COVID-19 Vaccine (BNT162, PF-07302048; COMIRNATY)

BLA STN 125742/45

Response to CBER Information Request of 14 March Regarding Additional Reactogenicity Data for Adolescents 12 Through 15 Years of Age

18 March 2022

1. INTRODUCTION

Reference is made to the sBLA to extend licensure of COMIRNATY to adolescents 12 through 15 years of age submitted to FDA on 16 Dec 2021 (Sequence number 0211).

Reference is also made to the Information Request received from CBER on 07 March 2022, the response to that request submitted by Pfizer/BioNTech on 11 March 2022 (Sequence number 0271), and the follow-up Information Request received from CBER on 14 March 2022.

Below, the request is shown in ***bold italics*** followed by Pfizer/BioNTech's response in plain text.

2. RESPONSES

2.1. Request 1

The review team has a follow-up question to Pfizer's response that was submitted in STN 125742.45.4 in response to the review team's 3/7/22 clinical and statistical questions.

You state that no additional reactogenicity data have been recorded in the e-diary since the EUA. However, we note that the numbers of placebo subjects who reported any headache, chills, and diarrhea post Dose 2 are 263, 73, and 43, respectively in the SDTM (1 Month Follow-up) datasets and the draft prescribing information, while the respective counts appear to be 264, 74, and 44 in the SDTM (6 Month Follow-up) datasets. Please clarify the discrepancy and provide updated reactogenicity tables as appropriate.

Response

With reference to reactogenicity (e-diary) data from Study C4591001 for participants 12 through 15 years of age, the SDTM datasets for the 6-month follow-up include e-diary data for one additional participant who received placebo, relative to the SDTM datasets for the 1-month follow-up. Although the diary data for this participant were saved in the e-diary application on the device on 07 January and 10 January 2021 (during the 1-month follow-up period), they were not synced with the server until 07 April 2021 and were included in the data transfer of 08 April 2021. Such a delay in data synchronization can occur if the participant has connection issues that cannot be resolved, in which case the data are saved on the device and transmitted the next time there is a successful connection.

The reactogenicity tables for local reactions and systemic events by maximum severity have been updated and are provided in Table 1 and Table 2, respectively. There is no change to the results for local reactions, while data for systemic events have changed for headache, chills, and diarrhea, as noted in the request. Tables for onset and duration of reactogenicity events have not been updated, as changes to the tables would be minimal, and the label would not be impacted.

Table 1. Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Subjects 12 Through 15 Years of Age (Reactogenicity Subset) – Safety Population

		Vaccine Group (as Administered)					
		BNT162b2 (30 µg)			Placebo		
		12-15 Years			12-15 Years		
Dose	Local Reaction	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])
1	Redness[d]						
	Any	1127	65 (5.8)	(4.5, 7.3)	1127	12 (1.1)	(0.6, 1.9)
	Mild	1127	44 (3.9)	(2.9, 5.2)	1127	11 (1.0)	(0.5, 1.7)
	Moderate	1127	20 (1.8)	(1.1, 2.7)	1127	1 (0.1)	(0.0, 0.5)
	Severe	1127	1 (0.1)	(0.0, 0.5)	1127	0	(0.0, 0.3)
	Grade 4	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	Swelling[d]						
	Any	1127	78 (6.9)	(5.5, 8.6)	1127	11 (1.0)	(0.5, 1.7)
	Mild	1127	55 (4.9)	(3.7, 6.3)	1127	9 (0.8)	(0.4, 1.5)
	Moderate	1127	23 (2.0)	(1.3, 3.0)	1127	2 (0.2)	(0.0, 0.6)
	Severe	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	Grade 4	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	Pain at the injection site[e]						
	Any	1127	971 (86.2)	(84.0, 88.1)	1127	263 (23.3)	(20.9, 25.9)
	Mild	1127	467 (41.4)	(38.5, 44.4)	1127	227 (20.1)	(17.8, 22.6)
	Moderate	1127	493 (43.7)	(40.8, 46.7)	1127	36 (3.2)	(2.2, 4.4)
	Severe	1127	11 (1.0)	(0.5, 1.7)	1127	0	(0.0, 0.3)
	Grade 4	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	Any local reaction[f]	1127	976 (86.6)	(84.5, 88.5)	1127	271 (24.0)	(21.6, 26.7)
2	Redness[d]						
	Any	1097	55 (5.0)	(3.8, 6.5)	1078	10 (0.9)	(0.4, 1.7)
	Mild	1097	29 (2.6)	(1.8, 3.8)	1078	8 (0.7)	(0.3, 1.5)
	Moderate	1097	26 (2.4)	(1.6, 3.5)	1078	2 (0.2)	(0.0, 0.7)
	Severe	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Grade 4	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Swelling[d]						
	Any	1097	54 (4.9)	(3.7, 6.4)	1078	6 (0.6)	(0.2, 1.2)
	Mild	1097	36 (3.3)	(2.3, 4.5)	1078	4 (0.4)	(0.1, 0.9)
	Moderate	1097	18 (1.6)	(1.0, 2.6)	1078	2 (0.2)	(0.0, 0.7)
	Severe	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Grade 4	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Pain at the injection site[e]						
	Any	1097	866 (78.9)	(76.4, 81.3)	1078	193 (17.9)	(15.7, 20.3)
	Mild	1097	466 (42.5)	(39.5, 45.5)	1078	164 (15.2)	(13.1, 17.5)
	Moderate	1097	393 (35.8)	(33.0, 38.7)	1078	29 (2.7)	(1.8, 3.8)
	Severe	1097	7 (0.6)	(0.3, 1.3)	1078	0	(0.0, 0.3)
	Grade 4	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Any local reaction[f]	1097	872 (79.5)	(77.0, 81.8)	1078	198 (18.4)	(16.1, 20.8)
Any dose	Redness[d]						
	Any	1131	97 (8.6)	(7.0, 10.4)	1129	18 (1.6)	(0.9, 2.5)
	Mild	1131	55 (4.9)	(3.7, 6.3)	1129	15 (1.3)	(0.7, 2.2)
	Moderate	1131	41 (3.6)	(2.6, 4.9)	1129	3 (0.3)	(0.1, 0.8)
	Severe	1131	1 (0.1)	(0.0, 0.5)	1129	0	(0.0, 0.3)

