)			
	3 µg (N[a]=11) n[b] (%)	**6 µg (N[a]=16) (N[a]=43) n[b] (%)**	**10 µg (N[a]=16) n[b] (%)**	**Total n[b] (%)**
Sex				
Male	6 (54.5)	9 (56.3)	10 (62.5)	25 (58.1)
Female	5 (45.5)	7 (43.8)	6 (37.5)	18 (41.9)
Race				
White	6 (54.5)	15 (93.8)	9 (56.3)	30 (69.8)
Black or African American	4 (36.4)	0	6 (37.5)	10 (23.3)
Asian	0	1 (6.3)	0	1 (2.3)
Multiracial	1 (9.1)	0	1 (6.3)	2 (4.7)
Ethnicity				
Hispanic/Latino	7 (63.6)	10 (62.5)	8 (50.0)	25 (58.1)
Non-Hispanic/non-Latino	4 (36.4)	6 (37.5)	8 (50.0)	18 (41.9)

Country				
United States	11 (100.0)	16 (100.0)	16 (100.0)	43 (100.0)
Age at Dose 1 (years[c])				
Mean (SD)	2.5 (0.52)	2.6 (0.81)	2.4 (0.62)	2.5 (0.67)
Median	3.0	2.0	2.0	2.0
Min, max	(2, 3)	(2, 4)	(2, 4)	(2, 4)
Obese[d]				
Yes	3 (27.3)	4 (25.0)	4 (25.0)	11 (25.6)
No	8 (72.7)	12 (75.0)	12 (75.0)	32 (74.4)
Baseline SARS-CoV-2 status				
Positive[e]	11 (100.0)	15 (93.8)	16 (100.0)	42 (97.7)
Negative[f]	0	1 (6.3)	0	1 (2.3)
Comorbidities[g]				
Yes	4 (36.4)	7 (43.8)	6 (37.5)	17 (39.5)
No	7 (63.6)	9 (56.3)	10 (62.5)	26 (60.5)

Numbers analysed

Table 6. Immunogenicity populations in C4591048 Substudy A Phase 1.

4th dose with XBB 1.5	**3 µg**	**6 µg**	**10 µg**	**Total**
6 months-<2y.				
Randomised	32 (100.0)	31 (100.0)	33 (100.0)	96 (100.0)
All available	29 (90.6)	26 (83.9)	29 (87.9)	84 (87.9)
4 doses Evaluable Imm. pop	12 (37.5)	17 (54.8)	16 (48.5)	45 (46.9)
2 y.-<5y.				
Randomised	23 (100)	24 (100)	24 (100)	71 (100.0)
All available	16 (69.9)	23 (95.8)	23 (95.8)	62 (87.3)
4 doses Evaluable Imm. pop	11 (47.8)	16 (66.7)	16 (66.7)	43 (60.6)
Total 6 months-<5y.				
Randomised	55 (100.0)	55 (100.0)	57 (100.0)	167 (100.0)
All available	45 (81.8)	49 (89.1)	52 (91.2)	146 (87.4)
4 doses Evaluable Imm. pop	23 (41.8)	33 (60.0)	32 (56.1)	88 (52.7)

Outcomes and estimation

At 1 month after Dose 4 (BNT162b2 [monovalent Omi XBB.1.5]) compared to 1 month after Dose 3, GMTs against Omicron XBB.1.5. were higher in participants who received 6 µg and 10 µg and trended higher in participants who received 3 µg in 6 months -<2 years group. No analysis of Geometric Mean Fold Rise and Seroresponse for Omicron XBB 1.5 virus strain was presented after dose 4.

Table 7. Neutralising antibody titre before and after vaccination, Phase 1.

Assay	Age Group	Dose/Sampling Time Point[a]	Vaccine Group (as Administered at Dose 4) C4591048 BNT162b2 (Omi XBB.1.5) 3 µg n[b]	3 µg GMT[c] (95% CI[c])	6 µg n[b]	6 µg GMT[c] (95% CI[c])	10 µg n[b]	10 µg GMT[c] (95% CI[c])
SARS-CoV-2 neutralisation assay - Omicron XBB.1.5 - NT50 (titre)	6 months to <2 years	3/1 Month[d]	10	2830.7 (1237.9, 6472.7)	12	2166.8 (1200.1, 3912.1)	11	2621.3 (1259.0, 5457.5)
		4/1 Month	11	5948.0 (1429.2, 24754.4)	17	9228.3 (5663.5, 15037.1)	15	11344.3 (5893.7, 21835.6)
	2 to <5 years	3/1 Month[d]	11	3439.9 (1580.1, 7488.6)	12	1543.0 (792.5, 3004.5)	13	2871.2 (1686.5, 4888.2)
		4/1 Month	10	9522.0 (4036.1, 22464.3)	16	6591.9 (4133.1, 10513.4)	16	10784.2 (6499.6, 17893.2)
	6 months to <5 years	3/1 Month[d]	21	3135.0 (1872.4, 5248.8)	24	1828.5 (1206.5, 2771.3)	24	2753.8 (1834.8, 4133.2)
		4/1 Month	21	7441.9 (3401.4, 16282.1)	33	7839.3 (5664.5, 10849.2)	31	11051.7 (7516.2, 16250.0)
SARS-CoV-2 neutralisation assay - Omicron BA.4/BA.5 - NT50 (titre)	6 months to <2 years	3/1 Month[d]	10	8988.4 (3591.6, 22494.4)	12	7689.3 (4533.3, 13042.5)	11	13183.6 (6741.6, 25781.4)
		4/1 Month	12	9385.3 (2433.6, 36195.0)	17	12860.1 (8437.1, 19601.8)	16	15631.9 (9210.4, 26530.4)
	2 to <5 years	3/1 Month[d]	11	10740.3 (6596.4, 17487.4)	13	8020.0 (5399.8, 11911.6)	13	15445.3 (8712.3, 27381.7)
		4/1 Month	11	17856.0 (10700.0, 29797.6)	16	12548.6 (9180.6, 17152.1)	16	18208.1 (11913.2, 27829.4)
	6 months to <5 years	3/1 Month[d]	21	9867.1 (6242.6, 15596.1)	25	7859.6 (5816.8, 10619.8)	24	14364.2 (9605.3, 21480.7)

Abbreviations: GMT = geometric mean titre; LLOQ = lower limit of quantitation; NA = not applicable; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein-binding; NE = not estimable; NT50 = 50% neutralising titre; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

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. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titres and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

d. Evaluable immunogenicity (3-Dose) population.

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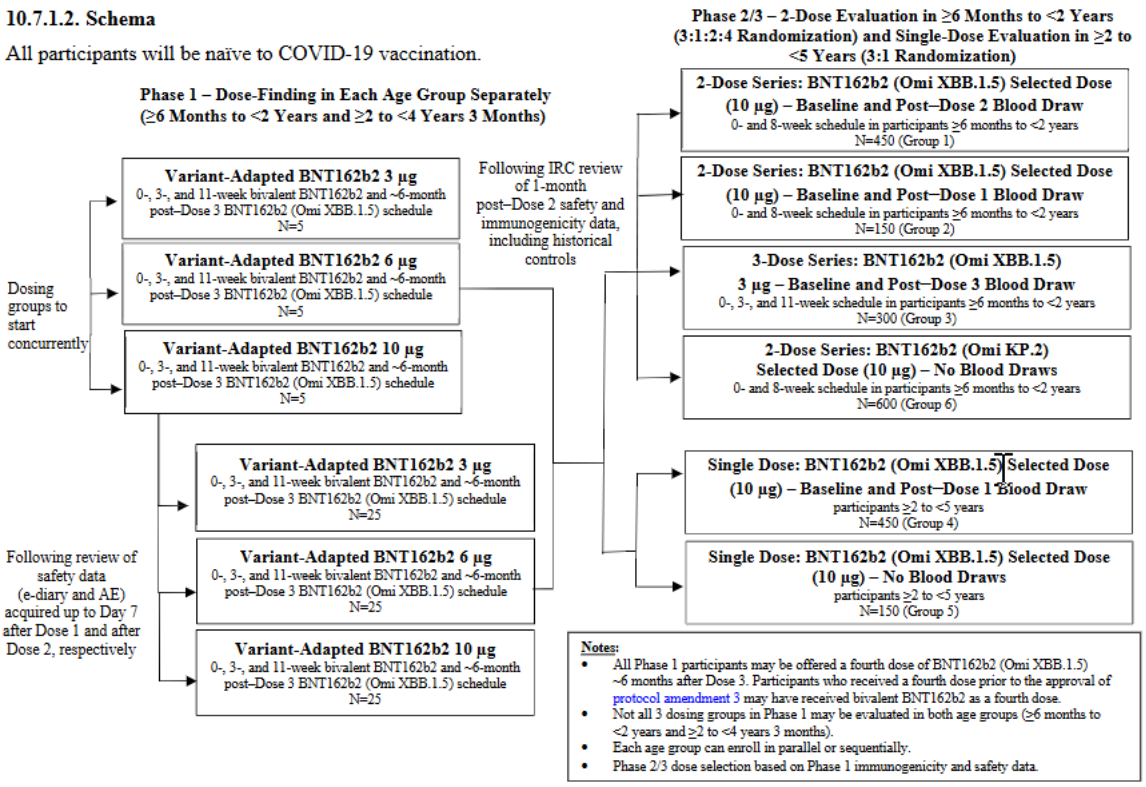
2.4.2. Main study

A Master Phase 1/2/3 Protocol to Investigate the Safety, Tolerability, and Immunogenicity of Variant-Adapted BNT162b2 RNA-Based Vaccine Candidate(s) in Healthy Children

2.4.2.1. – Substudy A phase 2/3 groups 1 through 5 – 6-month analysis

Methods

Figure 1: C4591048 Substudy A Phase 1/2/3 design



Study participants

Eligible study participants in Phase 2/3 were COVID-19 vaccine-naïve healthy male or female participants ≥6 months through<5 years at time of randomisation/enrolment.

Individuals were excluded from the study if they were immunocompromised or had a suspected immunodeficiency, bleeding diathesis or condition associated with prolonged bleeding, that would contraindicate an IM injection. Individuals were also excluded if there was any medical or laboratory abnormality that may increase the risk of study participation or make the participants inappropriate for the study. Individuals were excluded if they had a history of severe adverse reaction associated with a vaccine and/or severe allergic reaction (e.g., anaphylaxis) to any component of study intervention. Individuals were also excluded if they had received a medication intended to prevent COVID-19 or had a previous or current diagnosis of MIS-C.

Treatments

The participants received BNT162b2 (Omi XBB.1.5) 10 µg or 3 µg formulation.

Table 8: Treatment groups in Phase 2/3 reported as immunogenicity populations

6 months-<2 years			2 years-<5 years
G1 XBB.1.5 10 µg 2 doses	G2 XBB.1.5 10 µg 1 dose	G3 XBB.1.5 3 µg doses	G4 XBB.1.5 10 µg 1 dose

Objectives and Outcomes/endpoints

Table 9. SSA, Phase 2-3 immunogenicity objectives and endpoints

Objectives	Estimands	Endpoints
Primary immunogenicity		
To demonstrate the noninferiority with respect to the level of neutralising titres and seroresponse rate of the anti–Omicron XBB.1.5 immune response after 2 doses of BNT162b2 (Omi XBB.1.5) at the selected dose level of 10 µg, compared to after 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg in COVID-19 vaccine–naïve participants ≥6 months to <2 years of age.	In participants complying with the key protocol criteria (evaluable participants): • GMR, estimated by the ratio of the geometric mean of SARS-CoV-2 XBB.1.5–neutralising titres at 1 month after Dose 2 for participants who received 2 doses of BNT162b2 (Omi XBB.1.5) at the selected dose level of 10 µg to those at 1 month after Dose 3 for participants who received 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg • The difference in percentage of participants with seroresponse[a] to the XBB.1.5 strain between participants who received 2 doses of BNT162b2 (Omi XBB.1.5) at the selected dose level of 10 µg at 1 month after Dose 2 and participants who received 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg at 1 month after Dose 3	SARS-CoV-2 Omicron XBB.1.5–neutralising titres

To demonstrate the noninferiority with respect to the level of neutralising titres and seroresponse rate of the anti–Omicron XBB.1.5 immune response after a single dose of BNT162b2 (Omi XBB.1.5) at the selected dose level of 10 µg in COVID-19 vaccine–naïve participants ≥2 to <5 years of age, compared to after 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg in COVID-19 vaccine–naïve participants ≥6 months to <2 years of age without evidence of prior infection.	In participants complying with the key protocol criteria (evaluable participants): • GMR, estimated by the ratio of the geometric mean of SARS-CoV-2 Omicron XBB.1.5–neutralising titres at 1 month after study vaccination for participants ≥2 to <5 years of age who received a single dose of BNT162b2 (Omi XBB.1.5) at the selected dose level of 10 µg, to those at 1 month after Dose 3 for participants ≥6 months to <2 years of age without evidence of prior infection who received 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg • The difference in percentage of participants with seroresponse to the XBB.1.5 strain between participants ≥2 to <5 years of age who received a single dose of BNT162b2 (Omi XBB.1.5) at 1 month after study vaccination, and participants ≥6 months to <2 years of age without evidence of prior infection who received 3 doses of BNT162b2 (XBB.1.5) 3 µg at 1 month after Dose 3	SARS-CoV-2 Omicron XBB.1.5–neutralising titres
Objectives	**Estimands**	**Endpoints**
Secondary Immunogenicity:		
To describe the immune response elicited by BNT162b2 (Omi XBB.1.5) in COVID-19 vaccine–naïve participants ≥6 months to <5 years of age.	In participants complying with the key protocol criteria (evaluable participants) in each vaccine group and each age group • GMTs at each time point • GMFR from before the study vaccination to each subsequent time point • Percentages of participants with seroresponse[a] at each time point following vaccination	• SARS-CoV-2 Omicron XBB.1.5–neutralising titres
Exploratory		
To describe COVID-19 and severe COVID-19 cases.		• Confirmed COVID-19 cases • Confirmed severe COVID-19 cases • Strain sequencing of COVID-19 cases
To describe MIS-C cases.		• Confirmed cases as per CDC criteria
To describe the immune response to emerging SARS-CoV-2 variants.		• SARS-CoV-2 neutralising titres for Omicron sublineages and SARS-CoV-2 variants not already specified

Sample size

Phase 2/3 was planned to enrol approximately 2100 participants, which was in line with safety objectives.

Noninferiority of Anti–Omicron XBB.1.5 Immune Response for the First Primary Immunogenicity Objectives in Phase 2/3

All enrolled participants (approximately 450 from Group 1) receiving 2 doses of BNT162b2 (Omi XBB.1.5) at the selected dose level of 10 µg, and with baseline and 1-month post–Dose 2 blood draws and all enrolled participants (approximately 300 from Group 3) receiving 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg will be selected to evaluate the first primary immunogenicity objective. Assuming a 25% nonevaluable rate, approximately 337 evaluable participants in the 2-dose vaccine group and 225 evaluable participants in the 3-dose vaccine group will contribute to the immunogenicity evaluation. Each hypothesis test will be performed at a 1-sided alpha level of 0.025.

For comparisons based on GMR, common assay standard deviations in log scale for Omicron XBB.1.5–neutralising titres are assumed to be 1.5 based on data observed in Study C4591054. Table below provides the power to declare noninferiority, using a 1.5-fold margin. If the true GMR of Omicron XBB.1.5–neutralising titres after 2 doses of variant-adapted BNT162b2 at the selected dose level of 10 µg to after 3 doses of variant-adapted BNT162b2 3 µg is 1, then 337 evaluable participants in the 2-dose vaccine group and 225 evaluable participants in the 3-dose vaccine group will provide 88.0% power to declare noninferiority using a 1.5-fold margin. The assumptions of assay variability, true GMR, and the statistical power estimate may be adjusted based on emerging data.

Table 10: Power to demonstrate noninferiority under different assumptions of sample size in the 2-dose group

Number of Evaluable Participants in the 2-Dose Group (≥6 Months to <2 Years) and the 3-Dose Group (≥6 Months to <2 Years)	Assumed True GMR	Power
337 vs 225	1.0	88.0%

For comparisons based on seroresponse rate differences, Table below provides the power to demonstrate noninferiority. For example, if the seroresponse rate is 80% in participants who received 2 doses of BNT162b2 (Omi XBB.1.5) at the selected dose level of 10 µg and participants who received 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg, then 337 evaluable participants in the 2-dose vaccine group and 225 evaluable participants in 3-dose vaccine group will provide 80.6% power to demonstrate noninferiority using a 10% margin.

Table 11: Power to demonstrate noninferiority under different assumptions of sample size in the 2-dose group

Number of Evaluable Participants in the 2-Dose Group (≥6 Months to <2 Years) and the 3-Dose Group (≥6 Months to <2 Years)	Assumed Seroresponse Rate in the 2-Dose Group (≥6 Months to <2 Years) (%)	Assumed Seroresponse Rate in the 3-Dose Group (≥6 Months to <2 Years) (%)	Power
337 vs 225	80	80	80.6%

Noninferiority of Anti–Omicron XBB.1.5 Immune Response for the Second Primary Immunogenicity Objectives in Phase 2/3

All enrolled participants (approximately 450 from Group 4) ≥2 to <5 years of age receiving a single dose of BNT162b2 (Omi XBB.1.5) at the selected dose level of 10 µg, and all enrolled participants ≥6 months to <2 years of age without evidence of prior infection receiving 3 doses of BNT162b2 (XBB.1.5) 3 µg (approximately 150 based on an assumption of 50% seronegative rate) will be selected to evaluate the second primary immunogenicity objective. Assuming a 25% nonevaluable rate, approximately 337 and 112 evaluable participants in each of above-mentioned vaccine groups, respectively, will contribute to the immunogenicity evaluation. Each hypothesis test will be performed at a 1-sided alpha level of 0.025.

For comparisons based on GMR, common assay standard deviations in log scale for Omicron XBB.1.5–neutralising titres are assumed to be 1.5 based on data observed in Study C4591054. Table below provides the power to declare noninferiority, using a 1.5-fold margin, under different assumptions of true GMRs of SARS-CoV-2 Omicron XBB.1.5– neutralising titres at 1 month after study vaccination for participants ≥2 to <5 years of age who received BNT162b2 (Omi XBB.1.5) as a single dose to neutralising titres at 1 month after Dose 3 in participants ≥6 months to <2 years of age without evidence of prior infection who received 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg. For example, if the true GMR is 1.1, the study will have 86.3% power to declare noninferiority. If the true GMR is 1.15, the study will have 91.4% power to declare noninferiority.

Table 12: Power to demonstrate noninferiority under different assumptions of GMR

Number of Evaluable Participants in Single-Dose Group (≥2 to <5 Years) and 3-Dose Group (≥6 Months to <2 Years)	Assumed True GMR	Power
337 vs 112	1.0	69.6%
337 vs 112	1.10	86.3%
337 vs 112	1.15	91.4%
337 vs 112	1.20	94.8%

For comparisons based on seroresponse rate differences, Table below provides the power to demonstrate noninferiority under different assumptions of seroresponse rates for each comparative group, using a 10% margin. For example, if the seroresponse rate is 80% in both comparator groups, then the study has 56.6% power to demonstrate noninferiority using a 10% margin.

Table 13: Power to demonstrate noninferiority under different assumptions of seroresponse rate

Number of Evaluable Participants in the Single-Dose Group (≥2 to <5 Years) and the 3-Dose Group (≥6 Months to <2 Years)	Assumed Seroresponse Rate in the Single-Dose Group (≥2 to <5 Years) (%)	Assumed Seroresponse Rate in the 3-Dose Group (≥6 Months to <2 Years) (%)	Power
337 vs 112	90	90	75.0%
337 vs 112	85	90	21.7%
337 vs 112	80	80	56.6%
337 vs 112	75	80	17.2%
337 vs 112	70	70	48.6%
337 vs 112	65	70	15.4%

Randomisation and blinding

All participants were centrally assigned to study intervention using an IRT. his was a randomised study that was single-blinded (sponsor-unblinded) in Phase 1 and open label in Phase 2/3.

Statistical methods

See also Phase 1 statistical methods in dose-response study part.

For all the immunogenicity endpoints, the analysis will be based on the evaluable immunogenicity population. Analyses of the all-available immunogenicity population were also performed to confirm robustness of analysis results. Participants were summarized according to the vaccine group to which they were randomised.

Phase 2/3

Immunogenicity analyses were conducted to characterise SARS-CoV-2 Omicron XBB.1.5 neutralisation responses in COVID-19 vaccine–naïve participants ≥6 months to <2 years of age following a 2-dose regimen (10 µg) of BNT162b2 (Omi XBB.1.5), and in participants ≥2 to <5 years of age following a single dose (10 µg) of BNT162b2 (Omi XBB.1.5), as well as to compare these responses to those observed after a 3-dose regimen (3 µg) of BNT162b2 (Omi XBB.1.5) in participants ≥6 months to <2 years of age who were contemporaneously enrolled into Substudy A Phase 2/3.

The model-based GMR and associated 95% CI were calculated by exponentiating the difference in LS means and the corresponding CIs based on the analysis of logarithmically transformed assay results using a linear regression model that included the baseline neutralising titre, postbaseline infection status, and vaccine group as covariates.

GMR

The unadjusted GMR was calculated as the mean of the difference of logarithmically transformed assay results and exponentiating the mean. Two-sided CIs were obtained by calculating CIs using the Student t distribution for the mean difference of the logarithmically transformed assay results and exponentiating the confidence limits.

Difference in Seroresponse Rates

The adjusted difference in seroresponse rate between 2 vaccine groups and the associated 2-sided 95% CIs, were based on the Miettinen and Nurminen method stratified by baseline neutralising titre category (< median, ≥ median). The unadjusted difference in percentages of participants with seroresponse between the 2 comparison groups, and the associated 2-sided 95% CIs, were calculated using the Miettinen and Nurminen method.

GMTs for Phase 2/3 were calculated as described in Phase 1 above.

Statistical Hypothesis

Multiplicity: The 2 primary immunogenicity objectives will be evaluated sequentially using a 1-sided alpha of 0.025 in the order shown in Section below.

Within each objective, GMR and seroresponse difference will be assessed sequentially in the order specified. Both hypotheses within the first objective must be established before assessing the second. Therefore, the overall type I error is fully controlled.

The order of hypothesis tests:

1. Noninferiority of 2 doses of 10 µg (G2) vs 3 doses of 3 µg (G3) among ≥6 months to <2 years of age.
    a. GMT
    b. Seroresponse

2. Noninferiority of 1 dose of 10 µg in 2 years-<5 year olds (G4) vs 3 doses of 3 µg (G3) in ≥6 months to <2 years of age without evidence of prior SARS-COV-2 infection.

    c. GMT

    d. Seroresponse

Noninferiority of Anti–Omicron XBB.1.5 Immune Responses for the First Primary Immunogenicity Objective in Phase 2/3

The first primary immunogenicity objective is to demonstrate the noninferiority with respect to the level of neutralising titres and the seroresponse rate of the anti–Omicron XBB.1.5 immune response induced by 2 doses of BNT162b2 (Omi XBB.1.5) at the selected dose (10 µg) relative to the anti–Omicron XBB.1.5 response elicited by 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg in COVID-19 vaccine–naïve participants ≥6 months to <2 years of age. The primary objective will be evaluated by the following 2 hypotheses:

The first null hypothesis (H0) is

H0: $\ln(\mu 1) - \ln(\mu 2) \leq \ln(0.67)$ vs H1: $\ln(\mu 1) - \ln(\mu 2) > \ln(0.67)$

where ln(0.67) corresponds to a 1.5-fold margin for noninferiority and

- ln(µ1) is the natural log of the geometric mean of SARS-CoV-2 Omicron XBB.1.5–neutralising titres measured at 1 month after Dose 2 in participants who received 2 doses of BNT162b2 (Omi XBB.1.5) at the selected dose of 10 µg;

- ln(µ2) is the natural log of the geometric mean of SARS-CoV-2 Omicron XBB.1.5–neutralising titres measured at 1 month after Dose 3 in participants who received 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg.

The second null hypothesis (H0) is

H0: $p1-p2 \leq -10\%$ vs H1: $p1-p2 > -10\%$

where -10% is the noninferiority margin for seroresponse and

- p1 is the percentage of participants with seroresponse to Omicron XBB.1.5 at 1 month after Dose 2 in participants who received 2 doses of BNT162b2 (Omi XBB.1.5) at the selected dose of 10 µg;
- p2 is the percentage of participants with seroresponse to Omicron XBB.1.5 at 1 month after Dose 3 in participants who received 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg.

Noninferiority based on the GMR will be declared if the lower limit of the 2-sided 95% CI for the GMR is greater than 0.67 (1.5-fold criterion) and the point estimate of the GMR is ≥0.8; noninferiority based on seroresponse rate difference will be declared if the lower limit of the 2-sided 95% CI for the difference in percentages of participants with seroresponse is >-10%.

Noninferiority of Anti–Omicron XBB.1.5 Immune Responses for the Second Primary Immunogenicity Objective in Phase 2/3

The second primary immunogenicity objective is to demonstrate the noninferiority with respect to the level of neutralising titres and the seroresponse rate of the anti–Omicron XBB.1.5 immune response induced by a single dose of BNT162b2 (Omi XBB.1.5) at the selected dose of 10 µg in COVID-19 vaccine–naïve participants ≥2 to <5 years of age relative to the anti–Omicron XBB.1.5 response elicited by 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg in COVID-19 vaccine–naïve participants ≥6

months to <2 years of age without evidence of prior infection. The second primary immunogenicity objective will be evaluated by the following 2 hypotheses:

The first null hypothesis (H0) is

H0: ln(μ1) – ln(μ2) ≤ ln(0.67) vs H1: ln(μ1) – ln(μ2) > ln(0.67)

where ln(0.67) corresponds to a 1.5-fold margin for noninferiority and

- ln(μ1) is the natural log of the geometric mean of SARS-CoV-2 Omicron XBB.1.5–neutralising titres measured at 1 month after study vaccination in participants ≥2 to <5 years of age who received a single dose of BNT162b2 (Omi XBB.1.5) at the selected dose of 10 μg;

- ln(μ2) is the natural log of the geometric mean of SARS-CoV-2 Omicron XBB.1.5–neutralising titres measured at 1 month after Dose 3 in participants ≥6 months to <2 years of age without evidence of prior infection who received 3 doses of BNT162b2 (Omi XBB.1.5).

The second null hypothesis (H0) is

H0: p1-p2 ≤ −10% vs H1:p1-p2 > −10%

where -10% is the noninferiority margin for seroresponse and

- p1 is the percentage of participants with seroresponse to Omicron XBB.1.5 at 1 month after study vaccination in participants ≥2 to <5 years of age who received a single dose of BNT162b2 (Omi XBB.1.5) at the selected dose of 10 μg;
- p2 is the percentage of participants with seroresponse to Omicron XBB.1.5 at 1 month after Dose 3 in participants ≥6 months to <2 years of age without evidence of prior infection who received 3 doses of BNT162b2 (Omi XBB.1.5) 3 μg.

Noninferiority based on the GMR will be declared if the lower limit of the 2-sided 95% CI for the GMR is greater than 0.67 (1.5-fold criterion) and the point estimate of the GMR is ≥0.8; noninferiority based on seroresponse rate difference will be declared if the lower limit of the 2-sided 95% CI for the difference in percentages of participants with seroresponse is >-10%.

Results

Participant flow

Across dose levels, most randomised participants (99.3%) received at least 1 dose of BNT162b2 (Omi XBB.1.5) and most participants (91.6% in the 10-μg groups and 88.9% in the 3-μg group) completed the study. A total of 47 participants (7.7%) in the 10-μg groups and 32 participants (10.5%) in the 3-μg group withdrew from the study, with most due to withdrawal by parent/guardian. One participant (0.2%) in the 10-μg group was withdrawn from the study due to an AE (Table below).

Table 14. Disposition of All Randomised Participants - Substudy A - Phase 2/3 - 6 Months to <2 Years of Age.

	Vaccine Group (as Randomised)		
	BNT162b2 (Omi XBB.1.5)		
	10 μg (Group 1 and Group 2) n[a] (%)	**3 μg (Group 3) n[a] (%)**	**Total n[a] (%)**

Randomised[b]	608 (100.0)	306 (100.0)	914 (100.0)
Not vaccinated	4 (0.7)	2 (0.7)	6 (0.7)
Vaccinated	604 (99.3)	304 (99.3)	908 (99.3)
Dose 1	604 (99.3)	304 (99.3)	908 (99.3)
Dose 2	576 (94.7)	295 (96.4)	871 (95.3)
Dose 3	NA	286 (93.5)	286 (31.3)
Completed 1-month post-Dose 1 visit	596 (98.0)	NA	596 (65.2)
Completed 1-month post-Dose 2 visit	570 (93.8)	292 (95.4)	862 (94.3)
Completed 1-month post-Dose 3 visit	NA	284 (92.8)	284 (31.1)
Completed the study	557 (91.6)	272 (88.9)	829 (90.7)
Withdrawn from study	47 (7.7)	32 (10.5)	79 (8.6)
Reason for withdrawal from study			
Adverse event	1 (0.2)	0	1 (0.1)
Death	2 (0.3)	1 (0.3)	3 (0.3)
Lost to follow-up	17 (2.8)	9 (2.9)	26 (2.8)
Protocol deviation	3 (0.5)	5 (1.6)	8 (0.9)
Withdrawal by parent/guardian	23 (3.8)	17 (5.6)	40 (4.4)
Other	1 (0.2)	0	1 (0.1)

Note: Participants enrolled in Group 1 and Group 2 were planned to receive a 2-dose series of BNT162b2 (Omi XBB.1.5) at 10 µg on a 0- and 8-week schedule. Participants enrolled in Group 3 were planned to receive a 3-dose series of BNT162b2 (Omi XBB.1.5) at 3 µg on a 0-, 3-, and 11-week schedule.

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

b. These values are the denominators for the percentage calculations.

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Most of the randomised participants (99.4%) received study vaccination. Most participants (94.1%) completed the study. Thirty-seven participants (5.3%) withdrew from the study, with most withdrawals due to being lost to follow-up or withdrawal by parent/guardian (Table below).

Table 15. Disposition of All Randomised Participants - Substudy A - Phase 2/3 - 2 to 5 Years of Age.

	Vaccine Group (as Randomised)
	BNT162b2 (Omi XBB.1.5) 10 µg (Group 4 and Group 5) n[a] (%)
Randomised[b]	692 (100.0)
Not vaccinated	4 (0.6)
Vaccinated	688 (99.4)
Dose 1	688 (99.4)
Completed 1-month post-Dose 1 visit	678 (98.0)
Completed the study	651 (94.1)
Withdrawn from study	37 (5.3)
Reason for withdrawal from study	
Death	2 (0.3)
Lost to follow-up	20 (2.9)

Protocol deviation	2 (0.3)
Withdrawal by parent/guardian	13 (1.9)

Note: Participants enrolled in Group 4 and Group 5 were planned to receive a single dose of BNT162b2 (Omi XBB.1.5) at 10 µg.
Note: One participant of 2 to <5 years of age who was randomised into Group 3 in error and received Omi XBB.1.5 at 3 µg is also included.
Note: One participant of 2 to <5 years of age who was randomised into Group 1 in error and received 2 doses of Omi XBB.1.5 at 10 µg is also included.
a. n = Number of participants with the specified characteristic.
b. These values are the denominators for the percentage calculations.
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Recruitment

The Phase 2/3 study was initiated on 29 January 2024 and the analyses presented in this report are based on the data cutoff date of 23 July 2025 which is the LSLV of Groups 1-5.

Conduct of the study

The Phase 2/3 study for Groups 1 – 5 was conducted at 47 sites in the US (including Puerto Rico), Brazil, and South Africa.

Table 16: summary of protocol amendments

Date of Protocol Amendment	Amendment
03 October 2024	This protocol amendment revised the design of Substudy A Phase 2/3.
05 July 2024	This protocol amendment was predominantly targeted at Substudy E.
01 September 2023	This protocol amendment was in response to the recommendation from the FDA to simplify the COVID-19 vaccine series, including in individuals under 12 years of age. The main updates were to revise Substudy A Phase 2/3 study design and add Substudy E to evaluate a single age-appropriate dose of BNT162b2 (Omi XBB.1.5) in COVID-19 vaccine–naïve individuals ≥2 to <12 years of age.
01 August 2023	This protocol amendment is in response to the recommendations that the strain composition of COVID-19 vaccines, globally, be updated.
18 November 2022	This protocol amendment was predominantly targeted at Substudy C and was in response to the feedback and learnings from other related substudies in the master protocol.
21 October 2022	This protocol amendment was in response to the FDA feedback received on 23 September 2022, requesting changes to generate more data on the bivalent vaccine.

Baseline data

BNT162b2 (Omi XBB.1.5) 10 µg (Group 1)

Overall, 48.2% of the evaluable immunogenicity (2-Dose) population were female. A total of 64.6% of participants had evidence of prior SARS-CoV-2 infection at study baseline ("baseline positive"). The median age at study vaccination was 14.0 months. Most participants were from South Africa (315; 85.8%), with 37 (10.1%) from the United States and 15 (4.1%) from Brazil.

BNT162b2 (Omi XBB.1.5) 10 µg (Group 2)

Overall, 45.7% of the evaluable immunogenicity (single-Dose) population were female. A total of 62.1% of participants had evidence of prior SARS-CoV-2 infection at study baseline. The median age at

study vaccination was 14.0 months. Most participants were from South Africa (119; 85.0%), with 13 (9.3%) from the United States and 8 (5.7%) from Brazil.

BNT162b2 (Omi XBB.1.5) 3 µg (Group 3)

Overall, 49.1% of the evaluable immunogenicity (3-Dose) population were female. A total of 64.5% of participants had evidence of prior SARS-CoV-2 infection at study baseline. The median age at study vaccination was 14.0 months. Most participants were from South Africa (202; 86.3%), with 20 (8.5%) from the United States and 12 (5.1%) from Brazil.

BNT162b2 (Omi XBB.1.5) 10 µg (Group 4)

Overall, 50.4% of the evaluable immunogenicity (single-Dose) population were female. A total of 93.4% of participants had evidence of prior SARS-CoV-2 infection at study baseline. The median age at study vaccination was 3.0 years. Most participants were from South Africa (355; 75.5%), with 62 (13.2%) from the United States, 40 (8.5%) from Brazil, and 13 (2.8%) from Puerto Rico (Table below).

Table 17. Demographic Characteristics - C4591048 Substudy A Phase 2/3 Participants - Evaluable Immunogenicity Population - 6 Months to <5 Years of Age

	Vaccine Group (as Randomised) BNT162b2 (Omi XBB.1.5)			
	6 Months to <2 Years			**2 to <5 Years**
	10 µg (Group 1) (N[a]=367) n[b] (%)	**10 µg (Group 2) (N[a]=140) n[b] (%)**	**3 µg (Group 3) (N[a]=234) n[b] (%)**	**10 µg (Group 4) (N[a]=470) n[b] (%)**
Sex				
Male	190 (51.8)	76 (54.3)	119 (50.9)	233 (49.6)
Female	177 (48.2)	64 (45.7)	115 (49.1)	237 (50.4)
Race				
White	31 (8.4)	13 (9.3)	15 (6.4)	56 (11.9)
Black or African American	263 (71.7)	99 (70.7)	179 (76.5)	334 (71.1)
American Indian or Alaska Native	0	1 (0.7)	0	1 (0.2)
Asian	1 (0.3)	1 (0.7)	1 (0.4)	2 (0.4)
Multiracial	11 (3.0)	2 (1.4)	5 (2.1)	12 (2.6)
Not reported	60 (16.3)	24 (17.1)	34 (14.5)	64 (13.6)
Unknown	1 (0.3)	0	0	1 (0.2)
Ethnicity				
Hispanic/Latino	34 (9.3)	13 (9.3)	22 (9.4)	83 (17.7)
Non-Hispanic/non-Latino	331 (90.2)	127 (90.7)	212 (90.6)	383 (81.5)
Not reported	2 (0.5)	0	0	4 (0.9)
Country				
Brazil	15 (4.1)	8 (5.7)	12 (5.1)	40 (8.5)
Puerto Rico	0	0	0	13 (2.8)
South Africa	315 (85.8)	119 (85.0)	202 (86.3)	355 (75.5)

United States	37 (10.1)	13 (9.3)	20 (8.5)	62 (13.2)
Age at Dose 1 (months/years[c])				
Mean (SD)	14.2 (5.06)	14.1 (5.03)	14.3 (5.30)	2.9 (0.81)
Median	14.0	14.0	14.0	3.0
Min, max	(6, 23)	(6, 23)	(6, 23)	(2, 4)
Obese[d]				
Yes	NA	NA	NA	54 (11.5)
No	NA	NA	NA	416 (88.5)
Baseline SARS-CoV-2 status				
Positive[e]	237 (64.6)	87 (62.1)	151 (64.5)	439 (93.4)
Negative[f]	121 (33.0)	45 (32.1)	77 (32.9)	25 (5.3)
Missing	9 (2.5)	8 (5.7)	6 (2.6)	6 (1.3)
Comorbidities[g]				
Yes	17 (4.6)	4 (2.9)	8 (3.4)	76 (16.2)
No	350 (95.4)	136 (97.1)	226 (96.6)	394 (83.8)

Abbreviations: MMWR = Morbidity and Mortality Weekly Report; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein-binding; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; NA = not applicable.
Note: Participants enrolled in Group 1 and Group 2 were planned to receive a 2-dose series of BNT162b2 (Omi XBB.1.5) at 10 µg on a 0- and 8-week schedule. Participants enrolled in Group 3 were planned to receive a 3-dose series of BNT162b2 (Omi XBB.1.5) at 3 µg on a 0-, 3-, and 11-week schedule. Participants enrolled in Group 4 were planned to receive a single dose of BNT162b2 (Omi XBB.1.5) at 10 µg.

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

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

c. The participant age at the study vaccination is in months for the age group ≥6 months to <2 years and in years for the age groups ≥2 years to <5 years.

d. Obese is defined as a body mass index (BMI) at or above the 95th percentile according to the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/data/zscore/bmiagerev.xls.

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

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

g. Number of participants who had at least 1 high-risk underlying condition, based on MMWR Morb Mortal Wkly Rep. 2020;69(32):1081-8 and CDC high-risk underlying conditions list last updated 09FEB2023 and/or obesity (BMI ≥ 95th percentile). Comorbidities were assessed at the first study visit.

PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adsl Table Generation: 25SEP2025 (03:42)

(Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adsl_s005_demo_evl_p2_5

Numbers analysed

Table 18. Immunogenicity populations in C4591048 Substudy A Phase 2/3

	6 months-<2 years			**2 years-<5 years**	**6 months-<5 years**
	G1 10 µg 2 doses n (%)	**G2 10 µg 1 dose n (%)**	**G3 3 µg 3 doses n (%)**	**G4 10 µg 1 dose n (%)**	**Total n (%)**
Randomised	456 (100.0)	152 (100.0)	306 (100.0)	518 (100.0)	1432 (100.0)
All Available immunogenicity population	409 (89.7)	142 (93.4)	271 (88.6)	485 (93.6)	1307 (91.3)
Evaluable immunogenicity population	367 (80.5)	140 (92.1)	234 (76.5)	470 (90.7)	1211 (84.6)
SARS-CoV-2 neg.			53 (17.3)		

Outcomes and estimation

Primary Immunogenicity

1-Month Post-Dose 2 (Group 1; 10 µg) to 1-Month Post-Dose 3 (Group 3; 3 µg)– Participants 6 Months to <2 Years of Age

Geometric Mean Ratio

Overall, the model-based GMR of SARS-CoV-2 Omicron XBB.1.5-neutralising titres between Group 1 (10 µg, 1 month after Omi XBB.1.5 Dose 2) and Group 3 (3 µg, 1 month after Omi XBB.1.5 Dose 3) was 1.51 (95% CI: 1.25, 1.82). Noninferiority based on the GMR was declared as the lower limit of the two-sided 95% confidence interval exceeded 0.67 (1.5-fold criterion), and the point estimate of the GMR was ≥0.8 (Table below).

The GMR was lower in the baseline SARS-CoV-2 negative subgroup (1.06; 95% CI: 0.77, 1.44) compared to the positive subgroup (1.81; 95% CI: 1.43, 2.30), but still showed comparable GMT in Group 1 compared to Group 3.

Table 19. Non-inferiority analysis for antibody titre, 6m- <2 y.

		Vaccine Group (as Randomised)				
		6 Months to <2 Years BNT162b2 (Omi XBB.1.5)				
		Group 1 10 µg 2 doses		Group 3 3 µg 3 doses		10 µg/ 3 µg
Assay	**Subgroup**	**n[a]**	**GMT[b] (95% CI[b])**	**n[a]**	**GMT[b] (95% CI[b])**	**GMR[c] (95% CI[c])**
SARS-CoV-2 neutralisation assay - Omicron XBB.1.5 - NT50 (titre)	Overall	352	8907.5 (7922.4, 10015.1)	224	5914.8 (5106.2, 6851.3)	1.51 (1.25, 1.82)
	Baseline SARS-CoV-2 status					
	Positive[d]	232	11097.1 (9576.7, 12859.0)	147	6123.7 (5087.7, 7370.7)	1.81 (1.43, 2.30)
	Negative[e]	119	5835.0 (4806.8, 7083.0)	77	5530.5 (4345.2, 7039.3)	1.06 (0.77, 1.44)

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

Note: Overall = irrespective of baseline SARS-CoV-2 status, including missing baseline status.

a. n = Number of participants with valid and determinate assay results for the specified assay at both baseline and at the given sampling time point.

b. GMTs and 2-sided 95% CIs were calculated by exponentiating the LSMeans and the corresponding CIs based on analysis of log-transformed assay results using a linear regression model with baseline log-transformed neutralising titres, postbaseline infection status and vaccine group as covariates.

c. GMRs and 2-sided 95% CIs were calculated by exponentiating the difference of LSMeans for the assay (Group 1 – Group 3) and the corresponding CIs based on the same regression model as stated above.

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

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

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Difference in Seroresponse Rates

Overall, the adjusted difference in percentage of participants with seroresponse to SARS-CoV-2 Omi XBB.1.5 between Group 1 (10 µg, 1 month after Omi XBB.1.5] Dose 2) and Group 3 (3 µg, 1 month after Omi XBB.1.5] Dose 3) was 1.28% (95% CI: –2.69, 5.26). Noninferiority based on seroresponse rate difference was declared, as the lower limit of the two-sided 95% confidence interval was greater than –10% (Table below).

The difference in seroresponse rates between Group 1 and Group 3 was similar in the baseline SARS-CoV-2 negative subgroup (–1.41%; 95% CI: –5.94, 3.13) compared to the positive subgroup (2.14%; 95% CI: –3.08, 7.35).

Table 20. Non-inferiority analysis for difference in Seroresponse Rates, 6m- <2 y.

		Vaccine Group (as Randomised)							
		6 Months to <2 Years BNT162b2 (Omi XBB.1.5)							
		Group 1 10 µg			Group 3 3 µg			Difference	
Assay	Subgroup	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])	%[d]	(95% CI[e])
SARS-CoV-2 neutralisation assay - Omicron XBB.1.5 - NT50 (titre)	Overall	352	335 (95.2)	(92.4, 97.2)	224	211 (94.2)	(90.3, 96.9)	1.28	(-2.69, 5.26)
	Baseline SARS-CoV-2 status								
	Pos[f]	232	217 (93.5)	(89.6, 96.3)	147	134 (91.2)	(85.4, 95.2)	2.14	(-3.08, 7.35)
	Ne[g]	119	117 (98.3)	(94.1, 99.8)	77	77 (100.0)	(95.3, 100.0)	-1.41	(-5.94, 3.13)

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

Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline. If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse.

Note: Overall = irrespective of baseline SARS-CoV-2 status, including missing baseline status.

a. N = number of participants with valid and determinate assay results for the specified assay both before vaccination and at the given sampling time point. This value is the denominators for the percentage calculations.

b. n = Number of participants with seroresponse for the given assay at the given sampling time point.

c. Exact 2-sided 95% CI, based on the Clopper and Pearson method.

d. Adjusted difference in proportions based on the Miettinen and Nurminen method stratified by baseline neutralising titre category (< median, ≥ median), expressed as a percentage (Group 1 - Group 3). For overall group, the median of baseline neutralising titres was calculated based on the pooled data in 2 comparator groups of all participants. For baseline positive group, the median of baseline neutralising titres was calculated based on the pooled data in 2 comparator groups of positive participants and for baseline negative group, the median of baseline neutralising titres was calculated based on the pooled data in 2 comparator groups of negative participants.

e. 2-Sided 95% CI, based on the Miettinen and Nurminen method for the difference in proportions stratified by baseline neutralising titre category (< median, ≥ median), expressed as a percentage.

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

Negative N-binding antibody result at Dose 1, negative NAAT result at Dose 1, and no medical history of COVID-19. PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adva Table Generation: 27SEP2025 (22:16) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adva_s003_diffserob_p2g1_evla

<u>Month Post-Dose-1 (Group 4; 10 µg; 2 through <5 years of age) to 1-Month Post-Dose 3 (Group 3; 3 µg; 6 months through <2 years of age)</u>

Geometric Mean Ratios

The unadjusted GMR comparing GMTs of SARS-CoV-2 Omicron XBB.1.5-neutralising titres at 1 month after a single dose of BNT162b2 (Omi XBB.1.5) in Group 4 (2 to <5 years; 10 µg) to those at 1 month after Dose 3 in Group 3 participants without evidence of infection up to 1 month after Dose 3 (6 months to <2 years; 3 µg) was 1.12 (95% CI: 0.86, 1.47). Noninferiority based on the GMR was declared, as the lower limit of the two-sided 95% confidence interval exceeded 0.67 (1.5-fold criterion), and the point estimate of the GMR was ≥0.8 (Table below).

In the baseline SARS-CoV-2 negative subgroup, the GMR was 0.14 (95% CI: 0.05, 0.36), which was lower than in the baseline positive subgroup (GMR: 1.26; 95% CI: 0.97, 1.63). Of note, the number of participants 2 to <5 years of age in the baseline negative subgroup was small (n=25), as most participants 2 to <5 years had prior exposure to SARS-CoV-2.

Table 21. Non- inferiority analysis for antibody titre, 2-<5 y. vs. 6m- <2 y. SARS-CoV-2 naïve

		Vaccine Group (as Randomised)				
		BNT162b2 (Omi XBB.1.5)				
Assay	Subgroup	Group 4 2 to <5 Years 10 µg 1 dose		Group 3 6 Months to <2 Years 3 µg 3 doses		2 to <5 Years 10 µg/ 6 Months to <2 Years 3 µg
		n[a]	GMT[b] (95% CI[b])	n[a]	GMT[b] (95% CI[b])	GMR[c] (95% CI[c])
SARS-CoV-2 neutralisation assay - Omicron XBB.1.5 - NT50 (titre)	Overall	470	6620.0 (5802.8, 7552.3)	53	5895.4 (4671.2, 7440.5)	1.12 (0.86, 1.47)
	Baseline SARS-CoV-2 status in Group 4					
	Positive[d]	439	7406.4 (6552.4, 8371.8)	53	5895.4 (4671.2, 7440.5)	1.26 (0.97, 1.63)
	Negative[e]	25	817.4 (318.5, 2097.7)	53	5895.4 (4671.2, 7440.5)	0.14 (0.05, 0.36)

Abbreviations: GMR = geometric mean ratio; GMT = geometric mean titre; LLOQ = lower limit of quantitation; NT50 = 50% neutralising titre; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Having no evidence of past SARS-CoV-2 infection up to 1-month post–Dose 3 for Group 3 participants was defined as having a negative N-binding antibody [serum] result at Dose 1 visit and 1-month post–Dose 3 visit; a negative NAAT [nasal swab] result at Dose 1, Dose 2 and Dose 3 visit, and any unscheduled visit up to the 1-month post–Dose 3 blood sample collection; and had no medical history of COVID-19.
Note: Overall = irrespective of baseline SARS-CoV-2 status, including missing baseline status.
a. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.
b. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titres and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.
c. GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titres (Group 4 2 to <5 Years – Group 3 6 Months to <2 Years) and the corresponding CI (based on the Student t distribution).
d. Positive N-binding antibody result at Dose 1, positive NAAT result at Dose 1, or medical history of COVID-19.
e. Negative N-binding antibody result at Dose 1, negative NAAT result at Dose 1, and no medical history of COVID-19.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adva Table Generation: 21SEP2025 (23:17)
(Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adva_s004_gmr_p2g4_evl

Difference in Seroresponse Rates

Overall, the unadjusted difference in percentage of participants with seroresponse to the SARS-CoV-2 Omi XBB.1.5 strain between participants 2 to <5 years of age who received a single 10 µg dose of BNT162b2 (Omi XBB.1.5) at 1 month after study vaccination in Group 4, and participants 6 months to <2 years of age without evidence of SARS-CoV-2 infection who received 3 doses of BNT162b2 (Omi XBB.1.5) 3 µg at 1 month after Dose 3 in Group 3 was -8.95 (95% CI: -11.92, -2.12). Noninferiority based on seroresponse rate difference was not met, as the lower limit of the two-sided 95% confidence interval was not greater than – 10% (Table below). Although the statistical criterion for noninferiority was missed, it was noted that participants 2 to <5 years of age achieved high seroresponse rate (91%) after a single dose of 10 µg BNT162b2 (Omi XBB.1.5) despite majority of participants being baseline SARS-CoV-2 positive.

In the baseline SARS-CoV-2 positive subgroup in Group 4, the unadjusted difference in percentage of participants with seroresponse was -7.85% (95% CI: –10.78, -1.02), similar to the overall unadjusted difference in seroresponse rates. In the baseline SARS-CoV-2 negative subgroup in Group 4, the unadjusted difference in percentage of participants with seroresponse was –28.00% (95% CI: –47.71, -14.22). Of note, the number of participants 2 to <5 years of age in the baseline negative subgroup was small (n=25), as most participants 2 to <5 years had prior exposure to SARS-CoV-2.

Table 22. Non-inferiority analysis for seroresponse rates 2-<5 y. vs. 6m- <2 y. SARS-CoV-2 naïve.

		Vaccine Group (as Randomised)							
		BNT162b2 (Omi XBB.1.5)							
		Group 4 2 to <5 Years 10 µg 1 dose			**Group 3 6 Months to <2 Years 3 µg 3 doses**			**Difference**	
Assay	**Subgroup**	**N[a]**	**n[b] (%)**	**(95% CI[c])**	**N[a]**	**n[b] (%)**	**(95% CI[c])**	**%[d]**	**(95% CI[e])**
SARS-CoV-2 neutralisation assay - Omicron XBB.1.5 - NT50 (titre)	Overall	458	417 (91.0)	(88.1, 93.5)	53	53 (100.0)	(93.3, 100.0)	-8.95	(-11.92, -2.12)
	Baseline SARS-CoV-2 status in Group 4								
	Positive[f]	433	399 (92.1)	(89.2, 94.5)	53	53 (100.0)	(93.3, 100.0)	-7.85	(-10.78, -1.02)
	Negative[g]	25	18 (72.0)	(50.6, 87.9)	53	53 (100.0)	(93.3, 100.0)	-28.00	(-47.71, -14.22)

Abbreviations: LLOQ = lower limit of quantitation; NT50 = 50% neutralising titre; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline. If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse.
Note: Having no evidence of past SARS-CoV-2 infection up to 1-month post-Dose 3 for Group 3 participants was defined as having a negative N-binding antibody [serum] result at Dose 1 visit and 1-month post-Dose 3 visit; a negative NAAT [nasal swab] result at Dose 1, Dose 2 and Dose 3 visit, and any unscheduled visit up to the 1-month post-Dose 3 blood sample collection; and had no medical history of COVID-19.
Note: Overall = irrespective of baseline SARS-CoV-2 status, including missing baseline status.
a. N = number of participants with valid and determinate assay results for the specified assay both before vaccination and at the given sampling time point. This value is the denominators for the percentage calculations.
b. n = Number of participants with seroresponse for the given assay at the given sampling time point.
c. Exact 2-sided 95% CI, based on the Clopper and Pearson method.
d. Difference in proportions, expressed as a percentage (Group 4 2 to <5 Years - Group 3 6 Months to <2 Years).
e. 2-Sided 95% CI, based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.
f. Positive N-binding antibody result at Dose 1, positive NAAT result at Dose 1, or medical history of COVID-19.
g. Negative N-binding antibody result at Dose 1, negative NAAT result at Dose 1, and no medical history of COVID-19.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adva Table Generation: 21SEP2025 (23:18)
(Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adva_s003_diffsero_p2g4_evl

Secondary Immunogenicity

1-Month Post-Dose 1 (Group 2; 10 µg) to 1-Month Post-Dose 3 (Group 3; 3 µg) – Participants 6 Months Through <2 Years of Age

Geometric Mean Ratio

Overall, the model-based GMR comparing GMTs of SARS-CoV-2 Omicron XBB.1.5-neutralising titres at 1 month after BNT162b2 (Omi XBB.1.5) Dose 1 in Group 2 (10 µg) to those at 1 month after Dose 3 in Group 3 (3 µg) was 0.40 (95% CI: 0.29, 0.55), indicating that GMTs were lower after a single 10 µg dose compared to the 3 doses of 3 µg group, suggesting that children 6 months to <2 years of age require more than 1 dose to mount an effective response. This is mainly driven by those who have no prior exposure to SARS-CoV-2, as indicated by a lower GMR of 0.07 (95% CI: 0.05, 0.12) in the baseline SARS-CoV-2 negative group. In baseline SARS-CoV-2 positive group, GMT after a single 10 µg dose was comparable to that after 3 doses of 3 µg (GMR: 1.02; 95% CI: 0.70, 1.48) (Table below).

Table 23. Non- inferiority analysis for antibody titres, 3x 3 µg vs. 1x 10 µg in 6m- <y.

		Vaccine Group (as Randomised)				
		6 Months to <2 Years BNT162b2 (Omi XBB.1.5)				
		Group 2 10 µg 1 dose		Group 3 3 µg 3 doses		10 µg/ 3 µg
Assay	Subgroup	n[a]	GMT[b] (95% CI[b])	n[a]	GMT[b] (95% CI[b])	GMR[c] (95% CI[c])
SARS-CoV-2 neutralisation assay - Omicron XBB.1.5 - NT50 (titre)	Overall	131	2448.4 (1897.6, 3159.0)	224	6196.1 (5101.6, 7525.5)	0.40 (0.29, 0.55)
	Baseline SARS-CoV-2 status					
	Positive[d]	86	6514.9 (4854.2, 8743.9)	147	6404.4 (5117.1, 8015.5)	1.02 (0.70, 1.48)
	Negative[e]	44	413.4	77	5650.2	0.07

	(286.1, 597.3)	(4282.7, 7454.4)	(0.05, 0.12)

Abbreviations: GMR = geometric mean ratio; GMT = geometric mean titre; LLOQ = lower limit of quantitation; NT50 = 50% neutralising titre; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Overall = irrespective of baseline SARS-CoV-2 status, including missing baseline status.
a. n = Number of participants with valid and determinate assay results for the specified assay at both baseline and at the given sampling time point.
b. GMTs and 2-sided 95% CIs were calculated by exponentiating the LSMeans and the corresponding CIs based on analysis of log-transformed assay results using a linear regression model with baseline log-transformed neutralising titres, postbaseline infection status and vaccine group as covariates.
c. GMRs and 2-sided 95% CIs were calculated by exponentiating the difference of LSMeans for the assay (Group 2 - Group 3) and the corresponding CIs based on the same regression model as stated above.
d. Positive N-binding antibody result at Dose 1, positive NAAT result at Dose 1, or medical history of COVID-19.
e. Negative N-binding antibody result at Dose 1, negative NAAT result at
Dose 1, and no medical history of COVID-19. PFIZER CONFIDENTIAL
SDTM Creation: 27AUG2025 (17:39) Source Data: adva Table Generation:
18SEP2025 (01:54) (Snapshot Date: 25AUG2025) Output File:
./nda2_ubped2/C4591048_A_CSR/adva_s004_gmrb_p2g2_evl

Difference in Seroresponse

Overall, the adjusted difference in the percentage of participants with seroresponse to Omicron XBB.1.5 between Group 2 (10 µg, 1 month after BNT162b2 [Omi XBB.1.5] Dose 1) and Group 3 (3 µg, 1 month after BNT162b2 [Omi XBB.1.5] Dose 3) was -14.62% (95% CI: −22.16, −7.07). The overall lower seroresponse rate observed in Group 2 than in Group 3 was mainly driven by the suboptimal response after a single 10 µg dose in those with no prior exposure to SARS-CoV-2. The adjusted differences in seroresponse rates between Group 2 and Group 3 was greater in the SARS-CoV-2 negative subgroup (−31.20%; 95% CI: −44.28, −18.12) than the difference between these vaccine groups in participants who were SARS-CoV-2 positive (−6.40%; 95% CI: −14.94, 2.14) (Table below).

Table 24. Non-inferiority analysis for seroresponse rates 3x 3 µg vs. 1x 10 µg in 6m- <y.

		Vaccine Group (as Randomised)					
		6 Months to <2 Years BNT162b2 (Omi XBB.1.5)					
		Group 2 10 µg 1 dose		Group 3 3 µg 3 doses			Difference
Assay	Subgroup	N[a]	n[b] (%) (95% CI[c])	N[a]	n[b] (%) (95% CI[c])	%[d]	(95% CI[c])
SARS-CoV-2 neutralisation assay - Omicron XBB.1.5 - NT50 (titre)	Overall	131	105 (80.2) (72.3, 86.6)	224	211 (94.2) (90.3, 96.9)	-14.62	(-22.16, -7.07)
	Baseline SARS-CoV-2 status						
	Positive[f]	86	74 (86.0) (76.9, 92.6)	147	134 (91.2) (85.4, 95.2)	-6.40	(-14.94, 2.14)
	Negative[g]	44	31 (70.5) (54.8, 83.2)	77	77 (100.0) (95.3, 100.0)	-31.20	(-44.28, -18.12)

Abbreviations: LLOQ = lower limit of quantitation; NT50 = 50% neutralising titre; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline. If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse.
Note: Overall = irrespective of baseline SARS-CoV-2 status, including missing baseline status.
a. N = number of participants with valid and determinate assay results for the specified assay both before vaccination and at the given sampling time point. This value is the denominators for the percentage calculations.
b. n = Number of participants with seroresponse for the given assay at the given sampling time point.
c. Exact 2-sided 95% CI, based on the Clopper and Pearson method.
d. Adjusted difference in proportions based on the Miettinen and Nurminen method stratified by baseline neutralising titre category (< median, ≥ median), expressed as a percentage (Group 2 - Group 3). For overall group, the median of baseline neutralising titres was calculated based on the pooled data in 2 comparator groups of all participants. For baseline positive group, the median of baseline neutralising titres was calculated based on the pooled data in 2 comparator groups of positive participants and for baseline negative group,

the median of baseline neutralising titres was calculated based on the pooled data in 2 comparator groups of negative participants.
e. 2-Sided 95% CI, based on the Miettinen and Nurminen method for the difference in proportions stratified by baseline neutralising titre category (< median, ≥ median), expressed as a percentage.
f. Positive N-binding antibody result at Dose 1, positive NAAT result at Dose 1, or medical history of COVID-19.

Negative N-binding antibody result at Dose 1, negative NAAT result at Dose 1, and no medical history of COVID-19. PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adva Table Generation: 27SEP2025 (22:25) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adva_s003_diffserob_p2g2_evla

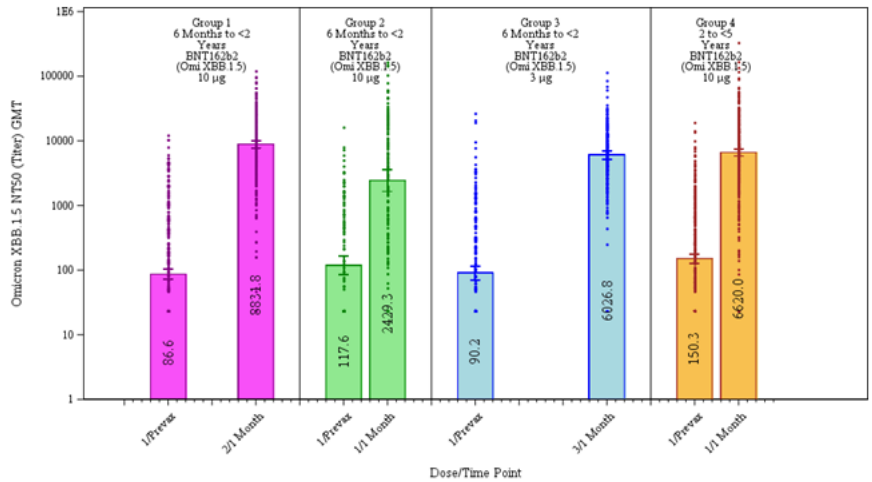
Descriptive Summary of Immune Responses – Participants 6 Months Through <5 Years of Age

Geometric Mean Titres

Across all evaluated groups (Groups 1 – 4), GMTs increased markedly after vaccination in both age cohorts and across all dosing groups. The highest GMTs were observed after two doses of BNT162b2 (Omi XBB.1.5) 10 µg (Group 1) or after three doses of BNT162b2 (Omi XBB.1.5) 3 µg in participants 6 months to <2 years (Group 3), or a single dose of BNT162b2 (Omi XBB.1.5) 10 µg in participants 2 to <5 years (Group 4), with values ranging from 6026.8 (95% CI: 5192.4, 6995.2) to 8831.8 (95% CI: 7785.3, 10018.9), depending on age and dose group. GMTs at 1 month after a single dose of BNT162b2 (Omi XBB.1.5) at 10 µg in participants 6 months to <2 years (Group 2) were lower compared to the reference primary vaccination schedule (three consecutive doses of 3 µg BNT162b2, Group 3).

- GMTs were generally higher in the SARS-CoV-2 positive subgroup compared to the negative subgroup.
- GMTs were generally similar across age, sex, race, ethnicity, and comorbidity (2 to <5 years of age) subgroups, with no clinically meaningful differences observed.

Figure 2: GMT and 95% CIs: SARS-CoV-2 neutralisation assay – Omicron XBB.1.5 – NT50 (titre) – C4591048 substudy A phase 2/3 participants – evaluable immunogenicity population



Abbreviations: GMT = geometric mean titer; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Dots represent individual antibody levels.
Note: Number within each bar denotes geometric mean.
Note: For Group 1 at 1-month post-dose2, for Group 2 at 1-Month post-dose1, for Group 3 at 1-month post-dose3 and for Group 4 at 1-month post-dose1.
PFIZER CONFIDENTIAL SDTM Creation: 18SEP2025 (01:50) Source Data: adva
Table Generation: 18SEP2025 (01:50) (Snapshot Date: 25AUG2025) Output File: /nda2_ubped2/C4591048_A_CSR/adva_f001_1_n2_evl

Geometric Mean Fold Rise

For participants 6 months to <2 years of age, the GMFR at 1 month after the first (Group 2) and second dose (Group 1) of BNT162b2 (Omi XBB.1.5) 10 µg were 22.4 (95% CI: 16.3, 30.8) and 102.5 (95% CI: 85.7, 122.6), respectively, while the GMFR at 1 month after Dose 3 of BNT162b2 (Omi XBB.1.5) 3 µg (Group 3) was 65.9 (95% CI: 51.7, 83.9). For participants 2 to <5 years of age who

received a single 10 µg dose (Group 4), the GMFR at 1-month post-vaccination was 43.4 (95% CI: 37.3, 50.6).

- GMFRs were generally similar or trended higher in the SARS-CoV-2 negative subgroup compared to the positive subgroup after Dose 2 or Dose 3 (Groups 1 and 3, 6 months to <2 years), but trended higher in the baseline SARS-CoV-2 positive subgroup 1-month post-Dose 1 in Groups 2 (6 months to <2 years) and 4 (2 to <5 years)
- GMFRs were generally similar across comorbidity (2 to <5 years) subgroups, with no clinically meaningful differences observed

Seroresponse Rates

For participants 6 months to <2 years of age, seroresponse rates at 1 month after the first dose (Group 2) and second dose (Group 1) of BNT162b2 (Omi XBB.1.5) 10 µg were 80.2% (95% CI: 72.3, 86.6) and 95.2% (95% CI: 92.4, 97.2), respectively, and after the third dose of BNT162b2 (Omi XBB.1.5) 3 µg (Group 3) were 94.2% (95% CI: 90.3, 96.9). In participants 2 to <5 years of age who received a single 10 µg dose (Group 4), the seroresponse rate at 1-month post-vaccination was 91.0% (95% CI: 88.1, 93.5).

- Among baseline SARS-CoV-2 negative participants, seroresponse rates trended higher after Dose 2 or Dose 3 of the series when compared to baseline SARS-CoV-2 positive participants (Groups 1 and 3, 6 months to <2 years). However, after the first dose, seroresponse rates in the negative subgroup trended lower than in the positive subgroup in Groups 2 (6 months to <2 years) and 4 (2 to <5 years).
- Seroresponse rates were generally consistent across sex, race, ethnicity, and comorbidity subgroups, with no clinically meaningful differences observed.

Table 25. Geometric Mean Titres, GMFR, Seroresponse by Subgroup - C4591048 Substudy A Phase 2/3 Participants - Evaluable Immunogenicity Population

C4591048 BNT162b2(Omi XBB.1.5)				
	6 Months to <2 Years			**2 to <5 Years**
	Group 1 10 µg 2 doses	**Group 2 10 µg 1 dose**	**Group 3 3 µg 3 doses**	**Group 4 10 µg 1 dose**
Geom. Mean Titre	**N**[b] GMT[c] (95% CI[c])	**N**[b] GMT[c] (95% CI[c])	**N**[b] GMT[c] (95% CI[c])	**N**[b] GMT[c] (95% CI[c])
Prevax GMT **all**	**352** 86.6 (71.7, 104.6)	**131** 117.6 (84.2, 164.2)	**224** 90.2 (71.0, 114,5)	**458** 150.3 (128.1, 176.)
Post last dose GMT **all**	**367** 8831.8 (7785.3, 10018.9)	**140** 2429.3 (1649.1, 3578.3)	**234** 6026.8 (5192.4, 6996.2	**470** 6620.0 (5802.8, 7552.3)
Prevax GMT SARS-COV-2 **negatives**	**119** 27.3 (24.9, 29.9)	**44** (30.5 (24.2, 38.6)	**77** 31.4 (25.3, 38.2)	**25** 37.0 (24.1, 56.6)
Post last dose GMT SARS-COV-2 **negatives**	**121** 5662.7 (4562.5, 7028.2)	**45** 388.7 (222.8, 678.2)	**77** 5642.9 (4641.2, 6860.7)	**25** 817.4 (318.5, 2097.7)
Prevax GMT SARS-COV-2 **positives**	**232** 157.4 (122.7, 202.1)	**86** 238.9 (156.2, 365.2)	**147** 157.5 (115.1, 215.5)	**433** 163.0 (138.3, 192.2)
Post last dose GMT SARS-COV-2 **positives**	**237** 11216.9 (9656.6, 13029.3)	**87** 6621.7 (4470.3, 9808.4)	**151** 6212.3 (5042.3, 7653.8)	**439** 7406.4 (6552.4, 8371.8)

GM Fold Rise all	**N**[b] GMFR (95% CI[c])	**N**[b] GMFR (95% CI[c])	**N**[b] GMFR (95% CI[c])	**N**[b] GMFR (95% CI[c])
Post last dose/ prevax	**392** 99.8 (84.2, 118.3)	**133** 22.4 (16.3, 30.8)	**257** 66.8 (53.3, 83.3)	**473** 43.9 (37.8, 51.0)
Seroresponse rate all	**N**[b] n (%) (95% CI[c])	**N**[b] n (%) (95% CI[c])	**N**[b] n (%) (95% CI[c])	**N**[b] n (%) (95% CI[c])
Post last dose	**392** 373 (95.2) (95.5, 97.1)	**133** 106 (79.7) (71.9, 86.2)	**257** 242 (94.2) (90.6, 96.7)	**473** 430 (90.9) (88.0, 93.3)

2.4.2.2. – Substudy E – Final 6-Month Analysis

Methods

Substudy E was a Phase 2/3 open-label study to evaluate the safety, tolerability, and immunogenicity of a single 10 µg dose of BNT162b2 (Omi XBB.1.5) in participants ≥5 to <12 years of age who were COVID-19 vaccine-naïve. Approximately 300 participants were to be enrolled.

This AR presents final immunogenicity and safety data from the 310 participants ≥5 to <12 years of age enrolled in Study C4591048 Substudy E.

Study participants

Eligible study participants were healthy male or female vaccine-naïve individuals ≥5 years to <12 years of age.

Treatments

Participants were intended to receive one 10 µg dose of BNT162b2 (Omi XBB.1.5).