Table 1. Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Subjects 12 Through 15 Years of Age (Reactogenicity Subset) – Safety Population

		Vaccine Group (as Administered)					
		BNT162b2 (30 µg)			Placebo		
		12-15 Years			12-15 Years		
Dose	Local Reaction	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])
	Grade 4	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	Swelling[d]						
	Any	1131	104 (9.2)	(7.6, 11.0)	1129	13 (1.2)	(0.6, 2.0)
	Mild	1131	69 (6.1)	(4.8, 7.7)	1129	10 (0.9)	(0.4, 1.6)
	Moderate	1131	35 (3.1)	(2.2, 4.3)	1129	3 (0.3)	(0.1, 0.8)
	Severe	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	Grade 4	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	Pain at the injection site[e]						
	Any	1131	1023 (90.5)	(88.6, 92.1)	1129	341 (30.2)	(27.5, 33.0)
	Mild	1131	394 (34.8)	(32.1, 37.7)	1129	283 (25.1)	(22.6, 27.7)
	Moderate	1131	612 (54.1)	(51.2, 57.0)	1129	58 (5.1)	(3.9, 6.6)
	Severe	1131	17 (1.5)	(0.9, 2.4)	1129	0	(0.0, 0.3)
	Grade 4	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	Any local reaction[f]	1131	1028 (90.9)	(89.1, 92.5)	1129	349 (30.9)	(28.2, 33.7)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 through Day 7 after each dose.
Note: Grade 4 reactions were classified by the investigator or medically qualified person.
a. N = number of subjects reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of subjects with the specified characteristic.
c. Exact 2-sided CI based on the Clopper and Pearson method.
d. Mild: >2.0 to 5.0 cm; moderate: >5.0 to 10.0 cm; severe: >10.0 cm; Grade 4: necrosis (redness and swelling categories) or exfoliative dermatitis (redness category only).
e. Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe pain at the injection site.
f. Any local reaction: any redness >2.0 cm, any swelling >2.0 cm, or any pain at the injection site.
PFIZER CONFIDENTIAL SDTM Creation: 05OCT2021 (18:31) Source Data: adfacevd Table Generation: 15MAR2022 (12:26)
(Data Cutoff Date: 02SEP2021, Database Snapshot Date: 27SEP2021) Output File: ./nda2_unblinded/C4591001_S_Peds_RR/adce_s010_lr_sev_ped_saf

Table 2. Systemic Events, by Maximum Severity, Within 7 Days After Each Dose – Subjects 12 Through 15 Years of Age (Reactogenicity Subset) – Safety Population

		Vaccine Group (as Administered)					
		BNT162b2 (30 µg)			Placebo		
		12-15 Years			12-15 Years		
Dose	Systemic Event	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])
1	Fever						
	≥38.0°C	1127	114 (10.1)	(8.4, 12.0)	1127	12 (1.1)	(0.6, 1.9)
	≥38.0°C to 38.4°C	1127	74 (6.6)	(5.2, 8.2)	1127	8 (0.7)	(0.3, 1.4)
	>38.4°C to 38.9°C	1127	29 (2.6)	(1.7, 3.7)	1127	2 (0.2)	(0.0, 0.6)
	>38.9°C to 40.0°C	1127	10 (0.9)	(0.4, 1.6)	1127	2 (0.2)	(0.0, 0.6)
	>40.0°C	1127	1 (0.1)	(0.0, 0.5)	1127	0	(0.0, 0.3)
	Fatigue[d]						
	Any	1127	677 (60.1)	(57.1, 62.9)	1127	457 (40.6)	(37.7, 43.5)
	Mild	1127	278 (24.7)	(22.2, 27.3)	1127	250 (22.2)	(19.8, 24.7)
	Moderate	1127	384 (34.1)	(31.3, 36.9)	1127	199 (17.7)	(15.5, 20.0)
	Severe	1127	15 (1.3)	(0.7, 2.2)	1127	8 (0.7)	(0.3, 1.4)
	Grade 4	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	Headache[d]						
	Any	1127	623 (55.3)	(52.3, 58.2)	1127	396 (35.1)	(32.3, 38.0)
	Mild	1127	361 (32.0)	(29.3, 34.8)	1127	256 (22.7)	(20.3, 25.3)
	Moderate	1127	251 (22.3)	(19.9, 24.8)	1127	131 (11.6)	(9.8, 13.6)
	Severe	1127	11 (1.0)	(0.5, 1.7)	1127	9 (0.8)	(0.4, 1.5)
	Grade 4	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	Chills[d]						
	Any	1127	311 (27.6)	(25.0, 30.3)	1127	109 (9.7)	(8.0, 11.5)
	Mild	1127	195 (17.3)	(15.1, 19.6)	1127	82 (7.3)	(5.8, 9.0)
	Moderate	1127	111 (9.8)	(8.2, 11.7)	1127	25 (2.2)	(1.4, 3.3)
	Severe	1127	5 (0.4)	(0.1, 1.0)	1127	2 (0.2)	(0.0, 0.6)
	Grade 4	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	Vomiting[e]						
	Any	1127	31 (2.8)	(1.9, 3.9)	1127	10 (0.9)	(0.4, 1.6)
	Mild	1127	30 (2.7)	(1.8, 3.8)	1127	8 (0.7)	(0.3, 1.4)
	Moderate	1127	0	(0.0, 0.3)	1127	2 (0.2)	(0.0, 0.6)
	Severe	1127	1 (0.1)	(0.0, 0.5)	1127	0	(0.0, 0.3)
	Grade 4	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	Diarrhea[f]						
	Any	1127	90 (8.0)	(6.5, 9.7)	1127	82 (7.3)	(5.8, 9.0)
	Mild	1127	77 (6.8)	(5.4, 8.5)	1127	72 (6.4)	(5.0, 8.0)
	Moderate	1127	13 (1.2)	(0.6, 2.0)	1127	10 (0.9)	(0.4, 1.6)
	Severe	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	Grade 4	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	New or worsened muscle pain[d]						
	Any	1127	272 (24.1)	(21.7, 26.7)	1127	148 (13.1)	(11.2, 15.2)
	Mild	1127	125 (11.1)	(9.3, 13.1)	1127	88 (7.8)	(6.3, 9.5)
	Moderate	1127	145 (12.9)	(11.0, 15.0)	1127	60 (5.3)	(4.1, 6.8)
	Severe	1127	2 (0.2)	(0.0, 0.6)	1127	0	(0.0, 0.3)

Table 2. Systemic Events, by Maximum Severity, Within 7 Days After Each Dose – Subjects 12 Through 15 Years of Age (Reactogenicity Subset) – Safety Population