Objectives and Outcomes/endpoints

Table 26: SSE, Phase 2-3 immunogenicity objectives and endpoints

Objectives	Estimands	Endpoints
Primary Immunogenicity	**Primary Immunogenicity**	**Primary Immunogenicity**

• To immunobridge the Omicron XBB.1.5 immune response elicited by a single dose of BNT162b2 (Omi XBB.1.5) between COVID-19 vaccine–naïve participants 5 to <12 years of age who received a single 10 µg dose of BNT162b2 (Omi XBB.1.5), and vaccine-experienced participants ≥12 years of age who received a single 30 µg dose of BNT162b2 (Omi XBB.1.5) in Study C4591054 – Substudy A.	In participants complying with the key protocol criteria (evaluable participants): • GMR estimated by the ratio of the geometric mean of SARS-CoV-2 Omicron XBB.1.5–neutralising titres at 1 month after study vaccination in COVID-19 vaccine–naïve participants 5 to <12 years of age who received a single dose of BNT162b2 (Omi XBB.1.5) to neutralising titres at 1 month after study vaccination in Study C4591054 – Substudy A vaccine-experienced participants ≥12 years of age. • The difference in percentage of participants with seroresponse to Omicron XBB.1.5 at 1 month after study vaccination between COVID19 vaccine–naïve participants 5 to <12 years of age who received a single 10 µg dose of BNT162b2 (Omi XBB.1.5), and vaccine-experienced participants ≥12 years of age who received a single 30 µg dose of BNT162b2 (Omi XBB.1.5) in Study C4591054 – Substudy A.	• SARS-CoV-2 Omicron XBB.1.5–neutralising titres
Objectives	**Estimands**	**Endpoints**
Secondary Immunogenicity:	**Secondary Immunogenicity:**	**Secondary Immunogenicity:**
To describe the immune response to BNT162b2 (Omi XBB.1.5) as a single dose in COVID-19 vaccine–naïve participants[a] ≥5 to <12 years of age.	In participants complying with the key protocol criteria (evaluable participants): • GMTs at baseline and 1 month after the study vaccination. • GMFR from baseline to 1 month after the study vaccination. • Percentages of participants with seroresponse[b] at 1 month after the study vaccination.	• SARS-CoV-2 Omicron XBB.1.5–neutralising titres.
Exploratory:	**Exploratory:**	**Exploratory:**
• To describe COVID-19 and severe COVID-19 cases.		• Confirmed COVID-19 cases. • Confirmed severe COVID-19 cases. • Strain sequencing of COVID-19 cases.
• To describe MIS-C cases.		• Confirmed cases as per CDC criteria.

a. The following participants will be used as a control for this objective: vaccine-experienced participants ≥12 years of age from Study C4591054 – Substudy A who received a single dose of BNT162b2 (Omi XBB.1.5) 30 µg.

b. Seroresponse is defined as achieving a ≥4-fold rise from the baseline (before the study vaccination). If the baseline measurement is below the LLOQ, the postvaccination measure of ≥4 × LLOQ is considered seroresponse.

Sample size

All participants ≥5 to <12 years of age from this substudy Group 2 receiving a single dose of BNT162b2 (Omi XBB.1.5) 10 µg, approximately 300 participants, and an approximately similar number of participants ≥12 years of age from Study C4591054 – Substudy A receiving a single dose of BNT162b2 (Omi XBB.1.5) 30 µg will be selected to evaluate the primary immunogenicity objective. Assuming a 25% nonevaluable rate, approximately 225 evaluable participants in each vaccine group will contribute to the immunogenicity evaluation. Each hypothesis test will be performed at a 1-sided alpha level of 0.025.

For comparison based on GMR, common assay standard deviations in log scale are assumed to be 1.5 based on data observed in Study C4591054. Table below provides the power to declare noninferiority, using a 1.5-fold margin, under different assumptions of true GMRs of SARS-CoV-2 Omicron XBB.1.5–neutralising titres at 1 month after study vaccination for participants who received a single dose of BNT162b2 (Omi XBB.1.5) 10 µg, to those at 1 month after study vaccination for Study C4591054 – Substudy A participants who received a single dose of BNT162b2 (Omi XBB.1.5) 30 µg. For example, if the true GMR is 1.05, then 225 evaluable participants in each arm will provide 89.3% power to declare noninferiority. If the true GMR is 1.0, the study will have 81.6% power to declare noninferiority. The assumptions of assay variability, true GMR, and the statistical power estimate may be adjusted based on emerging data.

Table 27: Power to demonstrate non-inferiority under different assumptions of GMR

Number of Evaluable Participants in Each Comparator Group	Assumed True GMR	Power
225	0.95	70.5%
225	1.0	81.6%
225	1.05	89.3%

For comparison based on seroresponse rate differences, Table below provides the power to demonstrate noninferiority under different assumptions of seroresponse rates for each comparative group, using a 10% margin. For example, if the seroresponse rate is 70% in both comparator groups, then the study has 64.0% power to demonstrate noninferiority using a 10% margin.

Table 28: Power to demonstrate non-inferiority under different assumptions of seroresponse rate

Number of Evaluable Participants in Each Comparator Group	Assumed Seroresponse Rate in Participants From This Substudy	Assumed Seroresponse Rate in Participants From Study C4591054 – Substudy A	Power
225	80	75	96.7
225	75	75	68.6
225	75	70	94.5
225	70	70	64.0

Randomisation and blinding

All participants were centrally assigned to study intervention using an IRT. This was an open-label substudy.

Statistical methods

For general considerations, see C4591048 Substudy A.

Analyses were performed to characterise Omicron XBB.1.5 neutralisation responses of COVID-19 vaccine-naïve participants ≥5 to <12 years of age following a single dose (10 µg) of BNT162b2 (Omi XBB.1.5) compared to COVID-19 vaccine-experienced participants ≥12 years of age following a single dose (30 µg) with BNT162b2 (Omi XBB.1.5) in Study C4591054 Substudy A.

Participants from Study C4591054 Substudy A were selected using stratified random sampling and were matched by baseline SARS-CoV-2 infection status with Study C4591048 Substudy E participants.

The validated SARS-CoV-2 authentic virus neutralisation assay was used to determine the neutralising titres.

GMTs and GMFRs with 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titres and fold rises, respectively, and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

Seroresponse was defined as achieving a ≥4-fold rise from baseline (before the study vaccination). If the baseline measurement was below the LLOQ, a postvaccination measure of ≥4 × LLOQ was considered seroresponse. The exact 2-sided 95% CIs for percentages of participants with seroresponse was calculated using the Clopper-Pearson method.

Model-Based GMR:

As the primary approach, the GMR and associated 95% CI was calculated by exponentiating the difference in LS means and the corresponding CIs based on the analysis of logarithmically transformed assay results using a linear regression model that includes the baseline neutralising titre, postbaseline infection status, and vaccine group as covariates.

Unadjusted GMR:

The GMR was calculated as the mean of the difference of logarithmically transformed assay results and exponentiating the mean. Two-sided CIs will be obtained by calculating CIs using the Student t distribution for the mean difference of the logarithmically transformed assay results and exponentiating the confidence limits.

Difference in Seroresponse

The primary approach to calculating the difference in seroresponse rate between 2 vaccine groups and the associated 2-sided 95% CIs, were based on the Miettinen and Nurminen method stratified by baseline neutralising titre category (< median, ≥ median). The unadjusted difference in percentages of participants with seroresponse between the 2 comparison groups, and the associated 2-sided 95% CIs, were calculated using the Miettinen and Nurminen method.

Statistical Hypothesis

The primary objective will be evaluated by the following 2 hypotheses:

<u>The first null hypothesis (H0) is</u>

H0: $\ln(\mu 1) - \ln(\mu 2) \leq \ln(0.67)$ vs H1: $\ln(\mu 1) - \ln(\mu 2) > \ln(0.67)$

where ln(0.67) corresponds to a 1.5-fold margin for noninferiority and

- $\ln(\mu 1)$ is the natural log of the geometric mean of SARS-CoV-2 Omicron XBB.1.5–neutralising titres measured at 1 month after study vaccination in COVID-19 vaccine-naïve participants ≥5 to <12 years of age who received a single dose of BNT162b2(Omi XBB.1.5) 10 µg;

- ln(μ2) is the natural log of the geometric mean of SARS-CoV-2 Omicron XBB.1.5–neutralising titres measured at 1 month after study vaccination in Study C4591054 – Substudy A vaccine-experienced participants ≥12 years of age who received a single dose of BNT162b2 (Omi XBB.1.5) 30 μg.

The second null hypothesis (H0) is

H0: p1-p2 ≤ −10% vs H1:p1-p2 > −10%

where -10% is the noninferiority margin for seroresponse and

- p1 is the percentage of participants with seroresponse to Omicron XBB.1.5 at 1 month after study vaccination in COVID-19 vaccine-naïve participants ≥5 to <12 years of age who received a single dose of BNT162b2 (Omi XBB.1.5) 10 μg;
- p2 is the percentage of participants with seroresponse to Omicron XBB.1.5 at 1 month after study vaccination in Study C4591054 – Substudy A vaccine-experienced participants ≥12 years of age who received a single dose of BNT162b2 (Omi XBB.1.5) 30 μg.

Immunobridging success based on the GMR will be declared if the lower limit of the 2-sided 95% CI for the GMR is greater than 0.67 (1.5-fold criterion) and the point estimate of the GMR is ≥0.8; immunobridging success based on seroresponse rate difference will be declared if the lower limit of the 2-sided 95% CI for the difference in percentages of participants with seroresponse is >-10%.

Results

Participant flow

Table 29: Disposition of All Assigned Participants - Substudy E.

	Vaccine Group (as Assigned)
	BNT162b2 (Omi XBB.1.5) 10 μg n[a] (%)
Assigned[b]	310
Not vaccinated	0
Vaccinated	310 (100.0)
Completed 1-month post–study vaccination visit (vaccination period)	307 (99.0)
Completed the study	287 (92.6)
Withdrawn from study	23 (7.4)
Reason for withdrawal from study	
Lost to follow-up	17 (5.5)
Protocol deviation	5 (1.6)
Withdrawal by parent/guardian	1 (0.3)

a. n = Number of participants with the specified characteristic.
b. This value is the denominator for the percentage calculations.
PFIZER CONFIDENTIAL SDTM Creation: 04NOV2024 (16:22) Source Data: adds Table Generation: 12NOV2024 (03:07) (Database snapshot date : 01NOV2024)

Recruitment

The study was initiated on 31 October 2023 and the analyses presented in this report are based on the LPLV date of 10 October 2024.

Conduct of the study

This study was conducted at 30 sites in the US, South Africa, and Brazil.

Baseline data

Immunogenicity Population

Demographic characteristics for participants in the evaluable immunogenicity populations from C4591048 SSE (Table below) were generally similar to those in the safety population. Between 1048 SSE and 1054 SSA vaccine groups, participants aged ≥5 to <12 years of age in the C4591048 group had higher proportions of Black or African American and Hispanic/Latino participants compared to the Study C4591054 comparator group of participants ≥12 years of age, due in part to enrolment of 5 to <12 year-old participants in both South Africa and Brazil in C4591048 SSE. Most participants in the C4591048 group were from the United States (194; 68.1%), with 61 from South Africa (21.4%), 28 from Brazil (9.8%), and 2 from Puerto Rico (0.7%). All participants in the C4591054 group were from the United States.

Table 30. Demographic Characteristics - C4591048 Substudy E and C4591054 Substudy A Participants - Evaluable Immunogenicity Population

	Vaccine Group (as Assigned)	
	C4591048 ≥5 to <12 Years BNT162b2 (Omi XBB.1.5) 10 µg (N[a]=285) n[b] (%)	C4591054 ≥12 Years BNT162b2 (Omi XBB.1.5) 30 µg (N[a]=302) n[b] (%)
Sex		
Male	132 (46.3)	126 (41.7)
Female	153 (53.7)	176 (58.3)
Race		
White	117 (41.1)	239 (79.1)
Black or African American	151 (53.0)	39 (12.9)
American Indian or Alaska Native	1 (0.4)	0
Asian	6 (2.1)	15 (5.0)
Native Hawaiian or other Pacific Islander	0	1 (0.3)
Multiracial	9 (3.2)	7 (2.3)
Not reported	1 (0.4)	0
Unknown	0	1 (0.3)
Ethnicity		
Hispanic/Latino	152 (53.3)	58 (19.2)
Non-Hispanic/non-Latino	133 (46.7)	242 (80.1)
Not reported	0	2 (0.7)
Country		
Brazil	28 (9.8)	0
Puerto Rico	2 (0.7)	0
South Africa	61 (21.4)	0
United States	194 (68.1)	302 (100.0)
Age (years) at study vaccination		

Mean (SD)	7.4 (1.97)	51.7 (18.77)
Median	7.0	53.5
Min, max	(5, 11)	(12, 82)
Obese[c]		
Yes	67 (23.5)	110 (36.4)
No	218 (76.5)	192 (63.6)
Baseline SARS-CoV-2 status		
Positive[d]	282 (98.9)	300 (99.3)
Negative[e]	3 (1.1)	2 (0.7)
Time from last dose of mRNA COVID-19 vaccine[f] (received prior to the study) to the study vaccination (months[g])		
n	NA	302
Mean (SD)		10.2 (1.75)
Median		10.7
Min, max		(5.5, 12.9)
≥5 to <7 Months		19 (6.3)
≥7 to <9 Months		59 (19.5)
≥9 to ≤12 Months		193 (63.9)
>12 Months		31 (10.3)
Time from last dose of mRNA COVID-19 vaccine[f] (received prior to the study) to the study vaccination (days)		
n	NA	302
Mean (SD)		285.8 (49.08)
Median		300.0
Min, max		(154, 360)
<150 Days		0
≥150 Days[h]		302 (100.0)

Abbreviations: NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein-binding; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; NA = not applicable.

a. N = number of participants in the specified group. These values are the denominators for the percentage calculations.

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

c. For participants 5 through 15 years of age, obesity is defined as a BMI at or above the 95th percentile from the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/data/zscore/bmiagerev.xls. Since the participant's age is only collected in years (C4591054 SSA only) and the BMI values in the CDC growth charts are only presented by age in months, the minimum 95th percentile value for that age was chosen for the obesity criteria. For participants ≥16 years of age obesity is defined as a BMI at or above 30.0 kg/m^2.

d. Positive N-binding antibody result at the study vaccination visit, positive NAAT result at the study vaccination visit, or medical history of COVID-19.

e. Negative N-binding antibody result at the study vaccination visit, negative NAAT result at the study vaccination visit, and no medical history of COVID-19.

f. The inclusion criteria for Study C4591054 SSA required the participant to have received at least 3 prior doses of a US-authorized mRNA COVID-19 vaccine with the most recent dose being a US-authorized Omicron BA.4/BA.5-adapted bivalent vaccine at least 150 days before study vaccination.

g. Month was calculated as 28 days.

h. Protocol-specified time frame.

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Numbers analysed

Table 31. Immunogenicity populations in C4591048 Substudy E Phase 2/3 and in C4591054 substudy A

	C4591048 ≥5 to <12 Years, XBB 1.5 10 µg n (%)	**C4591054 ≥12 Years, XBB 1.5 30 µg n (%)**	**Total n (%)**
Assigned	310 (100.0)	303 (100.0)	613 (100.0)
All available immunogenicity population	302 (97.4)	302 (99.7)	604 (98.5)
Evaluable immunogenicity population	285 (91.9)	302 (99.7)	587 (95.8)

Outcomes and estimation

Immunogenicity

Immunogenicity data are summarized below for C4591048 SSE vaccine-naïve participants ≥5 to <12 years of age following a single dose (10 µg) of BNT162b2 (Omi XBB.1.5) compared to C4591054 SSA vaccine-experienced participants ≥12 years of age following a single dose (30 µg) with BNT162b2 (Omi XBB.1.5).

Primary Immunogenicity

Geometric Mean Ratio

Omicron XBB.1.5

In the evaluable immunogenicity population, the primary model-based GMR of Omicron XBB.1.5-neutralising titres for the BNT162b2 (Omi XBB.1.5) 10 µg group to the BNT162b2 (Omi XBB.1.5) 30 µg group was 1.81 (2-sided 95% CI: 1.51, 2.16). The alternative model-based GMR by excluding post-baseline infection status from the model was identical to the primary model-based GMR. In addition, the model-based GMR from an additional supportive analysis in participants without evidence of post-baseline infection was similar to the primary model-based GMR. Unadjusted GMR was 1.48 (95% CI: 1.22, 1.79).

Immunobridging success based on the model-based GMR was declared since the lower limit of the 2-sided 95% CI for the GMR was greater than 0.67 (1.5-fold criterion) and the point estimate of the GMR was ≥0.8.

Table 32. Non- inferiority analysis for antibody titres in 5-< 12 y. compared to adults

	Vaccine Group (as Assigned)		
	C4591048 ≥5 to <12 Years	**C4591054 ≥12 Years**	**C4591048 ≥5 to <12 Years/ C4591054 ≥12 Years**
	BNT162b2 (Omi XBB.1.5) 10 µg	**BNT162b2 (Omi XBB.1.5) 30 µg**	
Assay	**n[a] GMT[b] (95% CI[b])**	**n[a] GMT[b] (95% CI[b])**	**GMR[c] (95% CI[c])**

SARS-CoV-2 neutralisation assay - Omicron XBB.1.5 - NT50 (titre)	285 6569.3 (5781.6, 7464.3)	300 3635.9 (3210.5, 4117.6)	1.81 (1.51, 2.16)

Abbreviations: GMR = geometric mean ratio; GMT = geometric mean titre; NT50 = 50% neutralising titre; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

a. n = Number of participants with valid and determinate assay results for the specified assay at both baseline and at the given sampling time point.

b. GMTs and 2-sided 95% CIs were calculated by exponentiating the LSMeans and the corresponding CIs based on analysis of log-transformed assay results using a linear regression model with baseline log-transformed neutralising titres, postbaseline infection status, and vaccine group as covariates.

c. GMRs and 2-sided 95% CIs were calculated by exponentiating the difference of LSMeans for the assay (C4591048 ≥5 to <12 Years - C4591054 ≥12 Years) and the corresponding CIs based on the same regression model as stated above.

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(Database snapshot date : C4591048 SSE [01NOV2024]/C4591054 SSA [03APR2024])

Difference in Seroresponse Rate

Omicron XBB.1.5

In the evaluable immunogenicity population, 88.8% of participants in the C4591048 BNT162b2 (Omi XBB.1.5) 10 µg group and 77.0% of participants in the C4591054 BNT162b2 (Omi XBB.1.5) 30 µg group achieved seroresponse to Omicron XBB.1.5. The adjusted difference in percentages of participants with seroresponse between the BNT162b2 (Omi XBB.1.5) 10 µg group and BNT162b2 (Omi XBB.1.5) 30 µg group was 8.97% (95% CI: 3.91, 14.02). Unadjusted difference in seroresponse rates was 11.77% (95% CI: 5.74, 17.84).

Immunobridging success based on seroresponse rate difference was declared since the lower limit of the 2-sided 95% CI for the adjusted difference in percentages of participants with seroresponse was >-10%.

Table 33. Non- inferiority analysis for seroresponses in 5-< 12 y. compared to adults

	Vaccine Group (as Assigned)		
	C4591048 ≥5 to <12 Years	**C4591054 ≥12 Years**	**C4591048 ≥5 to <12 Years- C4591054 ≥12 Years**
	BNT162b2 (Omi XBB.1.5) 10 µg	**BNT162b2 (Omi XBB.1.5) 30 µg**	**Difference**
Assay	**n[a] n[b] (%) (95% CI[c])**	**n[a] n[b] (%) (95% CI[c])**	**n[b] (%) (95% CI[c])**
SARS-CoV-2 neutralisation assay - Omicron XBB.1.5 - NT50 (titre)	285 253 (88.8) (84.5, 92.2)	300 231 (77.0) (71.8, 81.6)	8.97 (3.91, 14.02)

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

Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline. If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse.

a. N = number of participants with valid and determinate assay results for the specified assay both before vaccination and at the given sampling time point. This value is the denominators for the percentage calculations.

b. n = Number of participants with seroresponse for the given assay at the given sampling time point.

c. Exact 2-sided 95% CI, based on the Clopper and Pearson method.

d. Adjusted difference in proportions based on the Miettinen and Nurminen method stratified by baseline neutralising titre category (< median, ≥ median), expressed as a percentage (C4591048 ≥5 to <12 Years - C4591054 ≥12 Years). The median of baseline neutralising titres was calculated based on the pooled data in 2 comparator groups.

e. 2-Sided 95% CI, based on the Miettinen and Nurminen method for the difference in proportions stratified by baseline neutralising titre category (< median, ≥ median), expressed as a percentage.

PFIZER CONFIDENTIAL Source Data: adva Table Generation: 03DEC2024 (03:58)

(Database snapshot date : C4591048 SSE [01NOV2024]/C4591054 SSA [03APR2024])

Secondary Immunogenicity

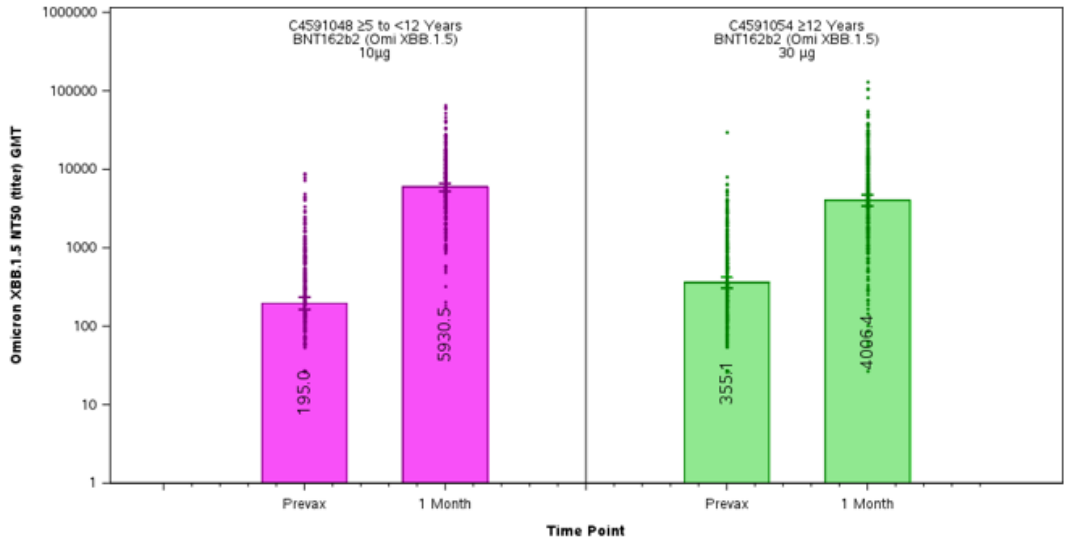
Geometric Mean Titres

Omicron XBB.1.5

Among both C4591048 participants and C4591054 participants in the evaluable immunogenicity population, GMTs against the Omicron XBB.1.5 variant were substantially higher at 1 month after study vaccination compared with that at prevaccination (Figure below).

GMTs against Omicron XBB.1.5 were lower in the C4591048 BNT162b2 (Omi XBB.1.5) 10 µg group compared to the C4591054 BNT162b2 (Omi XBB.1.5) 30 µg group at prevaccination. At 1 month after vaccination, GMTs were higher in the BNT162b2 (Omi XBB.1.5) 10 µg group compared to that in the comparator group (Figure below).

Figure 3: GMT and 95% CIs: SARS-CoV-2 neutralisation assay – Omicron XBB.1.5 – NT50 (titre) – C4591048 substudy E and substudy A participants – evaluable immunogenicity population



Abbreviations: GMT = geometric mean titer; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Dots represent individual antibody levels.
Note: Number within each bar denotes geometric mean.
PFIZER CONFIDENTIAL Source Data: adva Table Generation: 29NOV2024 (00:20)
(Database snapshot date : C4591048 SSE [01NOV2024]/C4591054 SSA [03APR2024])
Output File: ./nda2_ubped2/C4591048_E_1MPD_1054_A_Immuno/adva_f002_sars_50_p2_2_evl

Geometric Mean Fold Rise

Omicron XBB.1.5

GMFRs from before study vaccination to 1-month after vaccination against Omicron XBB.1.5 were higher in the C4591048 participants who received BNT162b2 (Omi XBB.1.5) 10 µg compared to that in the C4591054 participants who received BNT162b2 (Omi XBB.1.5) 30 µg (Table below).

Table 34. GMFR in 5-< 12 y. compared to adults

		Vaccine Group (as Assigned)			
		C4591048 ≥5 to <12 Years XBB.1.5) 10 µg		C4591054 ≥12 Years BNT162b2 (Omi BNT162b2 (Omi XBB.1.5) 30 µg	
Assay	Sampling Time Point[a]	n[b]	GMFR[c] (95% CI[c])	n[b]	GMFR[c] (95% CI[c])
SARS-CoV-2 neutralisation assay - Omicron XBB.1.5 - NT50 (titre)	1 Month	285	30.4 (25.3, 36.5)	300	11.3 (9.7, 13.2)

Abbreviations: GMFR = geometric mean fold rise; LLOQ = lower limit of quantitation; NT50 = 50% neutralising titre; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

a. Protocol-specified timing for blood sample collection.

b. n = number of participants with valid and determinate assay results for the specified assay both baseline and at the given sampling time point.

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

PFIZER CONFIDENTIAL Source Data: adva Table Generation: 03DEC2024 (02:20)

(Database snapshot date : C4591048 SSE [01NOV2024]/C4591054 SSA [03APR2024])

2.4.3. Discussion on clinical efficacy

The Comirnaty Omicron XBB 1.5 variant vaccine was approved by the European Commission on 15 May 2024, as recommended by the CHMP during procedure EMEA/H/C/005735/X/0199. There were no clinical data for Omicron XBB 1.5 at the time of approval. The clinical data to support the XBB 1.5 indication in 12 year and older was assessed recently in procedure EMA/VR/0000296341 and SmPC changes adopted in CHMP February 2026. Omicron XBB 1.5 formulations were withdrawn from the EU market (EMA/VR/0000303772). The Omicron XBB 1.5 immunogenicity information is presented in updated Omicron JN.1, KP.2 and LP.8 variant vaccines SmPCs.

The currently approved posology for children 6 months through <5 years of age is 3 µg dose of Comirnaty vaccine administered as a 3-dose primary series. The MAH applies to change the posology from 3 µg to 10 µg and dosing regimen reduction from 3-dose to a 2-dose primary course for 6 months to <2 years of age and to a single dose for 2 years to <5 years of age. Further, the MAH wishes to delete the 3 µg strength from the Comirnaty Marketing authorisation. In addition, the MAH provides clinical data to support the already approved 10 µg single dose posology in children from 5 to 11 years.

C4591048 is a master phase 1/2/3 protocol to investigate the safety, tolerability, and immunogenicity of variant adapted BNT162b2 RNA – based vaccine candidate(s) in healthy children, listed as a category 3 study in the RMP. This study has several substudies. In current application, the data to support the posology changes in 6 months to <5 years originates from Substudy A and the data to support usage in 5-< 12 year old children from Substudy E.

Age groups 6m-<2years and 2- <5 years

Design and conduct of clinical studies

C4591048 Substudy A is a randomised single-blinded (Sponsor-unblinded) study in Phase 1 and open-label in Phase 2/3. The proposed posology changes in children 6 months through <5 years of age base on results from study C4591048 phase 2/3, sub-study A (SSA) Groups 1-5.

- Substudy A: Phase 1 is a single-blinded, dose-finding study to evaluate the safety, tolerability, and immunogenicity of a 3-dose series of bivalent BNT162b2 (original/Omi BA.4/BA.5) administered on a 0-, 3-, and 11-week schedule (at 3, 6, or 10 µg), followed by a fourth dose with BNT162b2 Monovalent (Omi XBB.1.5) ~6 months after Dose 3, administered at the same dose level as was received for the primary vaccination series.

  This study was descriptive and no hypothesis testing was planned.

- Substudy A (Groups 1 – 4): Phase 2/3 is an open-label study evaluating the safety, tolerability, and immunogenicity of a of Omi XBB.1.5 administered in COVID-19 vaccine-naïve participants in children 6 m-< 5 years of age. Vaccine was administrated in 6 months-<2 year old children in 3 different posology groups.
    - G1 received a 2- dose schedule on a 0- and 8-week at the 10 µg dose,
    - G2 received a single dose at the 10 µg dose level and
    - G3 received the currently approved 3 dose schedule with at 3 µg dose level.
    - G4 Children at age 2-< 5 years received single dose of Omi XBB.1.5 at the 10 µg dose level.

The study was hypothesis tested. Non-inferior immune responses were evaluated. The GMR (ratio of GMTs) and seroresponse from all subgroups were compared to the same results from G3, which represents the currently approved posology for entire 6m-< 5 years age group. Seroresponse was defined as achieving a ≥4-fold rise from baseline (before the study vaccination). Noninferiority based on the GMR was be declared if the lower limit of the 2-sided 95% CI for the GMR is greater than 0.67 (1.5-fold criterion) and the point estimate of the GMR is ≥0.8; noninferiority based on seroresponse rate difference was declared if the lower limit of the 2-sided 95% CI for the difference in percentages of participants with seroresponse is >-10%. These non-inferiority margins are acceptable. The 2 primary immunogenicity objectives were evaluated sequentially using a 1-sided alpha of 0.025 in the order: G1/G3 GMR, G1/G3 Seroresponse, G4/G3 GMR, G4/G3 Seroresponse, which is also acceptable. The G2/G3 immunogenicity analysis was a secondary objective.

There are some unclarities with the G4/G3 analysis. In this analysis, only previously SARS-COV-2 naïve individuals were included, whereas in all other analysis all participants regardless of their SARS-COV-2 status were included. This selection potentially gives benefit for G4 group as SARS-COV-2 experienced population tend to respond with higher antibody titre than SARS-CoV-2 naive.

The Sample size calculation showed, that for G1/G3 analysis the required sample size to demonstrate non-inferior GMR and Seroresponse is 337/225. For non- inferiority analysis G4/G3 require 337/112 individuals.

Efficacy Results

Phase 1

The sample size for evaluable immunogenicity population receiving 4th dose with Omicron XBB 1.5 was low as at 3, 6, or 10 µg level 12, 17 and 16 children respectively were included in age group 6m-<2 years. The same low sample size age was observed in 2-< 5 year old group as evaluable immunogenicity population at 3, 6, or 10 µg level included 11, 16 and 16 participants.

Generally, the immunology results from Phase 1 show, that single dose of 10 µg Omicron XBB 1.5 vaccine is immunogenic in children, who have received 3 doses of bivalent Omicron vaccine earlier. The dose- response was recorded as at 10 µg level the GMTs were higher than in case of 3 and 6 µg. In conclusion, the Phase 1 results support the choice to evaluate 10 µg dose level in Phase 2/3.

Phase 2/3

The sample size followed the power calculation for primary non-inferiority analysis G1/G3 (337/225) as 367/ 234 individuals were included into the valuable immunogenicity population. In G4/ G3 SARS-CoV-2 negative population analysis, the actual numbers (470/53) differed from the planned sample size (337/112). The baseline demographic characteristics were comparable between subgroups.

In 6m-<2 years age group, it was shown that two doses of Omi XBB.1.5 at 10 µg were noninferior to three 3 µg doses against Omicron XBB.1.5 based on GMR (1.51 (95% CI: 1.25, 1.82)) and difference in seroresponse rates (1.28% (95% CI: –2.69, 5.26)) (G1/G3 analysis). Immune responses were generally consistent across age, sex, race, and baseline SARS-CoV-2 status.

GMTs, GMR (0.40 (95% CI: 0.29, 0.55) and seroresponse rate difference (-14.62% (95% CI: –22.16, –7.07) were lower after a single 10 µg dose of BNT162b2 (Omi XBB.1.5) when compared to after three 3 µg doses of BNT162b2 (Omi XBB.1.5) (G2/G3 analysis), primarily driven by lower GMR and seroresponse rates among those who had no prior exposure to SARS-CoV-2 compared to those who were baseline SARS-CoV-2 positive.

In 2- <5 years of age a single 10-µg dose Omi XBB.1.5 met non-inferiority based on GMR (1.12 (95% CI: 0.86, 1.47)), but not based on difference in seroresponse rates (-8.95 (95% CI: -11.92, -2.12)), when compared to three 3 µg doses of BNT162b2 (Omi XBB.1.5) in children 6-months to < 2 years without evidence of SARS-CoV-2 infection up to 1 month after Dose 3 (G4/G3 analysis).

The change in posology in 6m-< 2 years age group to replace 3 x 3 µg posology with 2 x 10 µg is supported as the non-inferiority of GMR and seroresponse were demonstrated. The reduction of number of doses to only 1 dose in 2-<5 year old group is not supported due to the following reasons:

a) The entire setup to compare antibody titres of older population including both SARS-CoV-2 negatives and positives with SARS-CoV-2 negative younger population. It is assumed, that the SARS-CoV-2 negative population responds with lower titre.

b) Power of this non-inferiority analysis is questionable as it was assumed 337 vs 112 participants. Instead, 470 vs 53 were included to the analysis.

c) The seroresponse rate difference non-inferiority analysis failed for G4 vs. G3.

d) The seroresponse after one 10 µg dose in baseline SARS-COV-2 negative subjects in G4 (2-<5 years) group was modest, about GMT 817 (at maximum 2097), compared to G3 baseline SARS-CoV-2 negative subjects receiving 3x 3 µg, which led to GMT 5643. Attempt to demonstrate non-inferiority between these baseline SARS-CoV-2 negative groups would fail.

e) In younger age group (G2) one dose of 10 µg vaccine was definitely not sufficient to induce non-inferior immune response in comparison to the 3 x 3 µg schedule.

There is a concern that a single 10 µg dose of Comirnaty does not provide sufficient protection for virus naïve children 2 to <5 years. The current EMA/ECDC recommendation states that children above 5 years of age should receive a single dose of vaccine, while children below 5 years of age without known vaccination or exposure to the virus should receive the primary vaccination schedule, under the assumption that a significant proportion remain seronegative. In EU, healthy children are not routinely vaccinated against COVID-19. The target group for this vaccination is children with serious comorbidities and therefore the best possible protection against the disease should be provided.

The MAH was asked to justify the usage of one dose of 10 µg Comirnaty in SARS-CoV-2 naïve children 2 to less than 5 years of age. The MAH answered that majority of the healthy children already have been exposed to COVID-19 for age 2-<5, the feasibility to conduct studies with COVID-19 unexposed children with serious comorbidities is limited. In the responses, the MAH agreed to change posology for 2 doses as primary schedule for COVID-19 vaccine- naïve children in entire 6 months to <5 years age group, which is considered acceptable.

Age group 5y-< 12 years

Design and conduct of clinical study

Study C4591048 Substudy E is an open-label study to evaluate the safety, tolerability, and immunogenicity of an updated BNT162b2 (Omi XBB.1.5) vaccine in participants 5 to <12 years of age who were COVID-19 vaccine-naïve. Participants received a single 10 µg dose of BNT162b2 (Omi XBB.1.5) as an approved posology describes in SmPC. For non-inferiority analysis for serology results from SSE (5-<12 y) a control group from Study C4591054 substudy A including vaccine experienced adults receiving 4th dose with Omicron XBB 1.5 was used. Study C4591054 compared immune responses after Omicron XBB 1.5 30 µg in individuals older than 12 years in vaccine experienced group (subgroup A) and in previously unvaccinated group (subgroup B).

The study was hypothesis tested. Non-inferior immune responses were evaluated in vaccine- naïve 5-<12 years age group vs. adults, who had received earlier versions of Comirnaty and received XBB 1.5 as their 4th dose of Covid-19 vaccine. The control group had median age 56 years (12-82), had received several vaccine doses earlier and received higher dose, 30 µg XBB 1.5. Immune responses tend to be lower after 55 years of age. The choice of the comparator group is not totally followed, as it seems that C4591054 Substudy B could been a better choice as these adults were also at least vaccine naive. One could have also selected younger adults into the comparison group.

Noninferiority based on the GMR was be declared if the lower limit of the 2-sided 95% CI for the GMR is greater than 0.67 (1.5-fold criterion) and the point estimate of the GMR is ≥0.8; noninferiority based on seroresponse rate difference was declared if the lower limit of the 2-sided 95% CI for the difference in percentages of participants with seroresponse is >-10%. These non-inferiority margins are acceptable. The sample size calculation show, that to demonstrate non-inferior immune response, 225 individuals are needed in both study arms.

Efficacy Results

The sample size followed the power calculation as 285/225 individuals were included to the evaluable immunogenicity population. The baseline characteristics differed between the study arms.

In the evaluable immunogenicity population, the primary model-based GMR of Omicron XBB.1.5-neutralising titres for the Omi XBB.1.5 10 µg group to the Omi XBB.1.5 30 µg group was 1.81 (2-sided 95% CI: 1.51, 2.16). 88.8% of participants in the 5-<12 years Omi XBB.1.5 10 µg group and 77.0% of participants in the adult Omi XBB.1.5 30 µg group achieved seroresponse to Omicron XBB.1.5. The

adjusted difference in percentages of participants with seroresponse between the 10 µg group and 30 µg group was 8.97% (95% CI: 3.91, 14.02).

Immunobridging success based on the model-based GMR and seroresponse rate difference was declared.

Regardless of the non-inferiority comparison, the immunogenicity data from C4591048 Substudy E supports the posology for 5-<12 year old group as the single 10 µg dose was immunogenic. This clinical data supports the current approved posology for this age group.

2.4.4. Conclusions on the clinical efficacy

The current approved posology for entire 6 months to < 5 years age group is 3 doses of 3 µg Comirnaty. The change in posology for 6m-< 2 year old children to replace 3 x 3µg with 2 x 10 µg Comirnaty is supported. The change in posology for 2 - <5 year old children to replace 3 x 3µg with 1 x 10 µg Comirnaty was not supported as the non-inferiority analysis of seroresponse difference failed and the immune response in SARS-CoV-2 naïve children after a single dose of 10 µg was modest compared to the approved 3 x 3µg posology. The MAH agreed to change posology for 2 doses x 10 µg as primary schedule for COVID-19 vaccine- naïve children in entire 6 months to <5 years age group.

The clinical data to support posology for 5-< 12 years old children as 1 dose of 10 µg Comirnaty is acceptable.

2.5. Clinical safety

Introduction

BNT162b-2 vaccine is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 months of age and older. This assessment report includes immunogenicity and safety data Study C4591048 Substudy A and E, to support an updated posology for infants and children from 6 months to <5 years of age from 3 µg to 10 µg. Furthermore, an updated dosing regimen from 3-dose to 2-dose primary course for 6 months to <2 years of age; and a single dose for 2 years to <5 years of age is proposed.

An updated RMP v15.2 has also been provided.

Study C4591048 is a Phase 1/2/3 master protocol initially designed to evaluate the safety, tolerability, and immunogenicity of variant-adapted BNT162b2 RNA-based vaccine candidate(s) in healthy children. Each substudy design is detailed separately in the respective substudy appendix of the master protocol. Substudies may be conducted in parallel, as required by the clinical plan, within the framework of the master protocol. Eligibility as related to age was designed to ensure participants receive the same level of dose throughout participation in the study.

Substudy A Phase 1 was the dose-finding portion of the study. It evaluates the safety, tolerability, and immunogenicity of a 3-dose series of bivalent BNT162b2, administered on a 0-, 3-, and 11-week schedule, followed by a fourth dose with BNT162b2 (Omi XBB.1.5) approximately 6 months after Dose 3, administered at the same dose level as was received for Dose 1 through Dose 3. Based on the currently authorized 3 µg BNT162b2 dose in individuals ≥6 months to <5 years of age, the dose-finding study included this same dose level (bivalent BNT162b2 3 µg) in addition to bivalent BNT162b2 6 and 10 µg. Following the 2023-2024 periodic strain change recommendation to update the COVID-19 vaccine to a monovalent Omicron XBB.1.5 composition, Pfizer/BioNTech evaluated BNT162b2 (Omi XBB.1.5) as a fourth dose in individuals who received 3 doses of bivalent BNT162b2 (original/Omi

BA.4/BA.5) in Substudy A Phase 1. Participants who received a fourth dose prior to the approval of protocol amendment 3 may have received bivalent BNT162b2 as a fourth dose.

Substudy A Phase 2/3 is the selected-dose portion of the study. The study design was revised to evaluate 2 doses of BNT162b2 (Omi XBB.1.5) at the dose level selected in Substudy A Phase 1 (10 µg), administered on a 0- and 8-week schedule, compared with 3 doses of BNT162b2 (Omi XBB.1.5) at the currently authorized 3 µg dose level in COVID19 vaccine–naïve individuals ≥6 months to <2 years of age, who were enrolled contemporaneously into Substudy A Phase 2/3. Substudy A Phase 2/3 also evaluated the safety, tolerability, and immunogenicity of a single dose of BNT162b2 (Omi XBB.1.5) 10 µg in COVID19 vaccine naïve participants ≥2 to <5 years of age, or BNT162b2 (Omi KP.2) in 6 months to <2 years of age for group 6. Approximately 2100 participants ≥6 months to <5 years of age were planned to be enrolled across 2 age groups: ~1500 participants in age group 1, ≥6 months to <2 years of age, and ~600 participants in age group 2, ≥2 to <5 years of age.

C4591048 Substudy E was a Phase 2/3 open-label study to evaluate the safety, tolerability, and immunogenicity of a single 10 µg dose of BNT162b2 (Omi XBB.1.5) in participants ≥5 to <12 years of age who were COVID-19 vaccine-naïve. Eligible study participants were healthy male or female vaccine-naïve individuals ≥5 years to <12 years of age. The safety population included a total of 310 participants.

Patient exposure

Substudy A

Disposition

Phase 1

Table 35: Disposition of All Randomised Participants - Substudy A - Phase 1 - 6 Months to <2 Years of Age

	Vaccine Group (as Randomised)			
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)			
	3 µg n[a] (%)	6 µg n[a] (%)	10 µg n[a] (%)	Total n[a] (%)
Randomised[b]	32 (100.0)	31 (100.0)	33 (100.0)	96 (100.0)
Not vaccinated	0	1 (3.2)	0	1 (1.0)
Vaccinated	32 (100.0)	30 (96.8)	33 (100.0)	95 (99.0)
Dose 1	32 (100.0)	30 (96.8)	33 (100.0)	95 (99.0)
Dose 2	31 (96.9)	29 (93.5)	31 (93.9)	91 (94.8)
Dose 3	30 (93.8)	27 (87.1)	31 (93.9)	88 (91.7)

	Vaccine Group (as Randomised)			
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)			
	3 µg n[a] (%)	6 µg n[a] (%)	10 µg n[a] (%)	Total n[a] (%)
Dose 4[c]	26 (81.3)	24 (77.4)	28 (84.8)	78 (81.3)
Completed 1-month post-Dose 2 visit	31 (96.9)	27 (87.1)	31 (93.9)	89 (92.7)
Completed 1-month post-Dose 3 visit	30 (93.8)	26 (83.9)	31 (93.9)	87 (90.6)
Completed 1-month post-Dose 4 visit	25 (78.1)	24 (77.4)	28 (84.8)	77 (80.2)
Completed the study	24 (75.0)	24 (77.4)	27 (81.8)	75 (78.1)
Withdrawn from study	8 (25.0)	6 (19.4)	6 (18.2)	20 (20.8)
Reason for withdrawal from study				
Lost to follow-up	2 (6.3)	2 (6.5)	2 (6.1)	6 (6.3)
Protocol deviation	1 (3.1)	0	1 (3.0)	2 (2.1)
Withdrawal by parent/guardian	5 (15.6)	4 (12.9)	3 (9.1)	12 (12.5)

a. n = Number of participants with the specified characteristic.
b. These values are the denominators for the percentage calculations.
c. All participants received BNT162b2 (Omi XBB.1.5) at the specified dose level at dose 4 except 2 participants who received Bivalent BNT162b2 (Original/Omi BA.4/BA.5) 3 µg.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adds Table Generation: 26SEP2025 (08:04) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adds_s002_disp_p1_2

One of the participants in the phase 1 6-Months to <2 years of age was excluded from the safety population due to not receiving study intervention. The safety population included 95 participants.

Table 36: Disposition of All Randomised Participants - Substudy A - Phase 1 - 2 to <5 Years of Age

	Vaccine Group (as Randomised)			
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)			
	3 µg n[a] (%)	6 µg n[a] (%)	10 µg n[a] (%)	Total n[a] (%)
Randomised[b]	23 (100.0)	24 (100.0)	24 (100.0)	71 (100.0)
Not vaccinated	0	0	0	0

	Vaccine Group (as Randomised)			
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)			
	3 µg n[a] (%)	6 µg n[a] (%)	10 µg n[a] (%)	Total n[a] (%)
Vaccinated	23 (100.0)	24 (100.0)	24 (100.0)	71 (100.0)
Dose 1	23 (100.0)	24 (100.0)	24 (100.0)	71 (100.0)
Dose 2	20 (87.0)	24 (100.0)	24 (100.0)	68 (95.8)
Dose 3	18 (78.3)	23 (95.8)	23 (95.8)	64 (90.1)
Dose 4[c]	13 (56.5)	23 (95.8)	20 (83.3)	56 (78.9)
Completed 1-month post-Dose 2 visit	18 (78.3)	23 (95.8)	23 (95.8)	64 (90.1)
Completed 1-month post-Dose 3 visit	15 (65.2)	23 (95.8)	22 (91.7)	60 (84.5)
Completed 1-month post-Dose 4 visit	13 (56.5)	22 (91.7)	20 (83.3)	55 (77.5)
Completed the study	13 (56.5)	21 (87.5)	20 (83.3)	54 (76.1)
Withdrawn from study	10 (43.5)	3 (12.5)	4 (16.7)	17 (23.9)
Reason for withdrawal from study				
Lost to follow-up	3 (13.0)	2 (8.3)	0	5 (7.0)
Protocol deviation	1 (4.3)	0	0	1 (1.4)
Withdrawal by parent/guardian	6 (26.1)	1 (4.2)	4 (16.7)	11 (15.5)

a. n = Number of participants with the specified characteristic.
b. These values are the denominators for the percentage calculations.
c. All participants received BNT162b2 (Omi XBB.1.5) at the specified dose level at dose 4.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adds Table Generation: 26SEP2025 (08:04) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adds_s002_disp_p1_5

All subjects received the study intervention; thus, the safety population included 71 participants.

Phase 2/3

Table 37: Disposition of All Randomised Participants - Substudy A - Phase 2/3 - 6 Months to <2 Years of Age

	Vaccine Group (as Randomised) BNT162b2 (Omi XBB.1.5)		
	10 µg (Group 1 and Group 2) n[a] (%)	3 µg (Group 3) n[a] (%)	Total n[a] (%)
Randomised[b]	608 (100.0)	306 (100.0)	914 (100.0)
Not vaccinated	4 (0.7)	2 (0.7)	6 (0.7)
Vaccinated	604 (99.3)	304 (99.3)	908 (99.3)
Dose 1	604 (99.3)	304 (99.3)	908 (99.3)
Dose 2	576 (94.7)	295 (96.4)	871 (95.3)
Dose 3	NA	286 (93.5)	286 (31.3)
Completed 1-month post-Dose 1 visit	596 (98.0)	NA	596 (65.2)
Completed 1-month post-Dose 2 visit	570 (93.8)	292 (95.4)	862 (94.3)
Completed 1-month post-Dose 3 visit	NA	284 (92.8)	284 (31.1)
Completed the study	557 (91.6)	272 (88.9)	829 (90.7)
Withdrawn from study	47 (7.7)	32 (10.5)	79 (8.6)
Reason for withdrawal from study			
Adverse event	1 (0.2)	0	1 (0.1)
Death	2 (0.3)	1 (0.3)	3 (0.3)
Lost to follow-up	17 (2.8)	9 (2.9)	26 (2.8)
Protocol deviation	3 (0.5)	5 (1.6)	8 (0.9)
Withdrawal by parent/guardian	23 (3.8)	17 (5.6)	40 (4.4)
Other	1 (0.2)	0	1 (0.1)

Note: Participants enrolled in Group 1 and Group 2 were planned to receive a 2-dose series of BNT162b2 (Omi XBB.1.5) at 10 µg on a 0- and 8-week schedule. Participants enrolled in Group 3 were planned to receive a 3-dose series of BNT162b2 (Omi XBB.1.5) at 3 µg on a 0-, 3-, and 11-week schedule.

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

b. These values are the denominators for the percentage calculations.

PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adds Table Generation: 18SEP2025 (22:00) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adds_s002_disp_p2_2

The safety population included 604 participants in the BNT162b2 (Omi XBB.1.5) 10 µg groups (Group 1 and Group 2) and 304 participants in the BNT162b2 (Omi XBB.1.5) 3 µg (Group 3). The six participants (0.7%) were excluded from the safety population due to not receiving study intervention.

Table 38: Disposition of All Randomised Participants - Substudy A - Phase 2/3 - 2 to <5 Years of Age

	Vaccine Group (as Randomised) **BNT162b2 (Omi XBB.1.5) 10 µg (Group 4 and Group 5) n[a] (%)**
Randomised[b]	692 (100.0)
Not vaccinated	4 (0.6)
Vaccinated	688 (99.4)
Dose 1	688 (99.4)
Completed 1-month post-Dose 1 visit	678 (98.0)
Completed the study	651 (94.1)
Withdrawn from study	37 (5.3)
Reason for withdrawal from study	
Death	2 (0.3)
Lost to follow-up	20 (2.9)
Protocol deviation	2 (0.3)
Withdrawal by parent/guardian	13 (1.9)

Note: Participants enrolled in Group 4 and Group 5 were planned to receive a single dose of BNT162b2 (Omi XBB.1.5) at 10 µg.
Note: One participant of 2 to <5 years of age who was randomised into Group 3 in error and received Omi XBB.1.5 at 3 µg is also included.
Note: One participant of 2 to <5 years of age who was randomised into Group 1 in error and received 2 doses of Omi XBB.1.5 at 10 µg is also included.
a. n = Number of participants with the specified characteristic.
b. These values are the denominators for the percentage calculations.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adds Table Generation: 18SEP2025 (22:00) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adds_s002_disp_p2_5

The total safety population included 688 participants. Four participants (0.6%) were excluded from the safety population due to participants not receiving study intervention.

Demographics

Phase 1

Participants 6 Months Through <2 Years of Age

Overall, 53.7% of the Phase 1 safety population 6 months through < 2 years of age were male. A total of 56.8% of participants had evidence of prior SARS-CoV-2 infection at study baseline ("baseline positive"). Most participants were White (67.4%), followed by Black or African American (22.1%), Multiracial (7.4%), and Asian (3.2%); Few participants (7.4%) had at least 1 high-risk underlying comorbidity. The median age at study vaccination was 10.0 months. All participants were from the United States. Median follow-up duration ranged from 16.1 to 16.5 months for after Doses 1 and from 6.4 to 6.5 months after Dose 4 across all vaccine groups. Most participants in each analysis set had follow-up periods exceeding 6 months.

Participants 2 Through <5 Years of Age

Overall, 56.3% of the Phase 1 safety population 2 through <5 years of age were male. A total of 95.8% of participants had evidence of prior SARS-CoV-2 infection at study baseline ("baseline positive"). Most participants were White (56.3%), followed by Black or African American (38.0%), Multiracial (4.2%), and Asian (1.4%); 33.8% of participants had at least 1 high-risk underlying comorbidity. The median age at study vaccination was 2.0 years.

Median follow-up duration ranged from 15.5 to 16.2 months after Doses 1, and from 6.4 to 6.5 months after Dose 4 across all vaccine groups. Most participants in each analysis set had follow-up periods exceeding 6 months.

Phase 2/3

Table 39: Demographic Characteristics - Substudy A - Phase 2/3 - 6 Months to <2 Years of Age - Safety Population

	Vaccine Group (as Administered at Dose 1)		
	BNT162b2 (Omi XBB.1.5)		
	10 µg (Group 1 and Group 2) (N[a]=604) n[b] (%)	3 µg (Group 3) (N[a]=304) n[b] (%)	Total (N[a]=908) n[b] (%)
Sex			
Male	317 (52.5)	156 (51.3)	473 (52.1)
Female	287 (47.5)	148 (48.7)	435 (47.9)
Race			
White	59 (9.8)	29 (9.5)	88 (9.7)
Black or African American	431 (71.4)	222 (73.0)	653 (71.9)
American Indian or Alaska Native	1 (0.2)	0	1 (0.1)
Asian	3 (0.5)	1 (0.3)	4 (0.4)

	Vaccine Group (as Administered at Dose 1) BNT162b2 (Omi XBB.1.5)		
	10 µg (Group 1 and Group 2) (N[a]=604) n[b] (%)	**3 µg (Group 3) (N[a]=304) n[b] (%)**	**Total (N[a]=908) n[b] (%)**
Multiracial	14 (2.3)	7 (2.3)	21 (2.3)
Not reported	95 (15.7)	45 (14.8)	140 (15.4)
Unknown	1 (0.2)	0	1 (0.1)
Ethnicity			
Hispanic/Latino	57 (9.4)	38 (12.5)	95 (10.5)
Non-Hispanic/non-Latino	545 (90.2)	266 (87.5)	811 (89.3)
Not reported	2 (0.3)	0	2 (0.2)
Country			
Brazil	33 (5.5)	28 (9.2)	61 (6.7)
South Africa	504 (83.4)	246 (80.9)	750 (82.6)
United States	67 (11.1)	30 (9.9)	97 (10.7)
Age at vaccination (months)			
Mean (SD)	14.2 (5.05)	14.1 (5.20)	14.1 (5.09)
Median	14.0	14.0	14.0
Min, max	(6, 23)	(6, 23)	(6, 23)
Baseline SARS-CoV-2 status			
Positive[c]	380 (62.9)	189 (62.2)	569 (62.7)
Negative[d]	201 (33.3)	103 (33.9)	304 (33.5)
Missing	23 (3.8)	12 (3.9)	35 (3.9)
Comorbidities[e]			
Yes	26 (4.3)	13 (4.3)	39 (4.3)
No	578 (95.7)	291 (95.7)	869 (95.7)

	Vaccine Group (as Administered at Dose 1) BNT162b2 (Omi XBB.1.5)		
	10 µg (Group 1 and Group 2) (N[a]=604) n[b] (%)	3 µg (Group 3) (N[a]=304) n[b] (%)	Total (N[a]=908) n[b] (%)

Abbreviations: MMWR = Morbidity and Mortality Weekly Report; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein-binding; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Participants enrolled in Group 1 and Group 2 were planned to receive a 2-dose series of BNT162b2 (Omi XBB.1.5) at 10 µg on a 0- and 8-week schedule. Participants enrolled in Group 3 were planned to receive a 3-dose series of BNT162b2 (Omi XBB.1.5) at 3 µg on a 0-, 3-, and 11-week schedule.
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. Positive N-binding antibody result at Dose 1, positive NAAT result at Dose 1, or medical history of COVID-19.
d. Negative N-binding antibody result at Dose 1, negative NAAT result at Dose 1, and no medical history of COVID-19.
e. Number of participants who had at least 1 high-risk underlying condition, based on MMWR Morb Mortal Wkly Rep. 2020;69(32):1081-8 and CDC high-risk underlying conditions list last updated 09FEB2023.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adsl Table Generation: 26SEP2025 (01:33) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adsl_s005_demo_p2_2

Median follow-up time from Dose 1 to the end of study was 8.5 months (10 µg) and 9.1 months (3 µg). Most participants who received Dose 2 (97.0%) and Dose 3 (95.1%) as their last dose had a follow up time ≥6 months after the last dose.

Table 40: Demographic Characteristics - Substudy A - Phase 2/3 - 2 to <5 Years of Age - Safety Population

	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (Group 4 and Group 5) (N[a]=688) n[b] (%)
Sex	
Male	348 (50.6)
Female	340 (49.4)
Race	
White	81 (11.8)
Black or African American	492 (71.5)
American Indian or Alaska Native	1 (0.1)
Asian	5 (0.7)
Multiracial	22 (3.2)

	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (Group 4 and Group 5) (N[a]=688) n[b] (%)
Not reported	86 (12.5)
Unknown	1 (0.1)
Ethnicity	
Hispanic/Latino	122 (17.7)
Non-Hispanic/non-Latino	562 (81.7)
Not reported	4 (0.6)
Country	
Brazil	53 (7.7)
Puerto Rico	19 (2.8)
South Africa	510 (74.1)
United States	106 (15.4)
Age at vaccination (years)	
Mean (SD)	2.9 (0.82)
Median	3.0
Min, max	(2, 4)
Obese[c]	
Yes	75 (10.9)
No	613 (89.1)
Baseline SARS-CoV-2 status	
Positive[d]	484 (70.3)
Negative[e]	196 (28.5)
Missing	8 (1.2)
Comorbidities[f]	

	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (Group 4 and Group 5) (N[a]=688) n[b] (%)
Yes	112 (16.3)
No	576 (83.7)

Abbreviations: MMWR = Morbidity and Mortality Weekly Report; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein-binding; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Participants enrolled in Group 4 and Group 5 were planned to receive a single dose of BNT162b2 (Omi XBB.1.5) at 10 µg.
Note: One participant of 2 to <5 years of age who was randomised into Group 3 in error and received Omi XBB.1.5 at 3 µg is also included.
Note: One participant of 2 to <5 years of age who was randomised into Group 1 in error and received 2 doses of Omi XBB.1.5 at 10 µg is also included.
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. Obese is defined as a body mass index (BMI) at or above the 95th percentile according to the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/data/zscore/bmiagerev.xls.
d. Positive N-binding antibody result at Dose 1 (Group 4 only), positive NAAT result at Dose 1, or medical history of COVID-19.
e. Negative N-binding antibody result at Dose 1 (Group 4 only), negative NAAT result at Dose 1, and no medical history of COVID-19.
f. Number of participants who had at least 1 high-risk underlying condition, based on MMWR Morb Mortal Wkly Rep. 2020;69(32):1081-8 and CDC high-risk underlying conditions list last updated 09FEB2023 and/or obesity (BMI ≥ 95th percentile).
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adsl Table Generation: 26SEP2025 (01:33) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adsl_s005_demo_p2_5

Median follow-up time after study vaccination was 6.3 months. Most participants (>95.9%) had ≥6 months of follow-up after the single dose of 10 µg.

Prior, Concomitant, and Post-Intervention Therapy

Phase 1

Participants 6 Months Through <2 Years of Age

Across the bivalent BNT162b2 (original/Omi BA.4/BA.5) groups, receipt of any concomitant (non-study) vaccine after Dose 1 ranged from 16 participants (48.5%) in the 10-µg group to 19 participants (57.6%) in the 3-µg group. Influenza vaccine was administered to 11 (33.3%) to 16 (48.5%) participants across dose groups. Other non-study vaccines received included hepatitis A vaccine (33.3%–48.5%), varicella zoster vaccine (20.7%–30.3%), and MMR vaccine (20.7%–33.3%).

Receipt of non-study COVID-19 vaccine after study vaccination was reported in 1 participant (3.0%) in the 10-µg group. Concomitant medication of Dtap-HepB-IPV (Pediatrix) was incorrectly coded to Paracetamol in one participant 6 months to <2 years of age in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 3 µg group following Dose 2.

No participants received prohibited medications.

Participants 2 Through <5 Years of Age

Across the bivalent BNT162b2 (original/Omi BA.4/BA.5) groups, receipt of any concomitant (non-study) vaccine after Dose 1 ranged from 0 participants in the 3 µg group and 3 participants (12.5%) in the 6 µg group for influenza vaccine, which was the only non-study vaccine in this age group.

Concomitant prohibited medication (prednisolone) received after Dose 1 was reported in 1 participant (4.3%) in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 3 µg group.

Phase 2/3

Participants 6 Months Through <2 Years of Age (Group 1 – 3)

BNT162b2 (Omi XBB.1.5) 10-µg Group

A total of 164 participants (27.2%) in the BNT162b2 (Omi XBB.1.5) 10-µg group received a non-study vaccine after first study vaccination.

The most administered non-study vaccines included measles vaccine (10.4%), diphtheria/hepatitis B/pertussis/tetanus/polio/Haemophilus influenzae type b combination vaccines (8.3%), and pneumococcal conjugate vaccines (7.5%). Other non-study vaccines administered included hepatitis A vaccine (3.6%), influenza vaccine (4.3%), MMR vaccine (3.0%), varicella zoster vaccine (1.5%), and meningococcal vaccine (0.2%). Receipt of a non-study COVID-19 vaccine was infrequent (0.2%).

No participants received prohibited medications.

BNT162b2 (Omi XBB.1.5) 3-µg Group

A total of 81 participants (26.6%) in the BNT162b2 (Omi XBB.1.5) 3-µg group received a non-study vaccine after first study vaccination.

The most commonly administered non-study vaccines included measles vaccine (12.5%), diphtheria/hepatitis B/pertussis/tetanus/polio/Haemophilus influenzae type b combination vaccines (6.6%), and pneumococcal conjugate vaccines (7.6%). Other non-study vaccines administered included hepatitis A vaccine (3.0%), influenza vaccine (3.6%), MMR vaccine (2.0%), varicella zoster vaccine (0.3%), and meningococcal vaccine (0.3%). Three participants (1.0%) received a non-study COVID-19 vaccine.

No participants received prohibited medications.

Participants 2 Through <5 Years of Age (Group 4 – 5)

BNT162b2 (Omi XBB.1.5) 10-µg Group

A total of 5 participants (0.7%) in the BNT162b2 (Omi XBB.1.5) 10-µg group received a non-study vaccine after study vaccination.

The non-study vaccines administered included diphtheria/pertussis/tetanus/polio combination vaccines (0.1–0.4%), hepatitis A vaccine (0.1%), hepatitis B vaccine (0.1%), Haemophilus influenzae type b (Hib) vaccine (0.1%), influenza vaccine (0.1%), inactivated influenza vaccine (0.1%), measles/mumps/rubella/varicella combination vaccines (0.1–0.3%), pneumococcal vaccines (0.1%), polio vaccine (0.1%), and varicella zoster vaccine (0.1%). No participants in this group received a non-study COVID-19 vaccine.

No participants received prohibited medications.

Exposure to BNT162b2 (Omi XBB.1.5)

Phase 1

Participants 6 Months Through <2 Years of Age (Bivalent BNT162b2 [Original/Omi BA.4/BA.5])

Across all dose groups, most participants received the correct dose at each scheduled vaccination; however, 2 participants received a dose different from their randomised assignment at one or more time points: 1 participant in the 6-µg group received 3-µg dose at Dose 2 and 1 participant in the 6-µg group received 3-µg dose at all 4 doses. Two participants received a fourth dose prior to the approval of Protocol Amendment 3 and therefore received bivalent BNT162b2 (original/Omi BA.4/BA.5) instead of BNT162b2 (Omi XBB.1.5).

Participants 2 Through <5 Years of Age (Bivalent BNT162b2 [Original/Omi BA.4/BA.5])

Of the 71 participants randomised, all (100.0%) received at least one dose of study vaccination. Most participants received the planned dose as randomised at each vaccination time point.

For Dose 4 (BNT162b2 Omi XBB.1.5), most participants in the 6-µg (91.7%) and 10-µg (83.3%) groups received the planned dose, compared to 56.5% in the 3-µg group. The lower proportion of participants in the 3-µg group receiving Dose 4 was primarily due to study withdrawals prior to this time point. One participant (4.2%) in the 6-µg group received BNT162b2 (Omi XBB.1.5) at the 10 µg dose for Dose 4, receiving an incorrect dose at one time point.

Phase 2/3

Participants 6 Months Through <2 Years of Age (Group 1 – 3)

Of the 914 participants randomised, 908 (99.3%) received at least one dose of study vaccination. Most participants received the planned dose as randomised at each vaccination time point. Most participants received the correct dose as assigned at each scheduled vaccination.

For Dose 2, 575 participants (94.6%) in the 10-µg group and 295 participants (96.4%) in the 3-µg group received the planned dose. One participant (0.2%) in the 10 µg group incorrectly received BNT162b2 (Omi XBB.1.5) 3 µg at Dose 2. In the 3-µg group, 286 participants (93.5%) received Dose 3 as planned.

Participants 2 Through <5 Years of Age (Group 4 – 5)

Of the 692 participants randomised, 688 (99.4%) received the study vaccination. Most participants (99.3%) received the planned 10-µg dose of BNT162b2 (Omi XBB.1.5), while one participant (0.1%) received a 3-µg dose due to a dosing error. Four participants (0.6%) did not receive study vaccine.

Substudy E

Disposition

Table 41: Disposition of All Assigned Participants - Substudy E

	Vaccine Group (as Assigned)
	BNT162b2 (Omi XBB.1.5) 10 µg n[a] (%)
Assigned[b]	310

	Vaccine Group (as Assigned) BNT162b2 (Omi XBB.1.5) 10 µg n[a] (%)
Not vaccinated	0
Vaccinated	310 (100.0)
Completed 1-month post–study vaccination visit (vaccination period)	307 (99.0)
Completed the study	287 (92.6)
Withdrawn from study	23 (7.4)
Reason for withdrawal from study	
Lost to follow-up	17 (5.5)
Protocol deviation	5 (1.6)
Withdrawal by parent/guardian	1 (0.3)

a. n = Number of participants with the specified characteristic.
b. This value is the denominator for the percentage calculations.
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The safety population included 310 participants. No participants were excluded from the safety population for any reason.

Demographics

Table 42: Demographic Characteristics - Substudy E - Safety Population

	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (N[a]=310) n[b] (%)
Sex	
Male	146 (47.1)
Female	164 (52.9)
Race	
White	128 (41.3)

	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (N[a]=310) n[b] (%)
Black or African American	164 (52.9)
American Indian or Alaska Native	1 (0.3)
Asian	6 (1.9)
Multiracial	10 (3.2)
Not reported	1 (0.3)
Ethnicity	
Hispanic/Latino	162 (52.3)
Non-Hispanic/non-Latino	148 (47.7)
Country	
Brazil	29 (9.4)
Puerto Rico	2 (0.6)
South Africa	65 (21.0)
United States	214 (69.0)
Age at the study vaccination (years)	
Mean (SD)	7.4 (1.98)
Median	7.0
Min, max	(5, 11)
Obese[c]	
Yes	78 (25.2)
No	232 (74.8)
Baseline SARS-CoV-2 status	
Positive[d]	306 (98.7)
Negative[e]	3 (1.0)
Missing	1 (0.3)

	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (N[a]=310) n[b] (%)
Comorbidities[f]	
Yes	109 (35.2)
No	201 (64.8)

Abbreviations: MMWR = Morbidity and Mortality Weekly Report; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein–binding; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
a. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
c. Obese is defined as a body mass index (BMI) at or above the 95th percentile according to the growth chart. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/data/zscore/bmiagerev.xls.
d. Positive N-binding antibody result at the study vaccination visit, positive NAAT result at the study vaccination visit, or medical history of COVID-19.
e. Negative N-binding antibody result at the study vaccination visit, negative NAAT result at the study vaccination visit, and no medical history of COVID-19.
f. Number of participants who had at least 1 high-risk underlying condition, based on MMWR. 2020;69(32):1081-8 and CDC high-risk underlying conditions list last updated 09FEB2023 and/or obesity (BMI ≥ 95th percentile).
PFIZER CONFIDENTIAL SDTM Creation: 04NOV2024 (16:22) Source Data: adsl Table Generation: 21NOV2024 (22:30) (Database snapshot date : 01NOV2024) Output File: ./nda2_ubped2/C4591048_E_CSR_Safety/adsl_s005_demo_p2_2

Prior, Concomitant, and Post-Intervention Therapy

One participant (0.3%) in the BNT162b2 (Omi XBB.1.5) 10-µg group received a non-study vaccine after study vaccination (Influenza vaccine). No participants received prohibited medications.

Exposure to BNT162b2 (Omi XBB.1.5)

All 310 assigned participants received BNT162b2 (Omi XBB.1.5) at the 10 µg dose level.