		Vaccine Group (as Administered)					
		BNT162b2 (30 µg)			Placebo		
		12-15 Years			12-15 Years		
Dose	Systemic Event	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])
	Grade 4	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	New or worsened joint pain[d]						
	Any	1127	109 (9.7)	(8.0, 11.5)	1127	77 (6.8)	(5.4, 8.5)
	Mild	1127	66 (5.9)	(4.6, 7.4)	1127	50 (4.4)	(3.3, 5.8)
	Moderate	1127	42 (3.7)	(2.7, 5.0)	1127	27 (2.4)	(1.6, 3.5)
	Severe	1127	1 (0.1)	(0.0, 0.5)	1127	0	(0.0, 0.3)
	Grade 4	1127	0	(0.0, 0.3)	1127	0	(0.0, 0.3)
	Any systemic event[g]	1127	877 (77.8)	(75.3, 80.2)	1127	636 (56.4)	(53.5, 59.4)
	Use of antipyretic or pain medication[h]	1127	413 (36.6)	(33.8, 39.5)	1127	111 (9.8)	(8.2, 11.7)
2	Fever						
	≥38.0°C	1097	215 (19.6)	(17.3, 22.1)	1078	7 (0.6)	(0.3, 1.3)
	≥38.0°C to 38.4°C	1097	107 (9.8)	(8.1, 11.7)	1078	5 (0.5)	(0.2, 1.1)
	>38.4°C to 38.9°C	1097	83 (7.6)	(6.1, 9.3)	1078	1 (0.1)	(0.0, 0.5)
	>38.9°C to 40.0°C	1097	25 (2.3)	(1.5, 3.3)	1078	1 (0.1)	(0.0, 0.5)
	>40.0°C	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Fatigue[d]						
	Any	1097	726 (66.2)	(63.3, 69.0)	1078	264 (24.5)	(21.9, 27.2)
	Mild	1097	232 (21.1)	(18.8, 23.7)	1078	133 (12.3)	(10.4, 14.5)
	Moderate	1097	468 (42.7)	(39.7, 45.7)	1078	127 (11.8)	(9.9, 13.9)
	Severe	1097	26 (2.4)	(1.6, 3.5)	1078	4 (0.4)	(0.1, 0.9)
	Grade 4	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Headache[d]						
	Any	1097	708 (64.5)	(61.6, 67.4)	1078	264 (24.5)	(21.9, 27.2)
	Mild	1097	302 (27.5)	(24.9, 30.3)	1078	170 (15.8)	(13.6, 18.1)
	Moderate	1097	384 (35.0)	(32.2, 37.9)	1078	93 (8.6)	(7.0, 10.5)
	Severe	1097	22 (2.0)	(1.3, 3.0)	1078	1 (0.1)	(0.0, 0.5)
	Grade 4	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Chills[d]						
	Any	1097	455 (41.5)	(38.5, 44.5)	1078	74 (6.9)	(5.4, 8.5)
	Mild	1097	221 (20.1)	(17.8, 22.6)	1078	53 (4.9)	(3.7, 6.4)
	Moderate	1097	214 (19.5)	(17.2, 22.0)	1078	21 (1.9)	(1.2, 3.0)
	Severe	1097	20 (1.8)	(1.1, 2.8)	1078	0	(0.0, 0.3)
	Grade 4	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Vomiting[e]						
	Any	1097	29 (2.6)	(1.8, 3.8)	1078	12 (1.1)	(0.6, 1.9)
	Mild	1097	25 (2.3)	(1.5, 3.3)	1078	11 (1.0)	(0.5, 1.8)
	Moderate	1097	4 (0.4)	(0.1, 0.9)	1078	1 (0.1)	(0.0, 0.5)
	Severe	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Grade 4	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Diarrhea[f]						
	Any	1097	65 (5.9)	(4.6, 7.5)	1078	44 (4.1)	(3.0, 5.4)
	Mild	1097	59 (5.4)	(4.1, 6.9)	1078	39 (3.6)	(2.6, 4.9)

Table 2. Systemic Events, by Maximum Severity, Within 7 Days After Each Dose – Subjects 12 Through 15 Years of Age (Reactogenicity Subset) – Safety Population