Reactogenicity

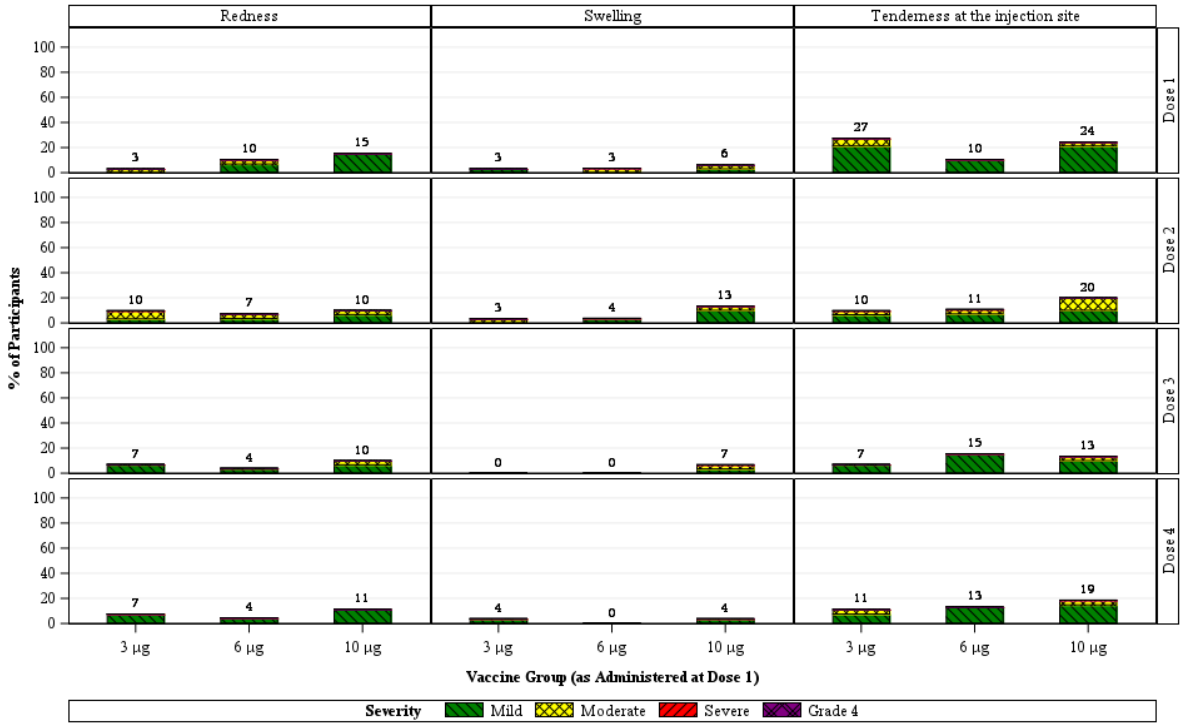
Substudy A

Local reactions

Phase 1

Participants 6 Months Through <2 Years of Age

Figure 4. Local Reactions, by Maximum Severity, Within 7 Days After Each Dose - Substudy A - Phase 1 - 6 Months to <2 Years of Age - Safety Population

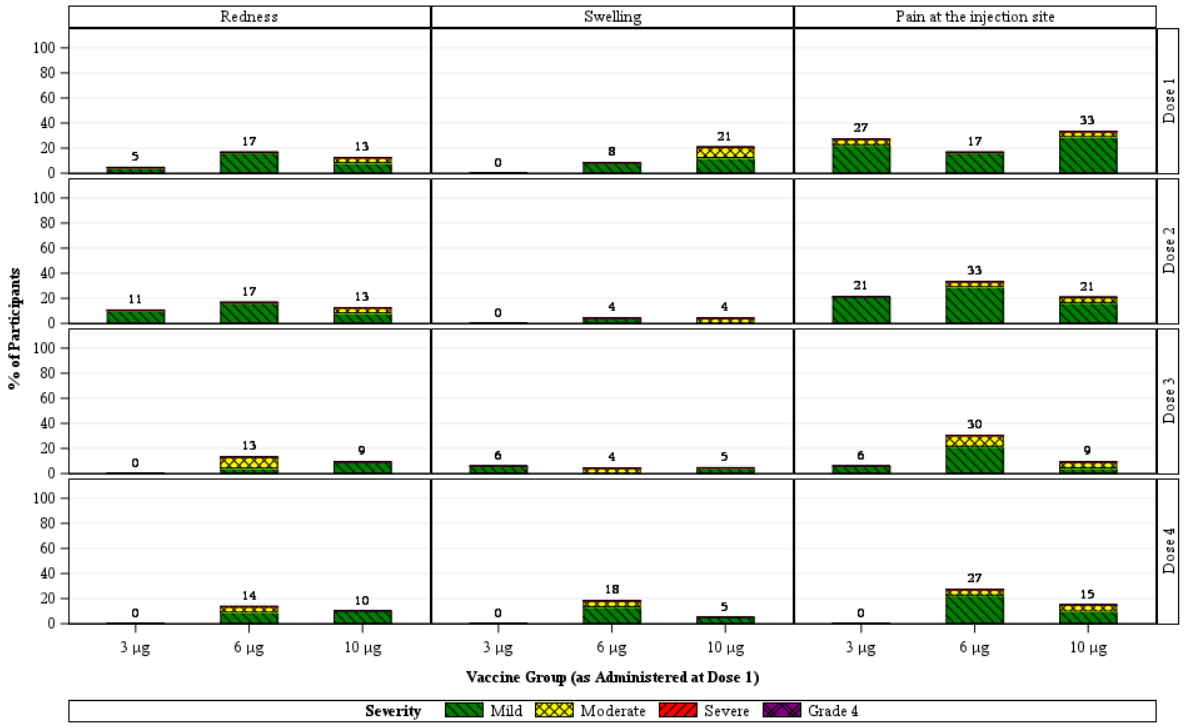


Note: The number above each bar denotes the percentage of participants reporting the reaction with any severity.
All participants received BNT162b2 (Omi XBB.1.5) at the specified dose level at dose 4 except 2 participants who received Bivalent BNT162b2 (Original/Omi BA.4 /BA.5) 3 µg.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adfacevd
Table Generation: 26SEP2025 (10:26) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adce_f001_lr_p1_2

All events after each dose (Doses 1 through 4) were mild or-to-moderate in severity. No Severe or Grade 4 local reactions were reported. The median onset for local reactions was typically within 1 to 2 days post-vaccination, with resolution usually within 1 to 3 days.

Individuals 2 Through <5 Years of Age

Figure 5. Local Reactions, by Maximum Severity, Within 7 Days After Each Dose - Substudy A - Phase 1 - 2 to <5 Years of Age - Safety Population



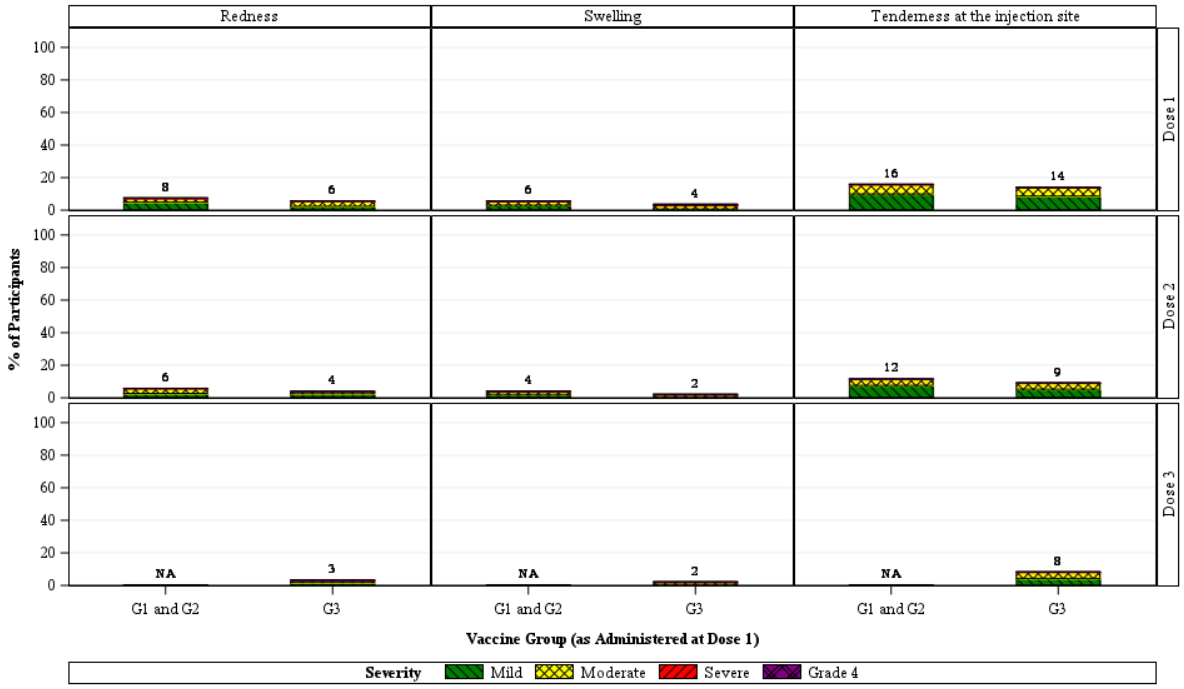
Note: The number above each bar denotes the percentage of participants reporting the reaction with any severity.
All participants received BNT162b2 (Omi XBB.1.5) at the specified dose level at dose 4.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adfacevd
Table Generation: 26SEP2025 (10:26) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adce_f001_lr_p1_5

Most events were mild or-to-moderate in severity. No Grade 4 reactions were reported. The median onset for local reactions was typically within 1 to 2 days post-vaccination, with resolution usually within 1 to 4 days.

Phase 2/3

Participants 6 Months Through <2 Years of Age (Group 1 – 3)

Figure 6. Local Reactions, by Maximum Severity, Within 7 Days After Each Dose - Substudy A - Phase 2/3 - 6 Months to <2 Years of Age - Safety Population

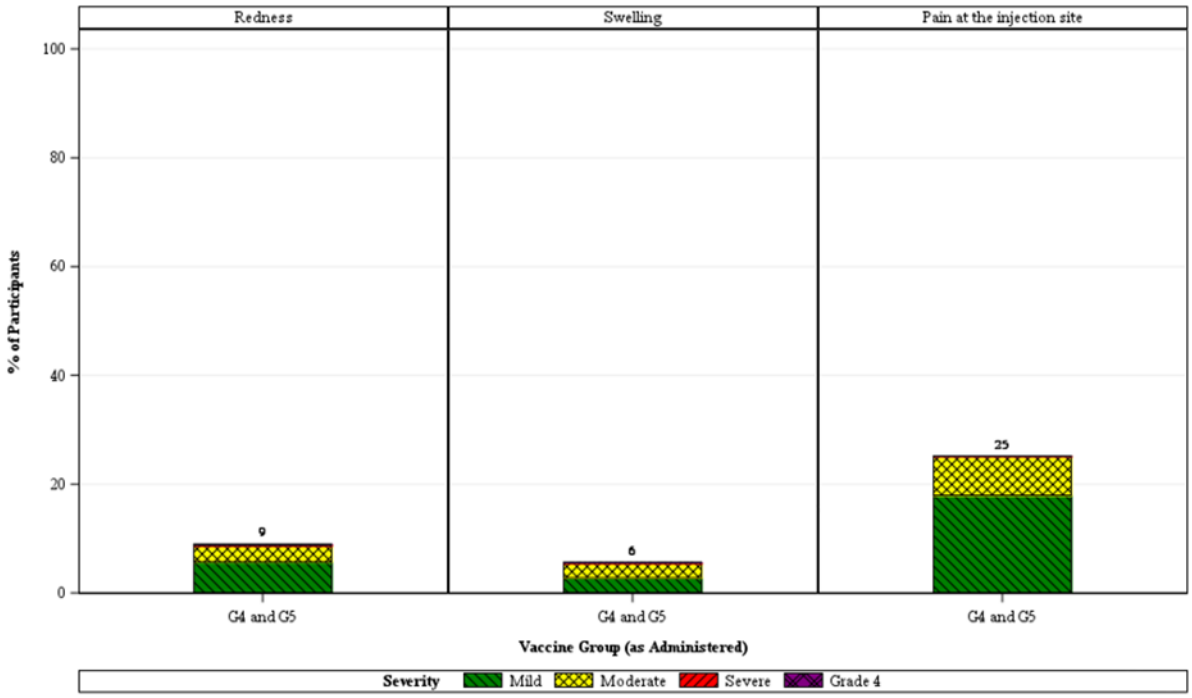


Abbreviation: NA = not applicable.
Note: The number above each bar denotes the percentage of participants reporting the reaction with any severity.
Note: Participants enrolled in Group 1 and Group 2 were planned to receive a 2-dose series of BNT162b2 (Omi XBB.1.5) at 10 µg on a 0- and 8-week schedule. Participants enrolled in Group 3 were planned to receive a 3-dose series of BNT162b2 (Omi XBB.1.5) at 3 µg on a 0-, 3-, and 11-week schedule.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adfacevd
Table Generation: 18SEP2025 (22:11) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adce_f001_lr_p2_2

The median onset for local reactions was 1-2 days, with most reactions resolving within 1 day. Most reactions were mild or moderate in severity. Severe reactions were rare, and no Grade 4 reactions were reported.

Individuals 2 Through <5 Years of Age (Group 4 – 5)

Figure 7. Local Reactions, by Maximum Severity, Within 7 Days After the Study Vaccination - Substudy A - Phase 2/3 – 2 to <5 Years of Age - Safety Population



Note: The number above each bar denotes the percentage of participants reporting the reaction with any severity.
Note: Participants enrolled in Group 4 and Group 5 were planned to receive a single dose of BNT162b2 (Omi XBB.1.5) at 10 µg.
Note: One participant of 2 to <5 years of age who was randomized into Group 3 in error and received Omi XBB.1.5 at 3 µg is also included.
Note: One participant of 2 to <5 years of age who was randomized into Group 1 in error and received 2 doses of Omi XBB.1.5 at 10 µg is also included.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adfacevd
Table Generation: 18SEP2025 (22:11) (Snapshot Date: 25AUG2025) Output File: /nda2_ubped2/C4591048_A_CSR/adce_f001_lr_p2_5

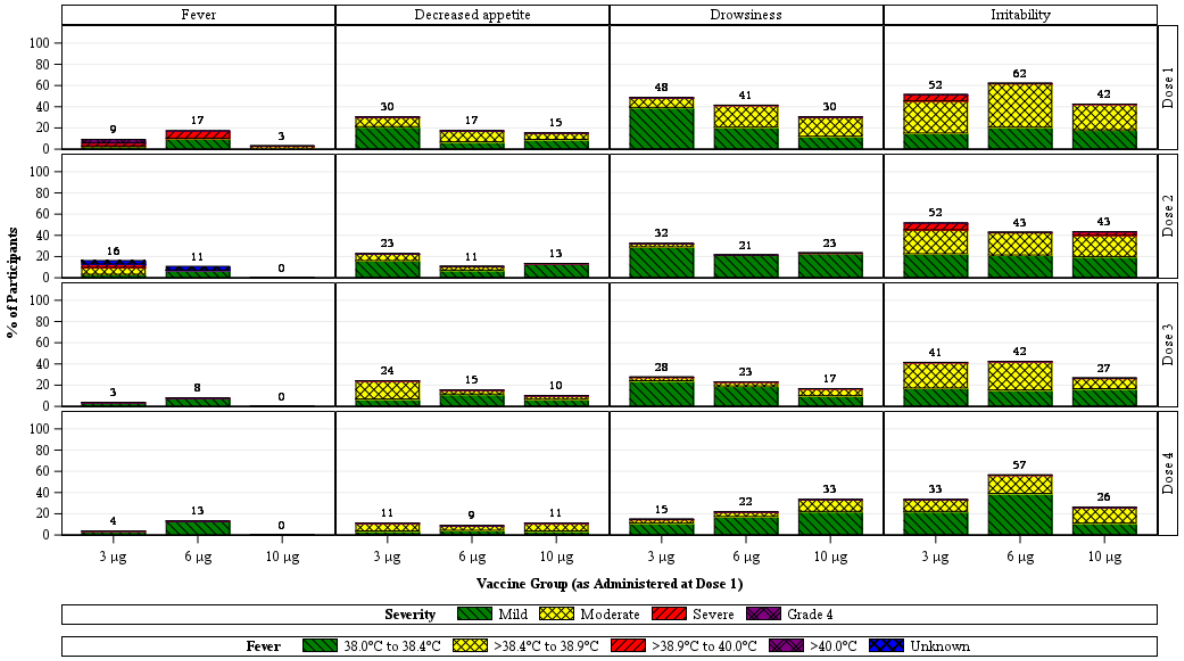
The median onset for local reactions was 1-2 days, with resolution typically within 1 day. Most reactions were mild or moderate in severity. Severe reactions were reported in <1%, and no Grade 4 reactions were reported.

Systemic events

Phase 1

Participants 6 Months Through <2 Years of Age

Figure 8. Systemic Events, by Maximum Severity, Within 7 Days After Each Dose - Substudy A - Phase 1 - 6 Months to <2 Years of Age - Safety Population



Note: The number above each bar denotes the percentage of participants reporting the event with any severity.
All participants received BNT162b2 (Omi XBB.1.5) at the specified dose level at dose 4 except 2 participants who received Bivalent BNT162b2 (Original/Omi BA.4 /BA.5) 3 µg.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adfacevd
Table Generation: 26SEP2025 (10:26) (Snapshot Date: 25AUG2025) Output File: /nda2_ubped2/C4591048_A_CSR/adce_f001_se_p1_2

Across the 3 dose groups, fevers ≥38.0°C were reported by 1 to 7 participants (3.0 to 21.2%) as follows:

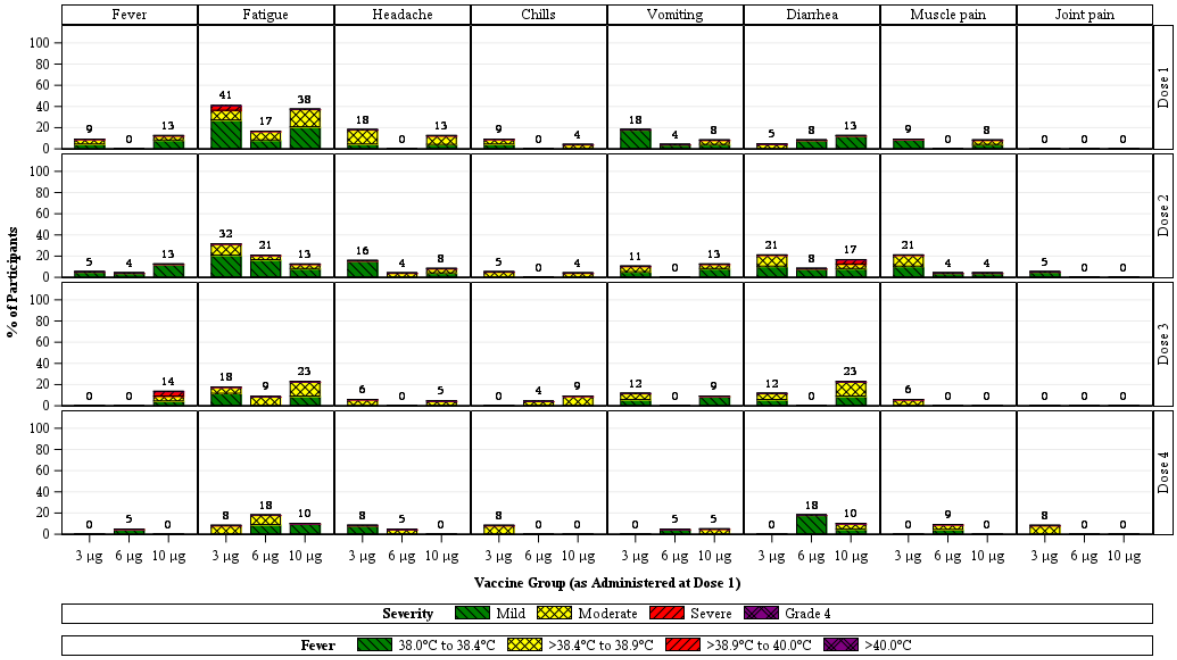
- In the 3 µg group, 2 (6.1%) participants reported a fever of >38.9°C to 40°C. In addition, 1 (3.0%) participant in the 3 µg group reported a fever >40.0°C.
- In the 6 µg group, 2 (6.9%) participants reported a fever of >38.9°C to 40°C. No participant in the 10 µg group reported a fever of >38.9°C.

Antipyretic or pain medication use was reported by 45.5% to 54.5% of participants after any dose of study vaccination across all 3 dose groups. In all 3 dose groups, most systemic events were mild or moderate in severity.

Across the dose groups, median onset for all systemic events ranged from 1.0 to 5.0 days after any dose and resolved with a median duration of 1.0 to 6.0 days.

Individuals 2 Through <5 Years of Age

Figure 9. Systemic Events, by Maximum Severity, Within 7 Days After Each Dose -Substudy A - Phase 1 - 2 to <5 Years of Age - Safety Population



Note: The number above each bar denotes the percentage of participants reporting the event with any severity.
All participants received BNT162b2 (Omi XBB.1.5) at the specified dose level at dose 4.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adfacevd
Table Generation: 26SEP2025 (10:26) (Snapshot Date: 25AUG2025) Output File: /nda2_ubped2/C4591048_A_CSR/adce_f001_se_p1_5

In the 10-µg group, 1 participant (4.2%) reported a fever of >38.9°C to 40°C.

Antipyretic or pain medication use was reported by 22.7% to 33.3% of participants after any dose of study vaccination across all three dose groups. In all three dose groups, most systemic events were mild or moderate in severity.

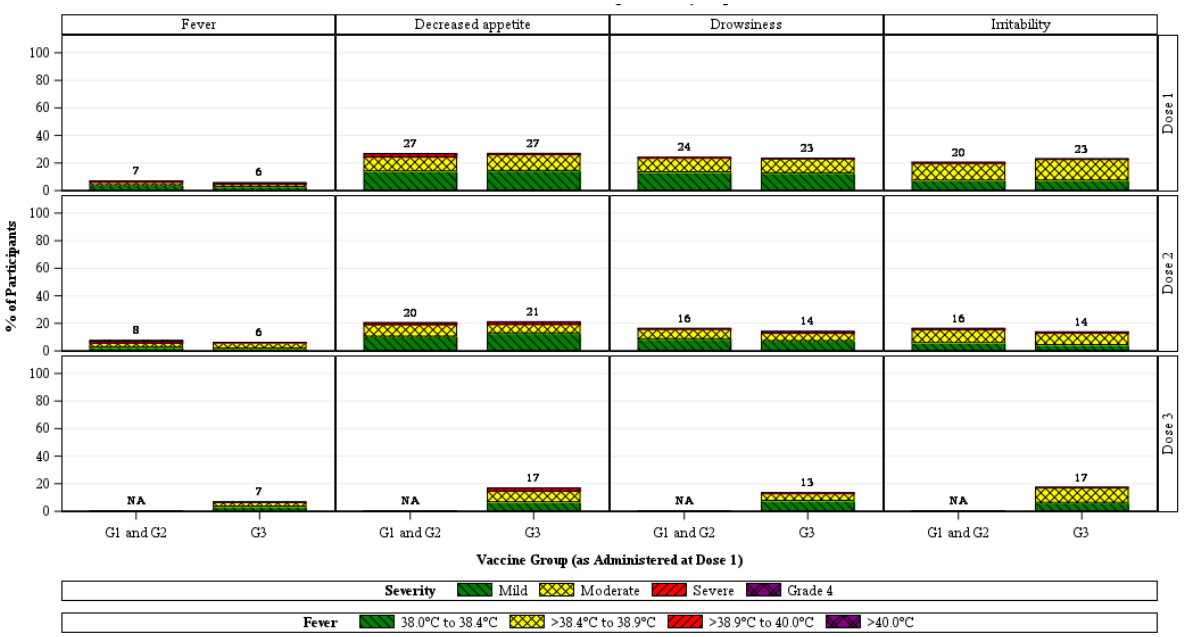
One participant (4.5%) in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 3-µg group, reported severe fatigue after any dose of study vaccine. One participant (4.2%) in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 10 µg group reported severe diarrhoea after any dose of study vaccine. No Grade 4 reactions were reported.

Across the dose groups, median onset for all systemic events ranged from 1.0 to 7.0 days after any dose and resolved with a median duration of 1.0 to 8.0 days.

Phase 2/3

Participants 6 Months Through <2 Years of Age (Group 1 – 3)

Figure 10. Systemic Events, by Maximum Severity, Within 7 Days After Each Dose - Substudy A - Phase 2/3 - 6 Months to <2 Years of Age - Safety Population



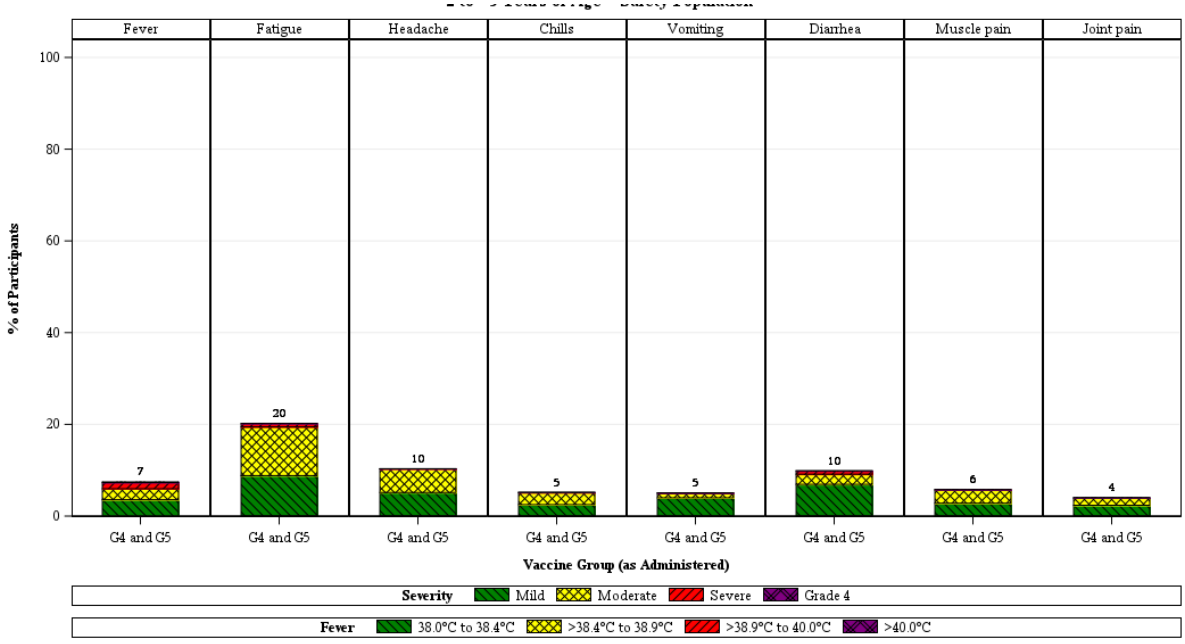
Abbreviation: NA = not applicable.
Note: The number above each bar denotes the percentage of participants reporting the event with any severity.
Note: Participants enrolled in Group 1 and Group 2 were planned to receive a 2-dose series of BNT162b2 (Omi XBB.1.5) at 10 µg on a 0- and 8-week schedule. Participants enrolled in Group 3 were planned to receive a 3-dose series of BNT162b2 (Omi XBB.1.5) at 3 µg on a 0-, 3-, and 11-week schedule.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adfacevd
Table Generation: 18SEP2025 (22:11) (Snapshot Date: 25AUG2025) Output File: /nda2_ubped2/C4591048_A_CSR/adce_f001_se_p2_2

In group 1 and 2, most systemic events were mild or moderate in severity. Any systemic event was reported in 55.8% of participants in the 10-µg groups. Decreased appetite was the most frequently reported systemic event after any dose, occurring in 35.6% of participants in the 10-µg groups. After any dose, drowsiness (31.3%), irritability (26.5%), and fever (12.3%) were also frequently reported. Severe events were uncommon (≤3.3%). No Grade 4 events were reported. Use of antipyretic or pain medication was reported in 21.4% of participants.

In group 3, most systemic events were mild or moderate in severity. Any systemic event was reported in 55.8%. Decreased appetite was the most frequently reported systemic event, occurring in 41.9% of participants in the 3-µg group. After any dose, drowsiness (32.3%), irritability (31.0%), and fever (15.2%) were also frequently reported. Severe events were uncommon (≤4.3%). Grade 4 fever (>40°C) was rare (0.3%). Use of antipyretic or pain medication was reported in 36.0% of participants.

Individuals 2 Through <5 Years of Age (Group 4 – 5)

Figure 11. Systemic Events, by Maximum Severity, Within 7 Days After the Study Vaccination - Substudy A - Phase 2/3 - 2 to <5 Years of Age - Safety Population



Note: The number above each bar denotes the percentage of participants reporting the event with any severity.
Note: Participants enrolled in Group 4 and Group 5 were planned to receive a single dose of BNT162b2 (Omi XBB.1.5) at 10 µg.
Note: One participant of 2 to <5 years of age who was randomized into Group 3 in error and received Omi XBB.1.5 at 3 µg is also included.
Note: One participant of 2 to <5 years of age who was randomized into Group 1 in error and received 2 doses of Omi XBB.1.5 at 10 µg is also included.
PFIZER CONFIDENTIAL SDTM Creation: 27AUG2025 (17:39) Source Data: adfacevd
Table Generation: 18SEP2025 (22:11) (Snapshot Date: 25AUG2025) Output File: /nda2_ubped2/C4591048_A_CSR/adce_f001_se_p2_5

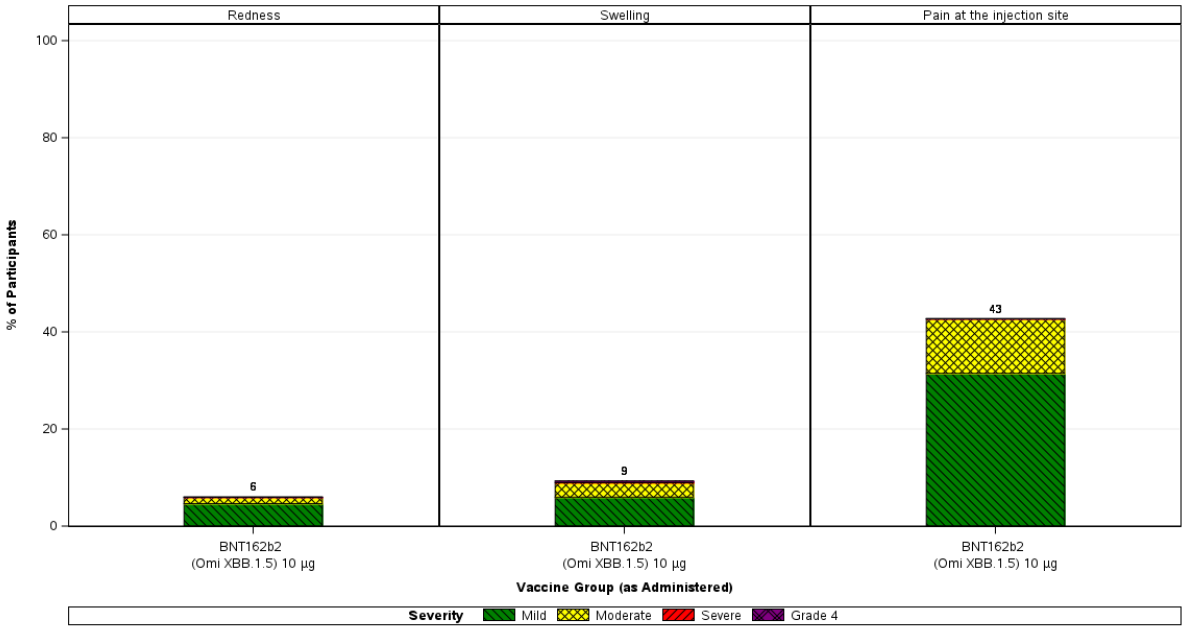
Most systemic events were mild or moderate in severity. Use of antipyretic or pain medication was reported in 14.4% of participants. The median onset for systemic events ranged from 1 to 4 days post-Dose 4, with most events resolving within 1 to 2 days.

Use of antipyretic or pain medication was reported in 14.4% of participants.

Substudy E

Local reactions

Figure 12. Local Reactions, by Maximum Severity, Within 7 Days After the Study Vaccination – Substudy E - Safety Population

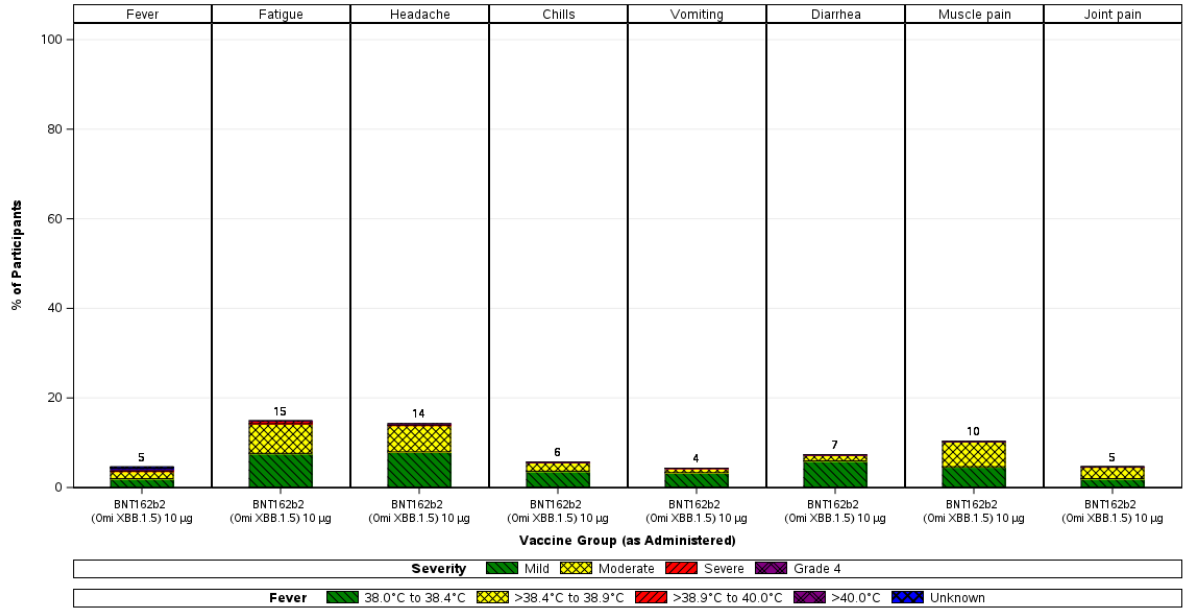


Note: The number above each bar denotes the percentage of participants reporting the reaction with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 04NOV2024 (16:22) Source Data: adfacevd
Table Generation: 12NOV2024 (03:02) (Snapshot Date: 01NOV2024) Output File: ./nda2_ubped2/C4591048_E_CSR_Safety/adce_f001_lr_p2_2

Most local reactions were mild or moderate in severity. Severe swelling was reported in 1 participant (0.3%) within 7 days after study vaccination, with the severe event on Day 2 reduced to moderate by Day 4. No Grade 4 local reactions were reported. The median onset for all local reactions was 1 to 2 days after study vaccination, and all events resolved within a median duration of 1 to 1.5 days after onset.

Systemic events

Figure 13. Systemic Events, by Maximum Severity, Within 7 Days After the Study Vaccination – Substudy E - Safety Population



Note: Severity was not collected for use of antipyretic or pain medication.
Note: The number above each bar denotes the percentage of participants reporting the event with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 04NOV2024 (16:22) Source Data: adfacevd
Table Generation: 12NOV2024 (03:02) (Snapshot Date: 01NOV2024) Output File: ./nda2_ubped2/C4591048_E_CSR_Safety/adce_f001_se_p2_2

Most systemic events were mild or moderate in severity. Severe fever (>40°C) was reported in 1 participant, severe fatigue in 2 participants, and severe headache in 1 participant. No Grade 4 systemic events were reported.

The median onset for all systemic events was 2 to 5 days after study vaccination, and all events resolved within a median duration of 1 to 2 days after onset. Antipyretics was used by 13% of the participants.

Adverse events

Substudy A

Phase 1

Participants 6 Months through <2 Years of Age

Table 43: Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 3 - Substudy A - Phase 1 - 6 Months to <2 Years of Age - Safety Population

	Vaccine Group (as Administered at Dose 1)					
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)					
	3 µg (N[a]=33)		6 µg (N[a]=29)		10 µg (N[a]=33)	
Adverse Event	**n[b] (%)**	**95% CI[c]**	**n[b] (%)**	**95% CI[c]**	**n[b] (%)**	**95% CI[c]**
Any adverse event	14 (42.4)	(25.5, 60.8)	10 (34.5)	(17.9, 54.3)	9 (27.3)	(13.3, 45.5)
Related[d]	2 (6.1)	(0.7, 20.2)	1 (3.4)	(0.1, 17.8)	1 (3.0)	(0.1, 15.8)
Severe	2 (6.1)	(0.7, 20.2)	0	(0.0, 11.9)	0	(0.0, 10.6)
Life-threatening	0	(0.0, 10.6)	0	(0.0, 11.9)	0	(0.0, 10.6)
Any serious adverse event	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)
Related[d]	0	(0.0, 10.6)	0	(0.0, 11.9)	0	(0.0, 10.6)
Severe	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)
Life-threatening	0	(0.0, 10.6)	0	(0.0, 11.9)	0	(0.0, 10.6)
Any nonserious adverse event	13 (39.4)	(22.9, 57.9)	10 (34.5)	(17.9, 54.3)	9 (27.3)	(13.3, 45.5)
Related[d]	2 (6.1)	(0.7, 20.2)	1 (3.4)	(0.1, 17.8)	1 (3.0)	(0.1, 15.8)
Severe	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)
Life-threatening	0	(0.0, 10.6)	0	(0.0, 11.9)	0	(0.0, 10.6)
Any adverse event leading to withdrawal	0	(0.0, 10.6)	0	(0.0, 11.9)	0	(0.0, 10.6)
Related[d]	0	(0.0, 10.6)	0	(0.0, 11.9)	0	(0.0, 10.6)
Serious	0	(0.0, 10.6)	0	(0.0, 11.9)	0	(0.0, 10.6)
Severe	0	(0.0, 10.6)	0	(0.0, 11.9)	0	(0.0, 10.6)
Life-threatening	0	(0.0, 10.6)	0	(0.0, 11.9)	0	(0.0, 10.6)
Death	0	(0.0, 10.6)	0	(0.0, 11.9)	0	(0.0, 10.6)

	Vaccine Group (as Administered at Dose 1)					
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)					
	3 µg (N[a]=33)		6 µg (N[a]=29)		10 µg (N[a]=33)	
Adverse Event	**n[b] (%)**	**95% CI[c]**	**n[b] (%)**	**95% CI[c]**	**n[b] (%)**	**95% CI[c]**

Note: One participant who received Dose 1, Dose 3, and Dose 4 at 6 µg, and Dose 2 at 3 µg was included in the 6 µg vaccine group.
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 event category. For "any adverse event," n = the number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI, based on the Clopper and Pearson method.
d. Assessed by the investigator as related to study intervention.
PFIZER CONFIDENTIAL SDTM Creation: 18SEP2025 (01:23) Source Data: adae Table Generation: 26SEP2025 (02:04) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adae_s130_1md3_p1_2

From Dose 4 Through 1-Month Post-Dose 4

Across all dose groups, AEs from Dose 4 through 1 month post–Dose 4. Any AE was reported in 3.7% of participants in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 3-µg group; no AEs were reported in the 6-µg or 10-µg groups. No related, severe, serious, life-threatening events, deaths, or withdrawals due to AEs occurred in any group.

From Dose 1 Through 6 Months After the Last Dose

Across all dose groups, AEs from study Dose 1 through 6 months after the last dose were mostly nonserious. The AE rates observed were 48.5% in the 3-µg, 37.9% in the 6 µg and 30.3% in the 10 µg groups. Related adverse events occurred infrequently across all groups (Range: 3.0%–6.1%). No life-threatening events, deaths, or withdrawals due to adverse events were reported in any dose group.

Participants 2 through <5 Years of Age

Table 44: Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 3 - Substudy A - Phase 1 - 2 to <5 Years of Age - Safety Population

	Vaccine Group (as Administered at Dose 1)					
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)					
	3 µg (N[a]=23)		6 µg (N[a]=24)		10 µg (N[a]=24)	
Adverse Event	**n[b] (%)**	**95% CI[c]**	**n[b] (%)**	**95% CI[c]**	**n[b] (%)**	**95% CI[c]**
Any adverse event	4 (17.4)	(5.0, 38.8)	11 (45.8)	(25.6, 67.2)	6 (25.0)	(9.8, 46.7)
Related[d]	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)
Severe	1 (4.3)	(0.1, 21.9)	0	(0.0, 14.2)	2 (8.3)	(1.0, 27.0)
Life-threatening	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)

	Vaccine Group (as Administered at Dose 1)					
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)					
	3 µg (N[a]=23)		6 µg (N[a]=24)		10 µg (N[a]=24)	
Adverse Event	**n[b] (%)**	**95% CI[c]**	**n[b] (%)**	**95% CI[c]**	**n[b] (%)**	**95% CI[c]**
Any serious adverse event	1 (4.3)	(0.1, 21.9)	0	(0.0, 14.2)	1 (4.2)	(0.1, 21.1)
Related[d]	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)
Severe	1 (4.3)	(0.1, 21.9)	0	(0.0, 14.2)	1 (4.2)	(0.1, 21.1)
Life-threatening	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)
Any nonserious adverse event	4 (17.4)	(5.0, 38.8)	11 (45.8)	(25.6, 67.2)	6 (25.0)	(9.8, 46.7)
Related[d]	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)
Severe	0	(0.0, 14.8)	0	(0.0, 14.2)	1 (4.2)	(0.1, 21.1)
Life-threatening	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)
Any adverse event leading to withdrawal	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)
Related[d]	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)
Serious	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)
Severe	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)
Life-threatening	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)
Death	0	(0.0, 14.8)	0	(0.0, 14.2)	0	(0.0, 14.2)

Note: One participant who received Dose 1, Dose 2, and Dose 3 at 6 µg, and Dose 4 at 10 µg was included in the 6 µg vaccine group.
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 event category. For "any adverse event," n = the number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI, based on the Clopper and Pearson method.
d. Assessed by the investigator as related to study intervention.
PFIZER CONFIDENTIAL SDTM Creation: 18SEP2025 (01:23) Source Data: adae Table Generation: 26SEP2025 (02:04) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adae_s130_1md3_p1_5

From Dose 4 Through 1-Month Post-Dose 4

Across all dose groups, AEs from Dose 4 through 1 month post–Dose 4 were infrequent and nonserious. Any AE was reported in 4.8% of participants in the 10-µg group; no AEs were reported in

the 3-µg or 6-µg groups. No related, severe, serious, life-threatening events, deaths, or withdrawals due to AEs occurred in any group.

Through 6 Months After the Last Dose

Across all dose groups, AEs from study Dose 1 through 6 months after the last dose were mostly nonserious. The AE rates observed were 17.4% in the 3-µg, 45.8% in the 6 µg and 25% in the 10 µg groups. No related adverse events were reported in any group. No life-threatening events, deaths, or withdrawals due to adverse events were reported in any dose group.

Phase 2/3

Participants 6 Months through <2 Years of Age (Group 1 – 3)

Table 45: Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After the Last Dose - Substudy A - Phase 2/3 - 6 Months to <2 Years of Age - Safety Population

	Vaccine Group (as Administered at Dose 1) BNT162b2 (Omi XBB.1.5)			
	10 µg (Group 1 and Group 2) (N[a]=604)		3 µg (Group 3) (N[a]=304)	
Adverse Event	**n[b] (%)**	**95% CI[c]**	**n[b] (%)**	**95% CI[c]**
Any adverse event	72 (11.9)	(9.4, 14.8)	36 (11.8)	(8.4, 16.0)
Related[d]	3 (0.5)	(0.1, 1.4)	2 (0.7)	(0.1, 2.4)
Severe	11 (1.8)	(0.9, 3.2)	8 (2.6)	(1.1, 5.1)
Life-threatening	2 (0.3)	(0.0, 1.2)	0	(0.0, 1.2)
Any serious adverse event	14 (2.3)	(1.3, 3.9)	9 (3.0)	(1.4, 5.5)
Related[d]	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Severe	9 (1.5)	(0.7, 2.8)	7 (2.3)	(0.9, 4.7)
Life-threatening	2 (0.3)	(0.0, 1.2)	0	(0.0, 1.2)
Any nonserious adverse event	61 (10.1)	(7.8, 12.8)	30 (9.9)	(6.8, 13.8)
Related[d]	2 (0.3)	(0.0, 1.2)	2 (0.7)	(0.1, 2.4)
Severe	2 (0.3)	(0.0, 1.2)	2 (0.7)	(0.1, 2.4)
Life-threatening	0	(0.0, 0.6)	0	(0.0, 1.2)
Any adverse event leading to withdrawal	4 (0.7)	(0.2, 1.7)	0	(0.0, 1.2)

	Vaccine Group (as Administered at Dose 1) BNT162b2 (Omi XBB.1.5)			
	10 µg (Group 1 and Group 2) (N[a]=604)		3 µg (Group 3) (N[a]=304)	
Adverse Event	**n[b] (%)**	**95% CI[c]**	**n[b] (%)**	**95% CI[c]**
Related[d]	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Serious	3 (0.5)	(0.1, 1.4)	0	(0.0, 1.2)
Severe	2 (0.3)	(0.0, 1.2)	0	(0.0, 1.2)
Life-threatening	2 (0.3)	(0.0, 1.2)	0	(0.0, 1.2)
Death	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)

Note: Participants enrolled in Group 1 and Group 2 were planned to receive a 2-dose series of BNT162b2 (Omi XBB.1.5) at 10 µg on a 0- and 8-week schedule. Participants enrolled in Group 3 were planned to receive a 3-dose series of BNT162b2 (Omi XBB.1.5) at 3 µg on a 0-, 3-, and 11-week schedule.
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 event category. For "any adverse event," n = the number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI, based on the Clopper and Pearson method.
d. Assessed by the investigator as related to study intervention.
PFIZER CONFIDENTIAL SDTM Creation: 18SEP2025 (01:23) Source Data: adae Table Generation: 21SEP2025 (23:14) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adae_s130_1md_p2_2

Dose 1 to 6 Months After the Last Dose

From Dose 1 to 6 months after the last dose any AE was reported in 94 participants (15.6%) in the BNT162b2 (Omi XBB.1.5) 10-µg groups and in 48 participants (15.8%) in the 3-µg group. Related (≤0.7%), severe (3.3%), and life-threatening AEs (≤0.5%) were rare and are discussed in relevant sections below.

Participants 2 through <5 Years of Age (Group 4 – 5)

Table 46: Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After the Study Vaccination - Substudy A - Phase 2/3 - 2 to <5 Years of Age - Safety Population

	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (Group 4 and Group 5) (N[a]=688)	
Adverse Event	**n[b] (%)**	**95% CI[c]**
Any adverse event	25 (3.6)	(2.4, 5.3)

Adverse Event	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (Group 4 and Group 5) (N[a]=688) n[b] (%)	95% CI[c]
Related[d]	0	(0.0, 0.5)
Severe	1 (0.1)	(0.0, 0.8)
Life-threatening	0	(0.0, 0.5)
Any serious adverse event	1 (0.1)	(0.0, 0.8)
Related[d]	0	(0.0, 0.5)
Severe	1 (0.1)	(0.0, 0.8)
Life-threatening	0	(0.0, 0.5)
Any nonserious adverse event	25 (3.6)	(2.4, 5.3)
Related[d]	0	(0.0, 0.5)
Severe	0	(0.0, 0.5)
Life-threatening	0	(0.0, 0.5)
Any adverse event leading to withdrawal	0	(0.0, 0.5)
Related[d]	0	(0.0, 0.5)
Serious	0	(0.0, 0.5)
Severe	0	(0.0, 0.5)
Life-threatening	0	(0.0, 0.5)
Death	0	(0.0, 0.5)

Note: Participants enrolled in Group 4 and Group 5 were planned to receive a single dose of BNT162b2 (Omi XBB.1.5) at 10 µg.
Note: One participant of 2 to <5 years of age who was randomised into Group 3 in error and received Omi XBB.1.5 at 3 µg is also included.
Note: One participant of 2 to <5 years of age who was randomised into Group 1 in error and received 2 doses of Omi XBB.1.5 at 10 µg is also included.
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 event category. For "any adverse event," n = the number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided CI, based on the Clopper and Pearson method.
d. Assessed by the investigator as related to study intervention.
PFIZER CONFIDENTIAL SDTM Creation: 18SEP2025 (01:23) Source Data: adae Table Generation: 21SEP2025 (23:14) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adae_s130_1md_p2_5

Through 6 Months After Study Vaccination

From study vaccination through 6 months after, 56 participants (8.1%) reported at least one AE. Most of these events were nonserious and included common childhood illnesses. No AEs were assessed as related to vaccination. The incidence of severe AEs (0.7%), life-threatening AEs (0.4%), and SAEs (1.5%) remained low. Two participants (0.3%) experienced AEs leading to withdrawal, including two fatal AEs (0.3%); none were considered related to study intervention.

Analysis of Adverse Events

Phase 1

Participants 6 Months through <2 Years of Age

From Dose 1 Through 1-Month Post-Dose 3

BNT162b2 (original/Omi BA.4/BA.5) 3 µg Group

Fourteen participants (42.4%) reported at least 1 AE from Dose 1 to 1-Month after Dose 3 with the most commonly reported detailed below:

Seven participants (21.2%) reported at least one AE from the SOC of Gastrointestinal disorders, with most reporting vomiting (12.1%), followed by teething, diarrhoea, constipation, and mouth ulceration (3.0% for each)

Six participants (18.2%) reported at least one AE from the SOC of Infections and infestations, with most reporting hand-foot-and-mouth disease (6.1%), followed by ear infection, otitis media, bronchiolitis, and conjunctivitis (3.0% for each).

BNT162b2 (original/Omi BA.4/BA.5) 6 µg Group

Ten AEs (34.5%) were reported, with the most commonly reported detailed below:

- Four participants (13.8%) reported at least one AE from the SOC of Gastrointestinal disorders, with most reporting teething (10.3%), followed by diarrhoea (3.4%)
- Three participants (10.3%) reported at least one AE from the SOC of Infections and infestations, with most reporting ear infection disease (6.9%), followed by otitis media (3.4%).

BNT162b2 (original/Omi BA.4/BA.5) 10 µg Group

Nine AEs (27.3%) were reported, with the most reported detailed below:

- Six participants (18.2%) reported at least one AE from the SOC of Infections and infestations, with most reporting otitis media (6.1%), followed by ear infection, furuncle, gastroenteritis, and respiratory syncytial virus (RSV infection) (3.0% for each).

Table 47: Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 3, by System Organ Class and Preferred Term - Substudy A - Phase 1 - 6 Months to <2 Years of Age - Safety Population

	Vaccine Group (as Administered at Dose 1)					
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)					
	3 µg (N[a]=33)		6 µg (N[a]=29)		10 µg (N[a]=33)	
System Organ Class Preferred Term	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**
Any adverse event	14 (42.4)	(25.5, 60.8)	10 (34.5)	(17.9, 54.3)	9 (27.3)	(13.3, 45.5)
Eye disorders	0	(0.0, 10.6)	0	(0.0, 11.9)	1 (3.0)	(0.1, 15.8)
Dacryostenosis acquired	0	(0.0, 10.6)	0	(0.0, 11.9)	1 (3.0)	(0.1, 15.8)
Gastrointestinal disorders	7 (21.2)	(9.0, 38.9)	4 (13.8)	(3.9, 31.7)	0	(0.0, 10.6)
Teething	1 (3.0)	(0.1, 15.8)	3 (10.3)	(2.2, 27.4)	0	(0.0, 10.6)
Vomiting	4 (12.1)	(3.4, 28.2)	0	(0.0, 11.9)	0	(0.0, 10.6)
Diarrhoea	1 (3.0)	(0.1, 15.8)	1 (3.4)	(0.1, 17.8)	0	(0.0, 10.6)
Constipation	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)
Mouth ulceration	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)
General disorders and administration site conditions	3 (9.1)	(1.9, 24.3)	0	(0.0, 11.9)	1 (3.0)	(0.1, 15.8)
Pyrexia	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	1 (3.0)	(0.1, 15.8)
Injection site induration	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)
Surgical failure	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)
Immune system disorders	2 (6.1)	(0.7, 20.2)	0	(0.0, 11.9)	0	(0.0, 10.6)
Drug hypersensitivity	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)

	Vaccine Group (as Administered at Dose 1)					
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)					
	3 µg (N[a]=33)		6 µg (N[a]=29)		10 µg (N[a]=33)	
System Organ Class Preferred Term	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**
Seasonal allergy	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)
Infections and infestations	6 (18.2)	(7.0, 35.5)	3 (10.3)	(2.2, 27.4)	6 (18.2)	(7.0, 35.5)
Ear infection	1 (3.0)	(0.1, 15.8)	2 (6.9)	(0.8, 22.8)	1 (3.0)	(0.1, 15.8)
Otitis media	1 (3.0)	(0.1, 15.8)	1 (3.4)	(0.1, 17.8)	2 (6.1)	(0.7, 20.2)
Hand-foot-and-mouth disease	2 (6.1)	(0.7, 20.2)	0	(0.0, 11.9)	0	(0.0, 10.6)
Bronchiolitis	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)
Conjunctivitis	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)
Furuncle	0	(0.0, 10.6)	0	(0.0, 11.9)	1 (3.0)	(0.1, 15.8)
Gastroenteritis	0	(0.0, 10.6)	0	(0.0, 11.9)	1 (3.0)	(0.1, 15.8)
Respiratory syncytial virus infection	0	(0.0, 10.6)	0	(0.0, 11.9)	1 (3.0)	(0.1, 15.8)
Reproductive system and breast disorders	1 (3.0)	(0.1, 15.8)	1 (3.4)	(0.1, 17.8)	0	(0.0, 10.6)
Penile adhesion	1 (3.0)	(0.1, 15.8)	1 (3.4)	(0.1, 17.8)	0	(0.0, 10.6)
Respiratory, thoracic and mediastinal disorders	0	(0.0, 10.6)	1 (3.4)	(0.1, 17.8)	0	(0.0, 10.6)
Nasal congestion	0	(0.0, 10.6)	1 (3.4)	(0.1, 17.8)	0	(0.0, 10.6)

	Vaccine Group (as Administered at Dose 1)					
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)					
	3 µg (N[a]=33)		6 µg (N[a]=29)		10 µg (N[a]=33)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Skin and subcutaneous tissue disorders	1 (3.0)	(0.1, 15.8)	2 (6.9)	(0.8, 22.8)	1 (3.0)	(0.1, 15.8)
Eczema	0	(0.0, 10.6)	1 (3.4)	(0.1, 17.8)	0	(0.0, 10.6)
Rash	0	(0.0, 10.6)	0	(0.0, 11.9)	1 (3.0)	(0.1, 15.8)
Urticaria	1 (3.0)	(0.1, 15.8)	0	(0.0, 11.9)	0	(0.0, 10.6)
Urticaria chronic	0	(0.0, 10.6)	1 (3.4)	(0.1, 17.8)	0	(0.0, 10.6)

Note: MedDRA (v28.0) 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 event. For "any adverse 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: 18SEP2025 (01:23) Source Data: adae Table Generation: 26SEP2025 (02:04) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adae_s150_1md3_soc_p1_2

From Dose 4 Through 1-Month Post-Dose 4

One participant (3.7%) reported at least one AE from the SOC of Infections and infestations (conjunctivitis)

From Dose 1 Through 6-Month After the Last Dose

Across all dose groups, nonserious AEs from Dose 4 through 1 month after the last dose was 30.3% for the bivalent BNT162b2 (original/Omi BA.4/BA.5) 10-µg group, 37.9% for the 6-µg group, and 48.5% 3-µg group. Related adverse events occurred infrequently across all groups (range: 3.0%–6.1%). No life-threatening events, deaths, or withdrawals due to adverse events were reported in any dose group.

Participants 2 through <5 Years of Age

From Dose 1 Through 1-Month Post-Dose 3

BNT162b2 (original/Omi BA.4/BA.5) 3 µg Group

Four AEs (17.4%) were reported, with the most reported detailed below:

Two participants (8.7%) reported at least one AE from the SOC of Infections and infestations, with these reported as chronic tonsilitis and pharyngitis streptococcal (4.3% for each).

BNT162b2 (original/Omi BA.4/BA.5) 6 µg Group

Eleven AEs (45.8%) were reported, with the most reported detailed below:

- Five participants (20.8%) reported at least one AE from the SOC of Infections and infestations, with most reporting conjunctivitis (12.5%), followed by impetigo and otitis externa (4.2% for each).
- Four participants (16.7%) reported at least one AE from the SOC of Injury, poisoning, and procedural complications, with most reporting skin laceration (8.3%), followed by arthropod bite, fall, and mouth injury (4.2% for each)
- Three participants (12.5%) reported at least one AE from the SOC of Skin and subcutaneous tissue disorders, with reporting of atopic dermatitis, dry skin, eczema, and pityriasis alba (4.2% for each).

BNT162b2 (original/Omi BA.4/BA.5) 10 µg Group

Six AEs (25.0%) were reported, with the most reported detailed below:

- Two participants (8.3%) reported at least one AE from the SOC of Infections and infestations, with similar reports of fungal skin infection, viral gastroenteritis, tonsillitis, and urinary tract infection (4.2% for each).
- Two participants (8.3%) reported at least one AE from the SOC of Injury, poisoning, and procedural complications, with equal reports of fall, accidental exposure to product, and contusion (4.2% for each).
- Two participants (8.3%) reported at least one AE from the SOC of Skin and subcutaneous tissue disorders, with all reported as diaper dermatitis (8.3%).

Table 48: Number (%) of Participants Reporting at Least 1 Adverse Event from Dose 1 to 1 Month After Dose 3, by System Organ Class and Preferred Term – Substudy A – Phase 1 – 2 to <5 Years of Age – Safety Population

	Vaccine Group (as Administered at Dose 1)					
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)					
	3 µg (N[a]=23)		6 µg (N[a]=24)		10 µg (N[a]=24)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any adverse event	4 (17.4)	(5.0, 38.8)	11 (45.8)	(25.6, 67.2)	6 (25.0)	(9.8, 46.7)
Ear and labyrinth disorders	1 (4.3)	(0.1, 21.9)	0	(0.0, 14.2)	0	(0.0, 14.2)

	Vaccine Group (as Administered at Dose 1)					
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)					
	3 µg (N[a]=23)		6 µg (N[a]=24)		10 µg (N[a]=24)	
System Organ Class Preferred Term	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**
Ear pain	1 (4.3)	(0.1, 21.9)	0	(0.0, 14.2)	0	(0.0, 14.2)
Gastrointestinal disorders	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Constipation	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Infections and infestations	2 (8.7)	(1.1, 28.0)	5 (20.8)	(7.1, 42.2)	2 (8.3)	(1.0, 27.0)
Conjunctivitis	0	(0.0, 14.8)	3 (12.5)	(2.7, 32.4)	0	(0.0, 14.2)
Chronic tonsillitis	1 (4.3)	(0.1, 21.9)	0	(0.0, 14.2)	0	(0.0, 14.2)
Fungal skin infection	0	(0.0, 14.8)	0	(0.0, 14.2)	1 (4.2)	(0.1, 21.1)
Gastroenteritis viral	0	(0.0, 14.8)	0	(0.0, 14.2)	1 (4.2)	(0.1, 21.1)
Impetigo	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Otitis externa	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Pharyngitis streptococcal	1 (4.3)	(0.1, 21.9)	0	(0.0, 14.2)	0	(0.0, 14.2)
Tonsillitis	0	(0.0, 14.8)	0	(0.0, 14.2)	1 (4.2)	(0.1, 21.1)
Urinary tract infection	0	(0.0, 14.8)	0	(0.0, 14.2)	1 (4.2)	(0.1, 21.1)
Injury, poisoning and procedural complications	1 (4.3)	(0.1, 21.9)	4 (16.7)	(4.7, 37.4)	2 (8.3)	(1.0, 27.0)
Fall	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	1 (4.2)	(0.1, 21.1)

	Vaccine Group (as Administered at Dose 1)					
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)					
	3 µg (N[a]=23)		6 µg (N[a]=24)		10 µg (N[a]=24)	
System Organ Class Preferred Term	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**
Skin laceration	0	(0.0, 14.8)	2 (8.3)	(1.0, 27.0)	0	(0.0, 14.2)
Accidental exposure to product	0	(0.0, 14.8)	0	(0.0, 14.2)	1 (4.2)	(0.1, 21.1)
Arthropod bite	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Contusion	0	(0.0, 14.8)	0	(0.0, 14.2)	1 (4.2)	(0.1, 21.1)
Mouth injury	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Skin abrasion	1 (4.3)	(0.1, 21.9)	0	(0.0, 14.2)	0	(0.0, 14.2)
Nervous system disorders	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Speech disorder developmental	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Psychiatric disorders	0	(0.0, 14.8)	2 (8.3)	(1.0, 27.0)	0	(0.0, 14.2)
Behaviour disorder	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Behavioural insomnia of childhood	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Renal and urinary disorders	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Dysuria	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)

	Vaccine Group (as Administered at Dose 1)					
	Bivalent BNT162b2 (Original/Omi BA.4/BA.5)					
	3 µg (N[a]=23)		6 µg (N[a]=24)		10 µg (N[a]=24)	
System Organ Class Preferred Term	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**
Respiratory, thoracic and mediastinal disorders	2 (8.7)	(1.1, 28.0)	0	(0.0, 14.2)	1 (4.2)	(0.1, 21.1)
Asthma	1 (4.3)	(0.1, 21.9)	0	(0.0, 14.2)	0	(0.0, 14.2)
Cough	0	(0.0, 14.8)	0	(0.0, 14.2)	1 (4.2)	(0.1, 21.1)
Rhinorrhoea	1 (4.3)	(0.1, 21.9)	0	(0.0, 14.2)	0	(0.0, 14.2)
Skin and subcutaneous tissue disorders	0	(0.0, 14.8)	3 (12.5)	(2.7, 32.4)	2 (8.3)	(1.0, 27.0)
Dermatitis diaper	0	(0.0, 14.8)	0	(0.0, 14.2)	2 (8.3)	(1.0, 27.0)
Dermatitis atopic	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Dry skin	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Eczema	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)
Pityriasis alba	0	(0.0, 14.8)	1 (4.2)	(0.1, 21.1)	0	(0.0, 14.2)

Note: MedDRA (v28.0) 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 event. For "any adverse 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: 18SEP2025 (01:23) Source Data: adae Table Generation: 26SEP2025 (02:04) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adae_s150_1md3_soc_p1_5

From Dose 4 Through 1-Month Post-Dose 4

One participant (4.8%) reported at least one AE from the SOC of Infections and infestations (otitis media)

From Dose 1 Through 6-Month After the Last Dose

Across all dose groups, nonserious AEs from Dose 4 through 6 months after the last dose was 17.4% for the bivalent BNT162b2 (original/Omi BA.4/BA.5) 3-µg group, 25.0% for the 10-µg group, and 45.8% 6-µg group. Related adverse events occurred infrequently across all groups (range: 3.0%–6.1%). Severe events and SAEs were infrequently reported and are discussed in respectively section below.

No related, life-threatening events, deaths, or withdrawals due to adverse events were reported in any dose group.

Phase 2/3

Participants 6 Months through <2 Years of Age

In both dose groups, from Dose 1 to 1 month after the last dose, most AEs were reported in the Infections and infestations SOC (3-µg: 3 [6.3%]; 10-µg: 4 [6.0%]).

AE rates were generally consistent through 6 months after the last dose and by sex, SARS-CoV-2 status, and exclusion of Site 1163 data. AE rates tended slightly higher in Hispanic/Latino participants compared to non-Hispanic/non-Latino and in White participants compared to other ethnic and racial groups.

Table 49: Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After the Last Dose, by System Organ Class and Preferred Term – Substudy A – Phase 2/3 – 6 Months to <2 Years of Age – Safety Population

	Vaccine Group (as Administered at Dose 1) BNT162b2 (Omi XBB.1.5)			
	10 µg (Group 1 and Group 2) (N[a]=604)		3 µg (Group 3) (N[a]=304)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any adverse event	72 (11.9)	(9.4, 14.8)	36 (11.8)	(8.4, 16.0)
Blood and lymphatic system disorders	2 (0.3)	(0.0, 1.2)	2 (0.7)	(0.1, 2.4)
Anaemia	2 (0.3)	(0.0, 1.2)	1 (0.3)	(0.0, 1.8)
Microcytic anaemia	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Gastrointestinal disorders	8 (1.3)	(0.6, 2.6)	5 (1.6)	(0.5, 3.8)
Diarrhoea	1 (0.2)	(0.0, 0.9)	3 (1.0)	(0.2, 2.9)
Teething	3 (0.5)	(0.1, 1.4)	0	(0.0, 1.2)
Vomiting	1 (0.2)	(0.0, 0.9)	1 (0.3)	(0.0, 1.8)
Abdominal pain upper	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)

	Vaccine Group (as Administered at Dose 1)			
	BNT162b2 (Omi XBB.1.5)			
	10 µg (Group 1 and Group 2) (N[a]=604)		3 µg (Group 3) (N[a]=304)	
System Organ Class Preferred Term	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**
Constipation	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Haematochezia	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Rectal haemorrhage	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
General disorders and administration site conditions	4 (0.7)	(0.2, 1.7)	2 (0.7)	(0.1, 2.4)
Pyrexia	3 (0.5)	(0.1, 1.4)	1 (0.3)	(0.0, 1.8)
Drowning	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Fatigue	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Immune system disorders	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Drug hypersensitivity	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Infections and infestations	36 (6.0)	(4.2, 8.2)	19 (6.3)	(3.8, 9.6)
Gastroenteritis	4 (0.7)	(0.2, 1.7)	3 (1.0)	(0.2, 2.9)
Conjunctivitis	2 (0.3)	(0.0, 1.2)	3 (1.0)	(0.2, 2.9)
Upper respiratory tract infection	4 (0.7)	(0.2, 1.7)	1 (0.3)	(0.0, 1.8)
Impetigo	1 (0.2)	(0.0, 0.9)	3 (1.0)	(0.2, 2.9)
Oral candidiasis	2 (0.3)	(0.0, 1.2)	2 (0.7)	(0.1, 2.4)
Otitis media	2 (0.3)	(0.0, 1.2)	2 (0.7)	(0.1, 2.4)
Scabies	4 (0.7)	(0.2, 1.7)	0	(0.0, 1.2)
Ear infection	2 (0.3)	(0.0, 1.2)	1 (0.3)	(0.0, 1.8)
Bronchiolitis	0	(0.0, 0.6)	2 (0.7)	(0.1, 2.4)

	Vaccine Group (as Administered at Dose 1) BNT162b2 (Omi XBB.1.5)			
	10 µg (Group 1 and Group 2) (N[a]=604)		3 µg (Group 3) (N[a]=304)	
System Organ Class Preferred Term	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**
Hand-foot-and-mouth disease	2 (0.3)	(0.0, 1.2)	0	(0.0, 1.2)
Pneumonia	2 (0.3)	(0.0, 1.2)	0	(0.0, 1.2)
Rhinitis	2 (0.3)	(0.0, 1.2)	0	(0.0, 1.2)
Urinary tract infection	2 (0.3)	(0.0, 1.2)	0	(0.0, 1.2)
Abscess limb	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Body tinea	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Cellulitis	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Cutaneous larva migrans	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Encephalitis	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Erysipelas	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Escherichia urinary tract infection	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Eyelid infection	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Gastroenteritis astroviral	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Gastroenteritis rotavirus	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Infestation	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Lice infestation	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Oral herpes	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Pneumonia necrotising	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)

	Vaccine Group (as Administered at Dose 1)			
	BNT162b2 (Omi XBB.1.5)			
	10 µg (Group 1 and Group 2) (N[a]=604)		3 µg (Group 3) (N[a]=304)	
System Organ Class Preferred Term	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**
Sinusitis	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Subcutaneous abscess	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Tinea capitis	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Tracheobronchitis	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Urosepsis	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Varicella	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Injury, poisoning and procedural complications	5 (0.8)	(0.3, 1.9)	6 (2.0)	(0.7, 4.2)
Fall	4 (0.7)	(0.2, 1.7)	2 (0.7)	(0.1, 2.4)
Craniocerebral injury	2 (0.3)	(0.0, 1.2)	1 (0.3)	(0.0, 1.8)
Thermal burn	0	(0.0, 0.6)	2 (0.7)	(0.1, 2.4)
Burns second degree	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Foreign body aspiration	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Gingival injury	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Road traffic accident	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Skin abrasion	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Traumatic haemorrhage	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Metabolism and nutrition disorders	3 (0.5)	(0.1, 1.4)	0	(0.0, 1.2)
Underweight	3 (0.5)	(0.1, 1.4)	0	(0.0, 1.2)

	Vaccine Group (as Administered at Dose 1)			
	BNT162b2 (Omi XBB.1.5)			
	10 µg (Group 1 and Group 2) (N[a]=604)		3 µg (Group 3) (N[a]=304)	
System Organ Class Preferred Term	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**
Musculoskeletal and connective tissue disorders	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Joint swelling	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Nephroblastoma	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Nervous system disorders	2 (0.3)	(0.0, 1.2)	1 (0.3)	(0.0, 1.8)
Seizure	2 (0.3)	(0.0, 1.2)	0	(0.0, 1.2)
Febrile convulsion	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Renal and urinary disorders	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Dysuria	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Respiratory, thoracic and mediastinal disorders	10 (1.7)	(0.8, 3.0)	3 (1.0)	(0.2, 2.9)
Cough	4 (0.7)	(0.2, 1.7)	1 (0.3)	(0.0, 1.8)
Nasal congestion	2 (0.3)	(0.0, 1.2)	2 (0.7)	(0.1, 2.4)
Nasal obstruction	2 (0.3)	(0.0, 1.2)	0	(0.0, 1.2)
Choking	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Rhinitis allergic	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Skin and subcutaneous tissue disorders	9 (1.5)	(0.7, 2.8)	4 (1.3)	(0.4, 3.3)
Rash	3 (0.5)	(0.1, 1.4)	2 (0.7)	(0.1, 2.4)

	Vaccine Group (as Administered at Dose 1) BNT162b2 (Omi XBB.1.5)			
	10 µg (Group 1 and Group 2) (N[a]=604)		3 µg (Group 3) (N[a]=304)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Dermatitis	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Dermatitis allergic	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Dermatitis contact	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Dry skin	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Eczema	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Rash macular	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Rash morbilliform	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Rash vesicular	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Vascular disorders	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Aortic dilatation	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)

Note: MedDRA (v28.0) coding dictionary applied.
Note: Participants enrolled in Group 1 and Group 2 were planned to receive a 2-dose series of BNT162b2 (Omi XBB.1.5) at 10 µg on a 0- and 8-week schedule. Participants enrolled in Group 3 were planned to receive a 3-dose series of BNT162b2 (Omi XBB.1.5) at 3 µg on a 0-, 3-, and 11-week schedule.
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 event. For "any adverse 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: 18SEP2025 (01:23) Source Data: adae Table Generation: 18SEP2025 (01:50) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adae_s150_1md_soc_p2_2

Participants 2 through <5 Years of Age

Overall, 25 participants (3.6%) in the BNT162b2 (Omi XBB.1.5) 10-µg group (Groups 4 and 5) reported at least one AE from study vaccination through 1 month after the study vaccination. The most frequently reported AEs fell under the SOC Respiratory, thoracic and mediastinal disorders (7 [1.0%]).

The most common PTs included diarrhoea (3 [0.4%]) and cough (3 [0.4%]), Most events were mild or moderate in severity.

AE rates were generally consistent by sex, race, ethnicity, SARS-CoV-2 status, and exclusion of Site 1163 data.

Dose 1 to 6 Months After Study Vaccination

From Dose 1 to 6 months after study vaccination, any AE was reported in 56 participants (8.1%) in the BNT162b2 (Omi XBB.1.5) 10-µg group. Severe (0.7%) and life-threatening AEs (0.4%) were rare and are discussed in respectively section below. No related AEs were reported from Dose 1 to 6 months after study vaccination.

Table 50: Number (%) of Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After the Study Vaccination, by System Organ Class and Preferred Term – Substudy A – Phase 2/3 – 2 to <5 Years of Age – Safety Population

	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (Group 4 and Group 5) (N[a]=688)	
System Organ Class Preferred Term	**n[b] (%)**	**(95% CI[c])**
Any adverse event	25 (3.6)	(2.4, 5.3)
Gastrointestinal disorders	6 (0.9)	(0.3, 1.9)
Diarrhoea	3 (0.4)	(0.1, 1.3)
Mouth ulceration	2 (0.3)	(0.0, 1.0)
Vomiting	1 (0.1)	(0.0, 0.8)
Infections and infestations	6 (0.9)	(0.3, 1.9)
Body tinea	1 (0.1)	(0.0, 0.8)
Bronchiolitis	1 (0.1)	(0.0, 0.8)
Conjunctivitis	1 (0.1)	(0.0, 0.8)
Otitis media	1 (0.1)	(0.0, 0.8)
Rhinitis	1 (0.1)	(0.0, 0.8)
Urinary tract infection	1 (0.1)	(0.0, 0.8)
Injury, poisoning and procedural complications	1 (0.1)	(0.0, 0.8)
Thermal burn	1 (0.1)	(0.0, 0.8)
Metabolism and nutrition disorders	1 (0.1)	(0.0, 0.8)
Underweight	1 (0.1)	(0.0, 0.8)
Musculoskeletal and connective tissue disorders	1 (0.1)	(0.0, 0.8)
Muscle spasms	1 (0.1)	(0.0, 0.8)

System Organ Class Preferred Term	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (Group 4 and Group 5) (N[a]=688) n[b] (%)	(95% CI[c])
Respiratory, thoracic and mediastinal disorders	7 (1.0)	(0.4, 2.1)
Cough	3 (0.4)	(0.1, 1.3)
Nasal congestion	2 (0.3)	(0.0, 1.0)
Asthma	1 (0.1)	(0.0, 0.8)
Epistaxis	1 (0.1)	(0.0, 0.8)
Skin and subcutaneous tissue disorders	6 (0.9)	(0.3, 1.9)
Dermatitis	2 (0.3)	(0.0, 1.0)
Rash	2 (0.3)	(0.0, 1.0)
Rash maculo-papular	1 (0.1)	(0.0, 0.8)
Rash papular	1 (0.1)	(0.0, 0.8)

Note: MedDRA (v28.0) coding dictionary applied.
Note: Participants enrolled in Group 4 and Group 5 were planned to receive a single dose of BNT162b2 (Omi XBB.1.5) at 10 µg.
Note: One participant of 2 to <5 years of age who was randomised into Group 3 in error and received Omi XBB.1.5 at 3 µg is also included.
Note: One participant of 2 to <5 years of age who was randomised into Group 1 in error and received 2 doses of Omi XBB.1.5 at 10 µg is also included.
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 event. For "any adverse 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: 18SEP2025 (01:23) Source Data: adae Table Generation: 18SEP2025 (01:50) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adae_s150_1md_soc_p2_5

Related Adverse Events

Phase 1

6 Months Through <2 Years of Age

From Dose 1 to 6 months after the last dose, a total of 2 participants (6.1%) in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 3 µg group, 1 participant (3.4%) in the 6 µg group, and 1 participant (3.0%) in the 10 µg group reported adverse events assessed by the investigator as related to the study vaccine from Dose 1 to 6 months after the last dose.

In the 3 µg group, related AEs in 2 participants included diarrhoea (n=1), vomiting (n=2), and injection site induration (n=1).

In the 6 µg group, related AEs included diarrhoea (n=1).

In the 10 µg group, related AEs included rash (n=1).

2 Through <5 Years of Age

From Dose 1 to 6 months after the last dose, no AEs were assessed as related in any participants 2 years through 5 years of age across the three dose groups.

Phase 2/3

6 Months Through <2 Years of Age (Group 1 – 3)

A total of 2 participants (0.7%) in the BNT162b2 (Omi XBB.1.5) 3-µg group and 3 participants (0.5%) in the 10-µg group reported adverse events assessed by the investigator as related to the study vaccine from Dose 1 through 6 months after the last dose.

- In the 3-µg group, related AEs included diarrhoea (n=1; Grade 2; on Day 2 after Dose 1 and resolved within 5 days) and cough (n=1; Grade 1; on Day 1 after Dose 2 and resolved within 2 days).
- In the 10-µg group, related AEs included pyrexia (n=1; Grade 3; on Day 2 after Dose 2 and resolved within 5 days), gastroenteritis (n=1; Grade 2; on Day 3 after Dose 1 and resolved within 11 days), and rash (n=1; Grade 2; on Day 5 after Dose 1 and resolved within 11 days).

2 Through <5 Years of Age (Group 4 – 5)

No related AEs were reported.

Severe and Life-Threatening Adverse Events

Phase 1

Participants 6 Months Through <2 Years of Age

Three participants (9.1%) in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 3 µg group reported severe AEs from Dose 1 to 6 months after the last dose. Severe AEs included drug hypersensitivity (n=1; allergic reaction to amoxicillin Day 4 after Dose 2; not assessed as related), bronchiolitis (n=1; on Day 3 after Dose 3; not assessed as related), and lip injury (n=1; on Day 70 after Dose 3; not assessed as related). No severe AEs were reported in the 6 µg or 10 µg groups.

No life-threatening events or withdrawals due to severe adverse events were reported in any dose group.

Participants 2 through <5 Years of Age

One participant (4.3%) in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 3 µg group reported a severe AE (asthma; on Day 53 after Dose 2; not assessed as related to study vaccination) from Dose 1 to 6 months after the last dose. Two participants (8.3%) in the 10 µg group reported severe AEs, including gastroenteritis viral (n=1; on Day 1 after Dose 2; not assessed as related), tonsillitis (n=1; on Day 14 after Dose 2; not assessed as related), and dermatitis diaper (n=1; on Day 4 after Dose 2; not assessed as related). No severe AEs were reported in the 6 µg group.

No life-threatening events, or withdrawals due to severe adverse events were reported in any dose group.

Phase 2/3

Participants 6 Months Through <2 Years of Age (Group 1 – 3)

Severe AEs

A total of 10 participants (3.3%) in the BNT162b2 (Omi XBB.1.5) 3-µg group and 20 participants (3.3%) in the 10-µg group reported severe adverse events from Dose 1 to 6 months after the last dose. No severe or life-threatening AEs were assessed as related to study vaccination. VILKA?

Life-threatening AEs

Three participants (0.5%) in the BNT162b2 (Omi XBB.1.5) 10-µg group and one participant (0.3%) in the 3-µg group reported life-threatening AEs from Dose 1 to 6 months after the last dose. In the 10-µg group, life-threatening AEs included drowning (n=1), ill-defined disorder (n=1), and nephroblastoma (n=1). In the 3-µg group, a single life-threatening AE of road traffic accident (n=1) was reported.

Most life-threatening events in this age group were fatal; a child with nephroblastoma was withdrawn from the study to receive cancer treatment but eventually succumbed to the disease following withdrawal.

2 through <5 Years of Age (Group 4 – 5)

Severe AEs

A total of 5 participants (0.7%) in the BNT162b2 (Omi XBB.1.5) 10-µg group (Groups 4 and 5,) reported severe AEs from study vaccination to 6 months after the study vaccination. Severe AEs included infections (bronchiolitis (n=1), gastroenteritis viral, pneumonia, sinusitis) and injuries (fall, fracture).

Life-Threatening AEs

Three participants (0.4%) in the 10-µg group reported life-threatening AEs, including drowning, accident, and diabetic ketoacidosis.

Other Significant Adverse Events

Phase 1

The MAH has evaluated additional adverse events of interest for vaccines due to association with COVID-19. No participants in either age group reported an AE of interest through 6 months after study vaccination.

Phase 2/3

Participants 6 Months through <2 Years of Age (Group 1 – 3)

The MAH has evaluated additional adverse events of interest for vaccines due to association with COVID-19. Two participants (0.3%) in the BNT162b2 (Omi XBB.1.5) 10 µg group (Group 1 and Group 2) reported an AE of seizure during the study. Neither of these events were assessed as related to study vaccination.

Four participants (1.3%) in the BNT162b2 (Omi XBB.1.5) 3 µg group (Group 3) reported an AE of interest (febrile convulsion [n=3; not assessed as related] and encephalitis [n=1; not assessed as related]).

Participants 2 through <5 Years of Age (Group 4 – 5)

The MAH has evaluated additional adverse events of interest for vaccines due to association with COVID-19. One participant (0.1%) reported an AE of interest (type 1 diabetes mellitus/ diabetic

ketoacidosis; On Day 74 after Dose 1; assessed as not related to study vaccination by the investigator) during the study.

Clinical Assessments for Myocarditis or Pericarditis

Phase 1

Participants 6 Months through <2 Years of Age

Myocarditis/pericarditis is a protocol-specified AESI; no cases were reported in this age group from Dose 1 through 6 months after the last dose.

Bivalent BNT162b2 (Original/Omicron BA.4/BA.5) 3 µg group: One participant underwent protocol required clinical evaluation for potential myocarditis/pericarditis due to reporting shortness of breath 4 days post-Dose 3. Per investigator, ECG and troponin were not performed as the participant had an alternate diagnosis of bronchiolitis.

Participants 2 through <5 Years of Age

Myocarditis/pericarditis is a protocol-specified AESI; no cases were reported in this age group from Dose 1 through 6 months after the last dose.

No participants aged 2 through 5 years underwent evaluations for protocol-specified symptoms suggestive of potential myocarditis/pericarditis.

Phase 2/3

Participants 6 Months through <2 Years of Age

Myocarditis/pericarditis is a protocol-specified AESI; no cases were reported in this age group from Dose 1 through 6 -months after last dose.

Two participants 6 months to <2 years underwent protocol required clinical evaluations for potential myocarditis or pericarditis following vaccination:

In the BNT162b2 (Omi XBB.1.5) 10-µg group (Group 1), one 18-month-old White female experienced shortness of breath beginning on Day 26 after Dose 1, lasting 6 days. The participant was seen for a COVID illness visit during due to shortness of breath in conjunction with cold-like symptoms of cough, nasal congestion, rhinorrhoea, and sneezing. Per investigator, ECG and troponin were not performed as the shortness of breath was not deemed to be indicative of myocarditis/pericarditis. No alternative diagnosis was identified. This participant was not diagnosed with myocarditis or pericarditis.

In the BNT162b2 (Omi XBB.1.5) 3-µg group (Group 3), one 12-month-old female experienced shortness of breath on Day 17 after Dose 2, lasting 2 days. Cardiac workup included a normal troponin I and normal ECG. This participant was seen for a COVID illness visit due to shortness of breath in conjunction with symptoms of cough, difficulty feeding, and nasal congestion. The diagnosis was lower respiratory tract infection. This participant was not diagnosed with myocarditis or pericarditis.

Participants 2 through <5 Years of Age

Myocarditis/pericarditis is a protocol-specified AESI; no cases were reported in this age group from study vaccination through 6 -months postvaccination.

No participants 2 to <5 years of age underwent evaluation for potential myocarditis or pericarditis following vaccination in this study population.

Surveillance of COVID-19 Cases

Phase 1

Participants 6 Months through <2 Years of Age

After Dose 1 prior to Dose 2: No cases of COVID-19 occurrence were reported in any vaccine group during this interval.

After Dose 2 prior to Dose 3: One case in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 3 µg group (QNS) and three cases in the 6 µg group (Omicron BA.5.2, Omicron XBB.1.5.32, and Omicron XBB.1.16) were reported. No cases were reported in the 10 µg group. All cases met both protocol-defined and CDC-defined criteria for COVID-19.

After Dose 3 prior to Dose 4: One case in the bivalent BNT162b2 (original/Omi BA.4/BA.4) 6 µg group and three cases in the 10 µg group were reported. No cases were reported in the 3 µg group. SARS-CoV-2 strains identified included EG.5.1.15 (n=1, 6 µg group), XBB.1.5.72 (n=1, 10 µg group), XBB.1.16.20 (n=1, 10 µg group), and EU.1.1 (n=1, 10 µg group). All cases met both protocol-defined and CDC-defined criteria for COVID-19.

After Dose 4 (BNT162b2 [Omi XBB.1.5]): One case in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 3 µg group, two cases in the 6 µg group, and one case in the 10 µg group were reported. SARS-CoV-2 strains identified included KV.2 (n=1, 3 µg group), KW.1 (n1, 10 µg group), HV.1 (n=1, 6 µg group), and unknown (n=1, 6 µg group) due to insufficient quantities.

All cases met both protocol-defined and CDC-defined criteria for COVID-19. No severe cases were reported. No cases of MIS-C were reported.

None of the cases after any dose met the severe criteria per protocol. No cases of MIS-C were reported.

Participants 2 through <5 Years of Age

After Dose 1 prior to Dose 2: No cases of COVID-19 occurrence were reported in any vaccine group during this interval.

After Dose 2 prior to Dose 3: No cases of COVID-19 occurrence were reported in any vaccine group during this interval.

After Dose 3 prior to Dose 4: One case was reported in the 6 µg group (not determined due to insufficient quantity). No cases were reported in the 3 µg or 10 µg groups. The case met both protocol-defined and CDC-defined criteria for COVID-19. No severe cases were reported. No cases of MIS-C were reported.

After Dose 4 (BNT162b2 [Omi XBB.1.5]): One case (4.2%) was reported in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 6 µg group (unknown due to insufficient quantities). No cases were reported in the 3 µg or 10 µg groups. The case met both protocol-defined and CDC-defined criteria for COVID-19. No severe cases were reported. No cases of MIS-C were reported.

Phase 2/3

Participants 6 Months through <2 Years of Age (Group 1 – 3)

After Dose 1 prior to Dose 2:

Eight cases of COVID-19 occurrence were reported in the 10 µg groups (Group 1 and Group 2). All cases had available lineage data and were caused by Omicron subvariants: KP.3.3 (n=1), BA.2.86

(n=1), and LB.1.3 (n=1), with 5 cases having insufficient quantities for assessment. No cases were reported in the 3 µg group.

Most cases met both protocol-defined and CDC-defined criteria for COVID-19; a few cases met CDC-defined criteria only.

After Dose 2 prior to Dose 3:

Six cases of COVID-19 occurrence were reported in the 3 µg group during this interval. This interval does not apply to the 10 µg group, which followed a two-dose schedule.

After Dose 2:

Twenty-five cases were reported in the 10 µg groups (Group 1 and Group 2). Of these 25 cases, all with available lineage data were caused by Omicron subvariants: KP.2.3 (n=1), MC.13 (n=2), KP.3.1.1 (n=5), KP.2.2 (n=1), ML.2 (n=2), XEC (n=2), LB.1.3 (n=3), BA.2 (n=1), and 1 indetermined, with 7 cases having insufficient quantities for assessment. All cases met protocol-defined and CDC-defined criteria for COVID-19.

After Dose 3:

Eleven cases of COVID-19 occurrence were reported in the 3 µg group. Of these cases, all with available lineage data were caused by Omicron subvariants: KP.2.3 (n=1), XEC (n=1), MC.1 (n=1), LB.1.3 (n=1), with 7 cases having insufficient quantities for assessment. All cases met protocol-defined and CDC-defined criteria for COVID-19.

Severe COVID-19 cases

One protocol-defined severe case occurred in the 10 µg group following Dose 1 (and prior to Dose 2). The severe case met protocol-defined severity criteria of elevated respiratory rate for age and decreased oxygen saturation level; both vital signs were considered not clinically significant by the investigator. The severe case had insufficient quantity for sequencing. No severe cases were reported in the 3 µg group. No cases met CDC-defined criteria for severe COVID-19, and no cases of MIS-C were reported.

Participants 2 through <5 Years of Age (Group 4 – 5)

Eleven cases (1.6%) of COVID-19 occurrence were reported. Identified SARS-CoV-2 strains included Omicron sublineages (KP.2.1 [n=1], KP.2.3 [n=1], KP.3.3 [n=1], KP.3.4 [n=1], KR.4.1 [n=1], LB.1.3.1 [n=1]. Five cases were of unknown SARS-CoV-2 lineage due to indeterminate result or insufficient quantity for sequencing. Most cases met both protocol-defined and CDC-defined criteria for COVID-19; two cases met protocol-defined criteria for severe COVID-19, and no cases of MIS-C were reported.

Severe COVID-19 cases

Two protocol-defined severe cases occurred following Dose 1. These severe cases both fulfilled a single protocol-defined severity criterion (elevated respiratory rate) that was considered by the investigator as not clinically significant and were associated with Omicron subvariants: KP.2.1 (n=1) and KP.3.4 (n=1). No cases met CDC-defined criteria for severe COVID-19, and no cases of MIS-C were reported.

Substudy E

An overview of AEs reported from the study vaccination through 1 month after the study vaccination is shown in Table below. In total, 11 participants (3.5%) reported any AE. SAEs of acute gastroenteritis

and seizure were separately reported in 2 participants (0.6%), with seizure AE reported as related to vaccination. Three participants reported 4 severe AEs (1%) within 1 month after vaccination (Table below), including hyperglycaemia and seizure in 1 participant, non-cardiac chest pain in one participant and acute gastroenteritis in 1 participant. No life-threatening AEs, withdrawals due to AEs, or deaths were reported.

Eighteen (5.8%) participants reported any AEs from study vaccination to 6 months after study vaccination. One additional SAE of acute gastroenteritis with dehydration and 1 additional severe AE of acute gastroenteritis with dehydration was reported through 6 months after vaccination.

Table 51: Number (%) of Participants Reporting at Least 1 Adverse Event From the Study Vaccination to 1 Month After the Study Vaccination - Substudy E - Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (Omi XBB.1.5) 10 µg (N[a]=310)	
Adverse Event	**n[b] (%)**	**95% CI[c]**
Any adverse event	11 (3.5)	(1.8, 6.3)
Related[d]	4 (1.3)	(0.4, 3.3)
Severe	3 (1.0)	(0.2, 2.8)
Life-threatening	0	(0.0, 1.2)
Any serious adverse event	2 (0.6)	(0.1, 2.3)
Related[d]	1 (0.3)	(0.0, 1.8)
Severe	2 (0.6)	(0.1, 2.3)
Life-threatening	0	(0.0, 1.2)
Any nonserious adverse event	11 (3.5)	(1.8, 6.3)
Related[d]	3 (1.0)	(0.2, 2.8)
Severe	2 (0.6)	(0.1, 2.3)
Life-threatening	0	(0.0, 1.2)
Any adverse event leading to withdrawal	0	(0.0, 1.2)
Related[d]	0	(0.0, 1.2)
Serious	0	(0.0, 1.2)
Severe	0	(0.0, 1.2)

Adverse Event	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (N[a]=310) n[b] (%)	95% CI[c]
Life-threatening	0	(0.0, 1.2)
Death	0	(0.0, 1.2)

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 event category. For "any adverse event", n = the number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided 95% CI, based on the Clopper and Pearson method.
d. Assessed by the investigator as related to study intervention.
PFIZER CONFIDENTIAL SDTM Creation: 04NOV2024 (16:22) Source Data: adae Table Generation: 12NOV2024 (03:07) (Database snapshot date : 01NOV2024) Output File: ./nda2_ubped2/C4591048_E_CSR_Safety/adae_s130_1md2_p2_2

Analysis of Adverse Events

Table 52: Number (%) of Participants Reporting at Least 1 Adverse Event From the Study Vaccination to 1 Month After the Study Vaccination, by System Organ Class and Preferred Term - Substudy E - Safety Population

System Organ Class Preferred Term	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (N[a]=310) n[b] (%)	(95% CI[c])
Any adverse event	11 (3.5)	(1.8, 6.3)
Gastrointestinal disorders	4 (1.3)	(0.4, 3.3)
Abdominal pain upper	1 (0.3)	(0.0, 1.8)
Diarrhoea	1 (0.3)	(0.0, 1.8)
Gastritis	1 (0.3)	(0.0, 1.8)
Vomiting	1 (0.3)	(0.0, 1.8)
General disorders and administration site conditions	2 (0.6)	(0.1, 2.3)
Non-cardiac chest pain	1 (0.3)	(0.0, 1.8)
Pyrexia	1 (0.3)	(0.0, 1.8)

System Organ Class Preferred Term	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (N[a]=310) n[b] (%)	(95% CI[c])
Immune system disorders	1 (0.3)	(0.0, 1.8)
Milk allergy	1 (0.3)	(0.0, 1.8)
Infections and infestations	3 (1.0)	(0.2, 2.8)
Gastroenteritis	1 (0.3)	(0.0, 1.8)
Otitis media	1 (0.3)	(0.0, 1.8)
Periorbital cellulitis	1 (0.3)	(0.0, 1.8)
Metabolism and nutrition disorders	2 (0.6)	(0.1, 2.3)
Decreased appetite	1 (0.3)	(0.0, 1.8)
Hyperglycaemia	1 (0.3)	(0.0, 1.8)
Nervous system disorders	2 (0.6)	(0.1, 2.3)
Dizziness	1 (0.3)	(0.0, 1.8)
Seizure	1 (0.3)	(0.0, 1.8)
Respiratory, thoracic and mediastinal disorders	1 (0.3)	(0.0, 1.8)
Nasal congestion	1 (0.3)	(0.0, 1.8)
Skin and subcutaneous tissue disorders	1 (0.3)	(0.0, 1.8)
Alopecia areata	1 (0.3)	(0.0, 1.8)

Note: MedDRA (v27.0) 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 event. For "any adverse event", n = number of participants reporting at least 1 occurrence of any adverse event.
c. Exact 2-sided 95% CI, based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 04NOV2024 (16:22) Source Data: adae Table Generation: 12NOV2024 (03:07) (Database snapshot date : 01NOV2024) Output File: ./nda2_ubped2/C4591048_E_CSR_Safety/adae_s150_1md2_soc_p2_2

Related Adverse Events

Four participants reported AEs (1.3%) assessed by the investigator as related to the study vaccine from study vaccination to 6 months after study vaccination: upper abdominal pain, decreased appetite,

and dizziness in one participant (n=1); seizure (n=1), diarrhoea (n=1), and non-cardiac chest pain (n=1).

Severe and Life-Threatening Adverse Events

Four participants reported severe AEs from study vaccination to 6 months after study vaccination: hyperglycaemia and seizure in 1 participant (n=1), non-cardiac chest pain (n=1), acute gastroenteritis (n=1), and acute gastroenteritis with dehydration (n=1).

No life-threatening AEs were reported from study vaccination through 6 months after study vaccination.

Other Significant Adverse Events

Myocarditis/pericarditis is a protocol-specified AESI; no cases were reported in this age group from study vaccination through 6-months postvaccination.

The MAH evaluates additional adverse events of interest for vaccines due to association with COVID-19. One participant (0.3%) reported an AE of interest (seizure) during the study. No other AEs of interest were identified through 6 months after study vaccination.

Clinical Assessments for Myocarditis or Pericarditis

Cardiac Evaluations

Two participants underwent cardiac evaluation visits for protocol-specified potential myocarditis/pericarditis symptoms after study vaccination.

A participant reported chest pain, with headache and pyrexia, 5 days after vaccination with a start date of 17 March 2024. At the cardiac evaluation visit conducted on 18 March 2024 (5 days post vaccination), the participant had a normal troponin I, and an abnormal ECG finding of repolarization anomaly, specifically "alteration of repolarization in V1 and V5." At the protocol required cardiology evaluation on 03 April 2024 (17 days postvaccination), the participant had a normal ECG and a normal echocardiogram; the chest pain was determined to be chest pain without cardiac involvement. The symptom of chest pain was attributed to the AE "non-cardiac chest pain", with start date 17 March 2024 and end date 19 March 2024 (2 days duration).

One participant reported shortness of breath 10 days after vaccination. No protocol required assessments were performed, as the site physicians did not deem the symptoms to be of cardiac aetiology. The participant had a positive SARS-COV-2 NAAT result from the nasal swab collected during the concurrent COVID-19 illness surveillance visit.

Surveillance of COVID-19 Cases

Four cases (1.3%) of COVID-19 occurrence were reported after study vaccination, with the SARS-CoV-2 strains identified as JN.1.9 (n=1), KP.2.3 (n=1), and unknown (n=2) due to insufficient quantities. All 4 cases met both protocol-defined and CDC-defined criteria for COVID-19. None met the severe criteria per the protocol and CDC definitions. No cases of MIS-C were reported after study vaccination.

Serious adverse event/deaths/other significant events

Substudy A

Phase 1

Death

No deaths were reported from Dose 1 through 6 months after the last dose in any of the age groups.

Serious Adverse Events

6 Months Through <2 Years of Age

One participant (3.0%) in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 3 µg group reported an SAE of bronchiolitis, with the cause noted as unspecified organism(s). The event occurred with onset on Day 3 after Dose 3 and lasted 10 days.

No SAEs were reported in the bivalent BNT162b2 (original/Omi BA.4/BA.5) 6 µg and 10 µg groups.

2 through <5 Years of Age

BNT162b2 (original/Omi BA.4/BA.5) 3 µg group: One participant (4.3%) reported an SAE of asthma. The event occurred after Dose 2, with onset on Day 53 after Dose 2 and lasted 5 days. The event was not considered related to the vaccine by the investigator.

BNT162b2 (original/Omi BA.4/BA.5) 6 µg group: No SAEs were reported through 6 months after study vaccination.

BNT162b2 (original/Omi BA.4/BA.5) 10 µg group: One participant (4.2%) reported an SAE of tonsillitis. The event occurred after Dose 2, with onset on Day 14 after Dose 2 and lasted 19 days. The event was not considered related to the vaccine by the investigator.

Phase 2/3

Death

6 Months Through <2 Years of Age (Group 1 – 3)

A 15-month-old male participant (10-µg; Group 1) died on Day 11 after Dose 2, at 1.3 years of age. The primary cause of death was drowning and was assessed as not related to study intervention by the investigator. No secondary causes were listed.

An 8-month-old male participant (10-µg; Group 1) died on Day 96 after Dose 2, approximately 1.1 years of age. The primary cause of death was reported as an ill-defined disorder/unknown illness and was assessed as not related to study intervention by the investigator. No secondary causes were listed.

A 21-month-old male participant (3-µg; Group 3) died on Day 52 after Dose 3, approximately 1.8 years of age. The primary cause of death was reported as a motor vehicle accident and was assessed as not related to study intervention by the investigator. No secondary causes were listed.

2 through <5 Years of Age (Group 4 – 5)

A 2-year-old male participant (10-µg; Group 5) died on Day 87 after vaccination. The primary cause of death was drowning and was assessed as not related to study intervention by the investigator. No secondary causes were listed.

A 3-year-old female participant (10-µg; Group 5) died on Day 93 after vaccination. The primary cause of death was accident, specifically accidental falling of bricks on the child and was assessed as not related to study intervention by the investigator. No secondary causes were listed.

Serious Adverse Events

6 Months Through <2 Years of Age (Group 1 – 3)

A total of 14 participants (4.6%) in the BNT162b2 (Omi XBB.1.5) 3-µg group and 27 participants (4.5%) in the BNT162b2 (Omi XBB.1.5) 10-µg group reported at least one SAE from Dose 1 through 6 months after the last dose. In both groups, the most frequently reported event was gastroenteritis (n=5 in the 3-µg group and n= 4 in the 10-µg group). One participant in the BNT162b2 (Omi XBB.1.5) 10-µg group reported a SAE of pyrexia that was assessed as related to study intervention by the investigator; this event took place on Day 2 after Dose 2 (Table below).

Table 53: Number (%) of Participants Reporting at Least 1 Serious Adverse Event From Dose 1 to 6 Months After the Last Dose, by System Organ Class and Preferred Term - Substudy A - Phase 2/3 - 6 Months to <2 Years of Age - Safety Population

	Vaccine Group (as Administered at Dose 1)			
	BNT162b2 (Omi XBB.1.5)			
	10 µg (Group 1 and Group 2)m(N[a]=604)		3 µg (Group 3) (N[a]=304)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any adverse event	27 (4.5)	(3.0, 6.4)	14 (4.6)	(2.5, 7.6)
Blood and lymphatic system disorders	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Anaemia	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
General disorders and administration site conditions	3 (0.5)	(0.1, 1.4)	0	(0.0, 1.2)
Drowning	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Ill-defined disorder	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Pyrexia	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Infections and infestations	20 (3.3)	(2.0, 5.1)	10 (3.3)	(1.6, 6.0)
Gastroenteritis	4 (0.7)	(0.2, 1.7)	5 (1.6)	(0.5, 3.8)
Bronchiolitis	4 (0.7)	(0.2, 1.7)	2 (0.7)	(0.1, 2.4)
Upper respiratory tract infection	3 (0.5)	(0.1, 1.4)	0	(0.0, 1.2)

	Vaccine Group (as Administered at Dose 1)			
	BNT162b2 (Omi XBB.1.5)			
	10 µg (Group 1 and Group 2)m(N[a]=604)		3 µg (Group 3) (N[a]=304)	
System Organ Class Preferred Term	**n[b] (%)**	**(95% CI[c])**	**n[b] (%)**	**(95% CI[c])**
Pneumonia	2 (0.3)	(0.0, 1.2)	0	(0.0, 1.2)
Abscess limb	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Croup infectious	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Encephalitis	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Escherichia urinary tract infection	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Gastroenteritis viral	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Gastrointestinal viral infection	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Infestation	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Lower respiratory tract infection	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Otitis media	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Pneumonia necrotising	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Pneumonia viral	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Tonsillitis	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Tracheobronchitis	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Urinary tract infection	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Urosepsis	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Injury, poisoning and procedural complications	3 (0.5)	(0.1, 1.4)	4 (1.3)	(0.4, 3.3)
Thermal burn	2 (0.3)	(0.0, 1.2)	2 (0.7)	(0.1, 2.4)
Foreign body aspiration	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Near drowning	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)

System Organ Class Preferred Term	Vaccine Group (as Administered at Dose 1) BNT162b2 (Omi XBB.1.5) 10 µg (Group 1 and Group 2)m(N[a]=604) n[b] (%)	(95% CI[c])	3 µg (Group 3) (N[a]=304) n[b] (%)	(95% CI[c])
Road traffic accident	0	(0.0, 0.6)	1 (0.3)	(0.0, 1.8)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Nephroblastoma	1 (0.2)	(0.0, 0.9)	0	(0.0, 1.2)
Nervous system disorders	0	(0.0, 0.6)	2 (0.7)	(0.1, 2.4)
Febrile convulsion	0	(0.0, 0.6)	2 (0.7)	(0.1, 2.4)

Note: MedDRA (v28.0) coding dictionary applied.
Note: Participants enrolled in Group 1 and Group 2 were planned to receive a 2-dose series of BNT162b2 (Omi XBB.1.5) at 10 µg on a 0- and 8-week schedule. Participants enrolled in Group 3 were planned to receive a 3-dose series of BNT162b2 (Omi XBB.1.5) at 3 µg on a 0-, 3-, and 11-week schedule.
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 event. For "any adverse 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: 18SEP2025 (01:23) Source Data: adae Table Generation: 18SEP2025 (01:50) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adae_s150_cod_sae_p2_2

2 through <5 Years of Age (Group 4 – 5)

A total of 10 participants (1.5%) in the BNT162b2 (Omi XBB.1.5) 10-µg group (Groups 4 and 5, N=688) reported at least one SAE from study vaccination through 6 months after the study vaccination (Table below).

The most common SAEs were infections and infestations, including lower respiratory tract infection. No SAEs were assessed as related to study vaccination.

Table 54: Number (%) of Participants Reporting at Least 1 Serious Adverse Event From Dose 1 to 6 Months After the Study Vaccination, by System Organ Class and Preferred Term - Substudy A - Phase 2/3 - 2 to <5 Years of Age - Safety Population

System Organ Class Preferred Term	Vaccine Group (as Administered) BNT162b2 (Omi XBB.1.5) 10 µg (Group 4 and Group 5) (N[a]=688) n[b] (%)	(95% CI[c])
Any adverse event	10 (1.5)	(0.7, 2.7)
General disorders and administration site conditions	1 (0.1)	(0.0, 0.8)
Drowning	1 (0.1)	(0.0, 0.8)
Infections and infestations	6 (0.9)	(0.3, 1.9)
Lower respiratory tract infection	2 (0.3)	(0.0, 1.0)
Bronchiolitis	1 (0.1)	(0.0, 0.8)
Gastroenteritis	1 (0.1)	(0.0, 0.8)
Gastroenteritis viral	1 (0.1)	(0.0, 0.8)
Pneumonia	1 (0.1)	(0.0, 0.8)
Sinusitis	1 (0.1)	(0.0, 0.8)
Viral tonsillitis	1 (0.1)	(0.0, 0.8)
Injury, poisoning and procedural complications	2 (0.3)	(0.0, 1.0)
Accident	1 (0.1)	(0.0, 0.8)
Fracture	1 (0.1)	(0.0, 0.8)
Metabolism and nutrition disorders	1 (0.1)	(0.0, 0.8)
Diabetic ketoacidosis	1 (0.1)	(0.0, 0.8)

Note: MedDRA (v28.0) coding dictionary applied.
Note: Participants enrolled in Group 4 and Group 5 were planned to receive a single dose of BNT162b2 (Omi XBB.1.5) at 10 µg.
Note: One participant of 2 to <5 years of age who was randomised into Group 3 in error and received Omi XBB.1.5 at 3 µg is also included.
Note: One participant of 2 to <5 years of age who was randomised into Group 1 in error and received 2 doses of Omi XBB.1.5 at 10 µg is also included.
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 event. For "any adverse 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: 18SEP2025 (01:23) Source Data: adae Table Generation: 18SEP2025 (01:50) (Snapshot Date: 25AUG2025) Output File: ./nda2_ubped2/C4591048_A_CSR/adae_s150_cod_sae_p2_5

Substudy E

Death

No deaths were reported from study vaccination through 6 months after study vaccination.

Serious Adverse Events

Three participants (1%) reported SAEs from study vaccination through 6 months after study vaccination: gastroenteritis (n=2) and seizure (n=1). The seizure occurred in an 8-year-old male with no past medical history who, 13 days after vaccination, began to convulse while sleeping. There was no preceding illness or event, the seizure lasted 1-2 minutes and resolved without intervention. The participant was transported to an emergency department (ED) by emergency medical services (EMS) where a work-up was notable for a normal brain MRI and the electroencephalogram showing left temporal spikes. The participant also has an AE for "hyperglycaemia" as participant's guardian reported an elevated blood sugar measurement on EMS arrival, though his blood sugar was within normal limits in the ED, with no glucose lowering intervention. The participant was discharged from the ED with a prescription for twice daily levetiracetam, which he remained on through study completion. No further episodes of seizure occurred while in study follow-up. The participant was scheduled for follow-up with paediatric neurology but did not attend the appointment. The seizure event was considered related to the vaccination by PI, the MAH did not concur with the investigator's assessment.

Discontinuation due to adverse events

Substudy A

Phase 1

There were no discontinuations due to AEs reported from Dose 1 through 6 months after the last dose in either age group.

Phase 2/3

Participants 6 Months through <2 Years of Age (Group 1 – 3)

BNT162b2 (Omi XBB.1.5) 3-µg group (Group 3):

One participant in the 3-µg group was discontinued due to a road traffic accident (motor vehicle accident), with onset after Dose 3.

BNT162b2 (Omi XBB.1.5) 10-µg group (Groups 1 and 2):

Six participants in the 10-µg group (Groups 1 and 2) reported AEs that led to discontinuation:

- One participant was discontinued due to nephroblastoma (Wilm's Tumour) and anaemia, with onset after Dose 1.
- One participant was discontinued due to an ill-defined disorder/unknown illness, with onset after Dose 2.
- One participant was discontinued due to drowning, with onset after Dose 1.
- One participant was discontinued due to rash (assessed as related to study vaccination), with onset after Dose 1, but remained in the study for safety follow-up.
- One participant discontinued due to anaemia but remained in the study for safety follow-up.

Participants 2 through <5 Years of Age (Group 4 – 5)

Two participants were discontinued due to adverse events:

- One participant was discontinued due to drowning (death by drowning), with onset after Dose 1.
- One participant was discontinued due to accident (death by accidental falling of bricks on child), with onset after Dose 1.

Substudy E

There were no discontinuations due to AEs reported for participants throughout the study.

Post marketing experience

No data has been provided for the use of BNT162b2 at 10 µg in individuals 6 months <5 years of age.

2.5.1. Discussion on clinical safety

The presented safety data is based on the phase 1/2/3 study C4591048 Substudy A and E, with the aim to support an increased dose of BNT162b2 from 3 µg to 10 µg in infants and children 6 months to <5 years of age. The Applicant has also proposed an updated dosing regimen from 3-dose to 2-dose primary course for 6 months to <2 years of age and a single dose for 2 years to <5 years of age.

Substudy A phase 1 was a dose finding study where a 3-dose series of bivalent BNT162b2, administered on a 0-, 3-, and 11-week schedule was followed by a fourth dose with BNT162b2 (Omi XBB.1.5) approximately 6 months after Dose 3. The included doses were bivalent BNT162b2 at 3, 6 and 10 µg. Following the 2023-2024 periodic strain change recommendation to Omicron XBB.1.5, a fourth dose of BNT162b2 Omi XBB.1.5 was administered to individuals who had received 3 doses of bivalent BNT162b2 (original/Omi BA.4/BA.5) in Substudy A Phase 1. Participants who received a fourth dose prior to the approval of protocol amendment 3 may have received bivalent BNT162b2 as a fourth dose. The safety population included 95 participants for the children ≥6 months to <2 years of age that had received at least the first dose. In this age group at least three doses were administered to 88 children (92%) and 78 children received the fourth dose (81%). The safety population constituted 71 participants for the children ≥2 to <5 years of age that had received at least one dose. In this age group at least 3 doses were given to 64 (90%) children, and the fourth dose was given to 56 (79%) of the participants.

Substudy A phase 2/3 evaluated the selected dose BNT162b2 Omi XBB.1.5 at 10 µg administered on a 0- and 8-week schedule compared with 3 doses of BNT162b2 Omi XBB.1.5 at 3 µg, in COVID-19 vaccine–naïve children ≥6 months to <2 years of age. Furthermore, the safety was also evaluated for a single dose BNT162b2 Omi XBB.1.5 at 10 µg was administered to covid-19 vaccine–naïve children ≥2 to <5 years of age. For the children ≥6 months to <2 years of age the safety population included 604 participants that received at least one dose of BNT162b2 Omi XBB.1.5 at 10 µg (Group 1 and Group 2), of which 576 (95%) received the second dose. At least one dose was given to 304 participants in the BNT162b2 Omi XBB.1.5 at 3 µg (Group 3) and 286 (94%) received the third dose. For the children ≥2 to <5 years of age, the safety population included 688 participants which received the single dose BNT162b2 Omi XBB.1.5 at 10 µg. Most of the participants in both the younger (83%) and the older (74%) age groups were from South Africa.

Substudy E phase 2/3 evaluated a single dose of BNT162b2 Omi XBB.1.5 at 10 µg in covid-19 vaccine-naïve children ≥5 to <12 years of age. All assigned participants received the vaccination; the safety population included 310 participants. Most of the participants were from the US.

Reactogenicity

Phase 1

Among the children aged 6 months to <2 years of age tenderness at the injection site was the most reported local reaction, which was reported in 7-27% among the children receiving 3µg and in 13-24% of the children that received the dose 10 µg. In both doses the highest frequency was reported after dose 1. Redness was reported at a slightly higher frequency among children that received 10 µg (10-15%) compared to those receiving 3 µg (3-10%). Most of the local reactions were mild to moderate at intensity and resolved within 3 days. Regarding the systemic events in this age group no dose dependent pattern could be observed. Irritability was the most reported systemic event, with a frequency of 26-43% in the 10 µg group and in 33-52% of the children that received 3 µg. Fever was reported in 0-3% among the children that received 10 µg and in 3-16% of those receiving 3 µg. Most of the systemic events were mild and moderate at intensity and resolved within 1-6 days. One participant in the 3 µg group reported fever >40°C.

Among the children 2 to <5 years of age, pain at the injection site was the most reported local reaction, where a slightly higher frequency was observed in the 6 µg group (17-33%) compared to 3 µg (0-27%) and 10 µg (9-33%). For the lowest dose there was a clear relationship between number of doses and reduction in local reactions. This pattern was not observed for the 6 and 10 µg doses. Independent of dose, fatigue was the most reported systemic event with a frequency of 10-38% at 10 µg and 8-41% at 3 µg. Fever was reported at a clearly higher frequency after administration of the doses 1-3 at 10 µg (13-14%), whereas none in the 10 µg reported fever after the fourth dose. Among the children that received 3 µg, fever was reported at 9% after the first dose, 5% after the second dose and none of them reported fever after doses 3 and 4. Most systemic events were mild to moderate at intensity and resolved

Substudy A phase 2/3

The most reported local reaction in children 6 months to <2 years of age was tenderness at injection site which was reported at 16% and 12% after dose 1 and 2 respectively in the children that received 10 µg. In the groups that received 3 doses at 3 µg the frequency was 8-14%. Most local events were mild to moderate severity and resolved within 2 days. For the systemic events, a similar frequency was observed between the 3 µg and 10 µg for the first two doses. Decreased appetite was reported in 27% and 21% at dose 1 and 2 respectively in the 3 µg group and in 27% and 20% respectively in the 10 µg groups. Fever was reported in 6-7% among the children that received 3 µg and in 7-8% of those that received 10 µg.

Among children 2 to <5 years of age that received one dose XBB.1.5 at 10 µg reported 25% pain at injection site and 9% reported redness. These reactions were mostly mild to moderate at intensity and resolved within 1 day. In this group was fatigue (20%) the most reported systemic event followed by diarrhoea and headache (10% each). Fever was reported in 7% of the participants of which one reported fever >40°C. The median onset was 1-4 days post dosing and most events resolved within two days.

Substudy A phase 2/3

Pain at injection site (43%) was the most reported local reaction. Severe swelling was reported in one participant on D2. The median onset was 1-2 days post dosing with a median duration of 1-1,5 days.

Fatigue (15%) was the most reported systemic event followed by headache (14%) and muscle pain (10%). Fever was reported in 5% of the children. Most systemic events were mild or moderate in severity. Severe fever (>40°C) was reported in 1 participant, severe fatigue in 2 participants and severe headache in 1 participant. The median onset for all systemic events was 2 to 5 days after study vaccination, and all events resolved within a median duration of 1 to 2 days after onset.

Adverse Events

Phase 1

Any AEs were reported at 42% in the 3 µg group and in 27% of the 10 µg group of the youngest children. The few AEs considered related to treatment concerned reactogenicity. In the older age group, any AEs was reported in 25% of the children that received 10 µg and in 17% of those that received 3 µg. In the phase 1 study no SAEs or life-threatening AEs were reported.

Substudy A phase 2/3

In the youngest age group, any AEs were reported in 12% up to one month after last vaccination for both the participants that received 3µg and 10 µg. AEs considered related to treatment included diarrhoea (3 µg) and pyrexia (10 µg), one participant each. These PTs are already included in the SmPC. Life-threatening events were reported in three participants in the 10 µg group (drowning, ill-defined disorder and nephroblastoma) and one participant in the 3 µg group (road traffic accident) reported life-threatening AEs from Dose 1 to 6 months after the last dose. None of them were considered related to treatment, this assessment is agreed.

In the older age group, any AEs were reported in 4% of the participants up to one month after vaccination. None of them was considered related to treatment. A total of 5 participants (0.7%) in the 10-µg group reported severe AEs from study vaccination to 6 months after the study vaccination in the older age group. These AEs included infections (bronchiolitis (n=1), gastroenteritis viral, pneumonia, sinusitis) and injuries (fall, fracture). Three participants (0.4%) in the 10 µg group reported life-threatening AEs, including drowning, accident, and diabetic ketoacidosis. None of these events were considered related to treatment, this conclusion can be accepted.

Substudy E

Among the 310 participants aged 5-11 years, 11 (3,5%) reported any AEs up to one month after the single dose of study vaccination. Four participants reported AEs that were considered related to vaccination (upper abdominal pain, decreased appetite, and dizziness in one participant (n=1); seizure that occurred on D13 (n=1), diarrhoea (n=1), and non-cardiac chest pain (n=1). The chest pain was further evaluated, and cardiac aetiology could not be identified. No life-threatening events were reported. No events of myocarditis or pericarditis were reported.

Overall, based on the presented data, the reactogenicity profile when administer BNT162b2 XBB 1.5 at 10 µg appears to be in line with the reactogenicity reported after administration of BNT162b2 XBB 1.5 at 3 µg in children 6 months to <5 years of age. No new safety concerns have been identified.

2.5.2. Conclusions on clinical safety

Based on the presented data, an acceptable safety profile has been presented in the phase 1/2/3 study when Comirnaty XBB 1.5 at 10 µg was administered to children aged 6 months to 11 years of age. The reactogenicity profile when administered Comirnaty at 10 µg appears to be in line with reported reactogenicity after administration of Comirnaty at 3 µg. No new safety concerns have been identified,

it should however be kept in mind that given the included number of participants, no conclusions could be made for any less frequent occurring potential AEs.

2.5.3. PSUR cycle

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.>

2.6. Risk management plan

The MAH submitted an updated RMP version with this application.

The CHMP received the following PRAC Advice on the submitted Risk Management Plan:

The PRAC considered that the risk management plan version 17.0 is acceptable.

Safety concerns

Important Identified Risks	Myocarditis and Pericarditis
Important Potential Risks	None
Missing Information	Use in pregnancy and while breast feeding
	Use in immunocompromised patients
	Use in frail patients with co-morbidities (e.g., chronic obstructive pulmonary disease [COPD], diabetes, chronic neurological disease, cardiovascular disorders)
	Use in patients with autoimmune or inflammatory disorders
	Long term safety data

Pharmacovigilance plan

Study (*study short name, and title*) Status *(planned/on-going)*	**Country**	**Summary of Objectives**	**Safety concerns addressed**	**Milestone**	**Due dates**
Category 3					
C4591009 *Ongoing*	US	To assess the occurrence of pre-specified safety events of interest among individuals in the general US population and in subcohorts of interest within selected data sources participating in the US Sentinel System.	Myocarditis and pericarditis AESI-based safety events of interest Use in pregnancy Use in immunocompromised patients Long term safety data	Protocol submission:	31-Aug-2021
				Protocol amendment submission:	11-Jul-2022
				Monitoring report 1 submission:	31-Oct-2022
				Interim Analysis submission:	30-Apr-2024
				Final CSR submission:	31-Mar-2026

Study (*study short name, and title)* **Status** *(planned/on-going)*	Country	Summary of Objectives	Safety concerns addressed	Milestone	Due dates
C4591022 *Ongoing*	US/CA	To assess whether pregnant women receiving BNT162b2 experience increased risk of pregnancy and infant safety outcomes, including major congenital malformations, spontaneous abortion, stillbirth, preterm delivery, small for gestational age, and small for age postnatal growth to one year of age, relative to pregnant women who received no COVID-19 vaccines during pregnancy.	Use in pregnancy.	Interim reports submission:	12-Apr-2022
					31-Jan-2023
					31-Jan-2024
				Final CSR submission:	28-Feb-2026
C4591036 (former Pediatric Heart Network Study) *Ongoing*	US/CA	To characterise the clinical course, risk factors, long-term sequelae, and quality of life in children and young adults <21 years with acute post-vaccine myocarditis including myocarditis after the bivalent Omicron modified vaccine.	Myocarditis/pericarditis Long term safety data.	Protocol submission:	30-Nov-2021
				6-monthly interim study report**Error! Bookmark not defined.**:	30-June-2023
				Protocol amendment submission:	15-Dec-2022
				12-monthly interim study report**Error! Bookmark not defined.**:	30-June-2025
				Final CSR submission:	28-Feb-2031
C4591052 *Ongoing*	EU		Myocarditis/pericarditis Use in pregnancy AESI-based safety events of interest including vaccine associated enhanced disease in immunocompromised patients	Protocol synopsis submission:	04-Jan-2023
				Protocol submission	30-Apr-2023

Study (*study short name, and title)* **Status** *(planned/on-going)*	Country	Summary of Objectives	Safety concerns addressed	Milestone	Due dates
		Post-approval observational studies using real-world data are needed to assess the association between Pfizer-BioNTech COVID-19 bivalent Omicron-modified Vaccine and pre-specified safety events of interest among persons administered the vaccine in the overall EU population.	Use in frail patients with co-morbidities (e.g., chronic obstructive pulmonary disease [COPD], diabetes, chronic neurological disease, cardiovascular disorders) Use in patients with autoimmune or inflammatory disorders Long term safety	Final CSR submission	30-Apr-2026

Risk minimisation measures

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
Myocarditis and pericarditis	Routine risk minimisation measures: SmPC sections 4.4. and 4.8. Additional risk minimisation measures: None	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None. Additional pharmacovigilance activities: *Studies (Final CSR Due Date)* C4591036 [former Pediatric Heart Network study] (28-February 2031) is the key study for this safety concern however other ongoing noninterventional studies may also contribute safety information. C4591009 (31-Mar-2026) C4591052 (30-Apr-2026)
Use in pregnancy and while breast feeding	Routine risk minimisation measures: SmPC section 4.6; PL section 2. Additional risk minimisation measures: None	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None. Additional pharmacovigilance activities: *Studies (Final CSR Due Date)* C4591022 is the key study for this safety concern, however other ongoing non-interventional studies may also contribute safety information to this cohort. C4591009[a] (31-Mar-2026) C4591052[a] (30-Apr-2026)
Use in immunocompromised patients	Routine risk minimisation measures: SmPC sections 4.4 and 5.1.	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None. Additional pharmacovigilance activities:

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
	Additional risk minimisation measures: None	*Studies (Final CSR Due Date)* C4591009 (31-Mar-2026) C4591052 (*30-Apr-2026*)
Use in frail patients with co-morbidities (e.g., chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders)	Routine risk minimisation measures: SmPC section 5.1. Additional risk minimisation measures: None	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None. Additional pharmacovigilance activities: *Studies (Final CSR Due Date)* *C4591052 (30-Apr-2026)*
Use in patients with autoimmune or inflammatory disorders	Routine risk minimisation measures: None. Additional risk minimisation measures: None	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None. Additional pharmacovigilance activities: *Studies (Final CSR Due Date)* C4591052 (*30-Apr-2026*)
Long term safety data	Routine risk minimisation measures: None. Additional risk minimisation measures: None	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None. Additional pharmacovigilance activities: *Studies (Final CSR Due Date)* C4591009 (31-Mar-2026) C4591036 (former PHN) (28-Feb-2031) C4591052 (*30-Apr-2026*)

a. Please note that studies C4591009, C4591022 *and C4591052* address only "Use in pregnancy" and not "Breast feeding".

2.7. Update of the Product information

As a consequence of this amended indication wording in the 10 mcg strength formulations and change in posology, sections 4.1, 4.2, 4.8, 5.1, 6.3 and 6.6 of the SmPC for JN.1, KP.2 and LP.8.1 have been updated. The 3 µg strength SmPCs have been deleted. The labelling and Package Leaflet have been updated accordingly.

Editorial changes have been included throughout the product information.

2.7.1. User consultation

A justification for not performing a full user consultation with target patient groups on the package leaflet has been submitted by the MAH and has been found acceptable.

3. Benefit-Risk Balance

3.1. Therapeutic Context

3.1.1. Disease or condition

COVID-19 primarily manifest respiratory symptoms, such as cough and nasal congestion, and systemic symptoms, such as fever and chills; symptoms may be mild to severe. The clinical manifestations may also include loss of taste or smell, and the spectrum of illness from SARS-CoV-2 can range from asymptomatic infection to severe pneumonia, acute respiratory distress syndrome, respiratory failure, septic shock, multiple organ dysfunction or failure, and death. While COVID-19 is primarily a pulmonary disease, it can also lead to cardiac, dermatologic, haematologic, hepatic, neurologic, renal, and other complications, including thromboembolic events and peri- and myocarditis.

3.1.2. Available therapies

The most important way to prevent COVID-19 caused by SARS-CoV-2 is active immunisation through prophylactic vaccination. Other interventions include specific antiviral compounds, monoclonal antibodies and supportive care.

There are currently several efficacious COVID-19 vaccines approved that are updated on an annual or periodic basis to match the identified circulating viral strains to maximise protection.

The SARS-CoV-2 Omicron strain adapted vaccines Bimervax, Nuvaxovid, Spikevax and Comirnaty are authorised in EU. Other COVID-19 vaccine approved is Kostaive (self-amplifying mRNA). There are limited options for treatment of COVID-19. Antiviral treatments such as Paxlovid (nirmatrelvir/ritonavir) and Veklury (remdesivir) remain effective against current SARS-CoV-2 variants. Other therapies, designed to neutralise the virus by binding to its spike protein, face reduced efficacy as the virus continues to evolve.

3.1.3. Main clinical studies

C4591048 is a master phase 1/2/3 protocol to investigate the safety, tolerability, and immunogenicity of variant adapted Comirnaty in healthy children. This study has several substudies. In current application, the data to support the posology changes in 6 months to <5 years originates from Substudy A and the data to support usage in 5-< 12-year-old children from Substudy E.

C4591048 Substudy A is a randomised open-label in Phase 2/3. The proposed posology changes in children 6 months through <5 years of age base on results from sub-study A (SSA) Groups 1-4. G3 received the current approved schedule 3x 3 µg and the other groups 10 µg as two doses (G1) or one dose (G2) schema. The age group 2 y-< 5 years received one dose of 10 µg formulation (G4).

In Study C4591048 Substudy E (SSE) vaccine naïve children 5 to <12 years of age received one dose of 10 µg Omi XBB.1.5 as already approved posology. Serology results from SSE (5-<12 years of age) were compared to serology results from another study. This Study C4591054 substudy A including vaccine experienced adults, who received Omicron XBB 1.5 30 µg as their 4th dose of Comirnaty.

3.2. Favourable effects

In 6m-<2 years age group, two doses of Comirnaty XBB.1.5 at 10 µg were noninferior to three 3 µg doses against Omicron XBB.1.5 based on GMR (1.51 (95% CI: 1.25, 1.82)) and difference in seroresponse rates (1.28% (95% CI: –2.69, 5.26)) (G1/G3 analysis). The change in posology in 6m-<

2 years age group to replace 3x 3 µg posology with 2x 10 µg is supported as the non-inferiority of GMR and seroresponse were demonstrated.

In 2- <5 years of age a single 10-µg dose Omi XBB.1.5 met non-inferiority based on GMR (1.12 (95% CI: 0.86, 1.47)), but not based on difference in seroresponse rates (-8.95 (95% CI: -11.92, -2.12)), when compared to three 3 µg doses of BNT162b2 (Omi XBB.1.5) in children 6-months to < 2 years without evidence of SARS-CoV-2 infection up to 1 month after Dose 3 (G4/G3 analysis).

In the evaluable immunogenicity population, the primary model-based GMR (5-<12 y. 10- µg/ adults 30-µg) was 1.81 (2-sided 95% CI: 1.51, 2.16). 88.8% of participants in the 5-<12 years group and 77.0% of participants in the adult group achieved seroresponse to Omicron XBB.1.5. The adjusted difference in percentages of participants with seroresponse was 8.97% (95% CI: 3.91, 14.02). Immunobridging success based on the model-based GMR and seroresponse rate difference was declared. The immunogenicity data from C4591048 Substudy E supports the current posology for 5-<12-year-old children.

3.3. Uncertainties and limitations about favourable effects

The reduction of number of doses to only 1 dose in 2-<5 year old group was not supported, because the seroresponse rate difference non-inferiority analysis failed and the seroresponse after one 10 µg dose in baseline SARS-CoV-2 negative subjects in G4 (2-<5 years) group was modest, about 7- fold lower than in case of current approved 3x 3 µg posology. The MAH agreed to change posology for 2 doses as primary schedule for COVID-19 vaccine- naïve children in entire 6 months to <5 years age group.

3.4. Unfavourable effects

The safety evaluation is based on the phase 1/2/3 study C4591048 Substudies A and E.

In the phase 2/3 part of the study, a total of 604 children aged 6 months to <2 years, 692 children aged 2 years to <5 years and 310 children aged 5 to <12 years had received BNT162b2 XBB 1.5 at 10 µg. The youngest group received two doses with 8 weeks in between, whereas the children >2 years of age have received a single dose at 10 µg. As a control group in the youngest age group 304 children received BNT162b2 XBB 1.5 at 3 µg as a 3 dose primary series.

Supportive data from the phase 1 part of the study has also been provided where participants that already had received a primary series of 3 doses Comirnaty BA.4-5 then received a fourth dose of Comirnaty at either 3 µg, 6 µg or 10 µg. Among children aged 6 months to <2 years of age the following numbers received all four doses: 3 µg (n=26), 6 µg (n=24) and 10 µg (n=28). Among children aged 2 to <5 years of age the following numbers received all four doses: 3 µg (n=13), 6 µg (n=23) and 10 µg (n=20).

The most reported local reaction in children aged 6 months to <2 years of age was tenderness at injection site. In the phase 2/3 study this was reported in 16% after dose 1 and in 12% after dose 2 in those that received 10µg, the corresponding frequency at 3 µg was 14% and 9% respectively and 8% after dose 3.

The most reported local reaction in children aged 2 months to <2 years in the phase 2/3 study was pain at injection site (25%) followed by redness (9%) and swelling (6%) after single dose at 10 µg.

In children aged 6 months to <2 years of age in the phase 2/3, the most reported systemic events study was decreased appetite, which was identified in 20-27% of those receiving 10 µg compared to 17-27% of those receiving 3 µg. Fever was reported in 7% after dose 1 and in 8% after dose 2 in

those that received 10µg, the corresponding frequency at 3µt was 6% each after dose 1 and 2, and 7% after dose 3.

Among children aged 2 years to <5 years the most reported systemic event was fatigue (20%) followed by headache and chills (10% each). Fever was reported in 7% of the participants.

Among the children aged 5-<12 years of age the most reported local reaction after a single dose Comirnaty XBB 1.5 at 10 µg was pain at injection site (43%). The most reported systemic event was fatigue (15%) followed by headache (14%) and muscle pain (10%). Fever was reported in 5% of the participants.

Overall, most local and systemic events were mild to moderate at intensity in all age groups.

3.5. Uncertainties and limitations about unfavourable effects

Given the size of the study, possible adverse events that rarely occurs could not be captured in this study. However, the wide use of Comirnaty in both adults and children since its initial authorisation together with an acceptable reactogenicity profile presented in the clinical study C4591048 substudy A and E does not raise additional concerns.

3.6. Effects Table

Table 55: Effects Table for Comirnaty with the simplified posology

Effect	Short description	Unit	Treatment	Control	Uncertainties / Strength of evidence	References
Favourable Effects						
G1/G3 GMR (95% CI)	6m-2y. XBB 1.5 2x 10 µg / 3x 3 µg	1.5 (1.3, 1.8)	N= 352 GMT= 8908	N= 224 GMT = 5915	Non-inferiority demonstrated	C4591048 SSA Phase 2/3
Seroresponse rate difference		1.3% (-2.7, 5.3)	95.2%	94.2%	Non-inferiority demonstrated	C4591048 SSA Phase 2/3
G4/G3 GMR (95% CI)	2-5y. 1x 10 µg / 6m-2y virus neg. 3x 3 µg	1.1 (0.9, 1.5)	N= 439 GMT= 6620 N= 25 neg. GMT = 817	N= 53 GMT= 5895	Non-inferiority demonstrated Low GMT in SARS-COV-2 naïve	C4591048 SSA Phase 2/3
Seroresponse rate difference		-9.0 (-11.9, -2.1)	91%	100 %	No Non-inferiority.	C4591048 SSA Phase 2/3
SSE/adults GMR (95% CI)	5-< 12 y. 1x 10 µg / adults 1x 30 µg as 4th dose	1.8 (1.5, 2.2)	N= 285 GMT= 6569	N= 300 GMT= 3636	Non-inferiority demonstrated	C4591048 SSE Phase 2/3
Seroresponse rate difference		9.0% (3.9, 14.0)	89 %	77 %	Non-inferiority demonstrated	C4591048 SSE Phase 2/3
Unfavourable Effects Children aged 6 months to <2 years of age						
Tenderness at injection site Dose 1: 16% vs 14% Dose 2: 12% vs 9%			BNT 162b2 XBB 1.5 at 10 µg	BNT 162b2 XBB 1.5 at 3 µg	Pos: positive controlled study shows similar reactogenicity profile Neg: Limited study population to identify more rare AEs	Study C4591048 substudy A Phase 2/3
Decreased appetite Dose 1: 27% vs 27% Dose 2: 20% vs 21%						
Fever Dose 1: 7% vs 6% Dose 2: 8% vs 6%						

Effect	Short description	Unit	Treatment	Control	Uncertainties / Strength of evidence	References
Unfavourable Effects Children aged 2 years to <5 years of age						
Pain at injection site Single dose: 25%			BNT 162b2 XBB 1.5 at 10 µg	N/A	Pos: Acceptable reactogenicity profile, in line with what can be expected based on previous shown data. Neg: No positive control included. Limited study population to identify more rare AEs	Study C4591048 substudy A Phase 2/3
Fatigue Single dose: 20%				N/A		
Fever Single dose: 7%				N/A		

3.7. Benefit-risk assessment and discussion

3.7.1. Importance of favourable and unfavourable effects

To support the proposed change in both dose and primary schedule in children aged 6 months to <5 years of age, the MAH has presented a phase 1/2/3 study including the targeted age groups. In the phase 2/3 part of the study, a total of 604 children aged 6 months to <2 years old, 692 children aged 2 years to <5 years old and 310 children aged 5 to <12 years old had received Comirnaty XBB 1.5 at 10 µg. The youngest group received two doses with 8 weeks in between, whereas the children >2 years of age have received a single dose at 10 µg. As a control group in the youngest age group 304 children received Comirnaty XBB 1.5 at 3 µg as a 3 dose primary series.

The new posologies for children 6m-<5 years were evaluated in C4591048 Substudy A, groups 1-4. The change in posology in 6m-< 2 years age group to replace 3x 3 µg posology with 2x 10 µg Comirnaty is supported as the non-inferiority of GMR and seroresponse were demonstrated.

In children 2- <5 years of age a single 10-µg dose Omi XBB.1.5 met non-inferiority based on GMR, but not based on difference in seroresponse rates. The results from 2- <5 y vaccinated once with 10-µg were compared to younger 6m-<2 years old age group, who were SARS-CoV-2 negative at the baseline and received current 3x 3 µg posology. The antibody titres after a single dose of 10-µg in SARS-COV-2 negative 2- <5 years old populations were modest, about 7- fold lower compared to the approved 3x 3 µg posology in 6m-< 2y. Therefore, there is a concern that one dose of 10 µg does not provide the needed protection for SARS-CoV-2 naïve children in age group 2-<5 years old. The MAH agreed to change posology for 2 doses as primary schedule for COVID-19 vaccine- naïve children in entire 6 months to <5 years old age group.

In children 5-< 12 years old a single 10-µg dose Omi XBB.1.5 met non-inferiority based on GMR and seroresponse when compared to immunogenicity results from adult, who received a single 30 µg dose Omi XBB.1.5 as their 4th dose. The immunogenicity data from C4591048 Substudy E supports the current posology for 5-<12 years old children.

The evaluation of the safety profile is mainly based on reactogenicity data where comparable reactions was identified in the children aged 6 months to <2 years old receiving 3 µg or 10 µg. In children aged 2 to <5 years old, a single dose at 10 µg did not suggest any new safety concerns.

3.7.2. Balance of benefits and risks

A sufficient immune response has been demonstrated in children aged 6 months to <2 years old receiving 2 doses of BNT162b2 XBB 1.5 at 10 µg and in children 5 to <12 years old receiving a single dose of BNT162b2 XBB 1.5 at 10 µg. A single dose of BNT162b2 XBB 1.5 at 10 µg was also immunogenic in SARS-COV-2 experienced 2-<5 years old children, but immune response was modest among SARS-COV-2 naïve children. Therefore, there is a concern that one dose of 10 µg does not provide the needed protection for SARS-COV-2 naïve children in age group 2-<5 years old. The MAH agreed to change posology for 2 doses of 10 µg as primary schedule for COVID-19 vaccine- naïve children in entire 6 months to <5 years old age group.

Overall, an acceptable safety profile has been presented with a reactogenicity profile which for the youngest children was comparable as for 3 µg. In children aged 2 to <5 years old, a single dose at 10 µg did not suggest any new safety concerns.

3.8. Conclusions

The overall B/R of Comirnaty is currently positive.

4. Recommendations

Outcome

Based on the review of the submitted data, the CHMP considers the following group of variations acceptable and therefore recommends the variation to the terms of the Marketing Authorisation, concerning the following changes:

Variation(s) requested		**Type**
C.I.6.a	C.I.6.a Addition of a new therapeutic indication or modification of an approved one	Variation type II
C.I.7.b	C.I.7.b a strength	Variation type IB

A grouped application consisting of:

C.I.6.a. To modify the indication wording for Comirnaty 10 µg/dose formulations to include infants and children from 6 months to 4 years of age, as well as the change of primary vaccination regimen from 3-dose to a 2-dose primary course in this age group, based on sub-study A (SSA) phase 2/3 of study C4591048; as well as to support the authorised 10 µg single dose based on sub-study E (SSE) of study C4591048, listed as a category 3 study in the RMP. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 6.3 and 6.6 of the SmPC for JN.1, KP.2 and LP.8.1 have been updated. Study C4591048 is a master phase 1/2/3 protocol to investigate the safety, tolerability, and immunogenicity of variant adapted Comirnaty in healthy children. The updated RMP version 17.0 has also been approved. In addition, the MAH took the opportunity to implement minor editorial changes in the PI.

C.I.7.b. To delete the 3 µg strength from the Comirnaty Marketing authorisation (EU/1/20/1528/035-036, EU/1/20/1528/042, EU/1/20/1528/050).

The group of variations leads to amendments to the annex(es) I, IIIA, IIIB and to the Risk Management Plan (RMP).

Amendments to the marketing authorisation

In view of the data submitted with the group of variations, amendments to annex(es) I, IIIA, IIIB and to the Risk Management Plan (RMP) are recommended.

Paediatric data

Furthermore, the CHMP reviewed the available paediatric data of studies subject to the agreed Paediatric Investigation Plan P/0105/2024 and the results of these studies are reflected in the Summary of Product Characteristics (SmPC) and, as appropriate, the Package Leaflet.