		Vaccine Group (as Administered)					
		BNT162b2 (30 µg)			Placebo		
		12-15 Years			12-15 Years		
Dose	Systemic Event	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])
	Moderate	1097	6 (0.5)	(0.2, 1.2)	1078	5 (0.5)	(0.2, 1.1)
	Severe	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Grade 4	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	New or worsened muscle pain[d]						
	Any	1097	355 (32.4)	(29.6, 35.2)	1078	90 (8.3)	(6.8, 10.2)
	Mild	1097	152 (13.9)	(11.9, 16.0)	1078	51 (4.7)	(3.5, 6.2)
	Moderate	1097	197 (18.0)	(15.7, 20.4)	1078	37 (3.4)	(2.4, 4.7)
	Severe	1097	6 (0.5)	(0.2, 1.2)	1078	2 (0.2)	(0.0, 0.7)
	Grade 4	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	New or worsened joint pain[d]						
	Any	1097	173 (15.8)	(13.7, 18.1)	1078	51 (4.7)	(3.5, 6.2)
	Mild	1097	91 (8.3)	(6.7, 10.1)	1078	30 (2.8)	(1.9, 3.9)
	Moderate	1097	78 (7.1)	(5.7, 8.8)	1078	21 (1.9)	(1.2, 3.0)
	Severe	1097	4 (0.4)	(0.1, 0.9)	1078	0	(0.0, 0.3)
	Grade 4	1097	0	(0.0, 0.3)	1078	0	(0.0, 0.3)
	Any systemic event[g]	1097	904 (82.4)	(80.0, 84.6)	1078	440 (40.8)	(37.9, 43.8)
	Use of antipyretic or pain medication[h]	1097	557 (50.8)	(47.8, 53.8)	1078	95 (8.8)	(7.2, 10.7)
Any dose	Fever						
	≥38.0°C	1131	275 (24.3)	(21.8, 26.9)	1129	17 (1.5)	(0.9, 2.4)
	≥38.0°C to 38.4°C	1131	141 (12.5)	(10.6, 14.5)	1129	11 (1.0)	(0.5, 1.7)
	>38.4°C to 38.9°C	1131	100 (8.8)	(7.3, 10.6)	1129	3 (0.3)	(0.1, 0.8)
	>38.9°C to 40.0°C	1131	33 (2.9)	(2.0, 4.1)	1129	3 (0.3)	(0.1, 0.8)
	>40.0°C	1131	1 (0.1)	(0.0, 0.5)	1129	0	(0.0, 0.3)
	Fatigue[d]						
	Any	1131	876 (77.5)	(74.9, 79.9)	1129	538 (47.7)	(44.7, 50.6)
	Mild	1131	239 (21.1)	(18.8, 23.6)	1129	266 (23.6)	(21.1, 26.1)
	Moderate	1131	597 (52.8)	(49.8, 55.7)	1129	260 (23.0)	(20.6, 25.6)
	Severe	1131	40 (3.5)	(2.5, 4.8)	1129	12 (1.1)	(0.6, 1.8)
	Grade 4	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	Headache[d]						
	Any	1131	854 (75.5)	(72.9, 78.0)	1129	506 (44.8)	(41.9, 47.8)
	Mild	1131	324 (28.6)	(26.0, 31.4)	1129	303 (26.8)	(24.3, 29.5)
	Moderate	1131	499 (44.1)	(41.2, 47.1)	1129	194 (17.2)	(15.0, 19.5)
	Severe	1131	31 (2.7)	(1.9, 3.9)	1129	9 (0.8)	(0.4, 1.5)
	Grade 4	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	Chills[d]						
	Any	1131	557 (49.2)	(46.3, 52.2)	1129	160 (14.2)	(12.2, 16.3)
	Mild	1131	257 (22.7)	(20.3, 25.3)	1129	115 (10.2)	(8.5, 12.1)
	Moderate	1131	276 (24.4)	(21.9, 27.0)	1129	43 (3.8)	(2.8, 5.1)
	Severe	1131	24 (2.1)	(1.4, 3.1)	1129	2 (0.2)	(0.0, 0.6)

Table 2. Systemic Events, by Maximum Severity, Within 7 Days After Each Dose – Subjects 12 Through 15 Years of Age (Reactogenicity Subset) – Safety Population

		Vaccine Group (as Administered)					
		BNT162b2 (30 µg)			Placebo		
		12-15 Years			12-15 Years		
Dose	Systemic Event	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])
	Grade 4	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	Vomiting[e]						
	Any	1131	59 (5.2)	(4.0, 6.7)	1129	21 (1.9)	(1.2, 2.8)
	Mild	1131	54 (4.8)	(3.6, 6.2)	1129	18 (1.6)	(0.9, 2.5)
	Moderate	1131	4 (0.4)	(0.1, 0.9)	1129	3 (0.3)	(0.1, 0.8)
	Severe	1131	1 (0.1)	(0.0, 0.5)	1129	0	(0.0, 0.3)
	Grade 4	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	Diarrhea[f]						
	Any	1131	141 (12.5)	(10.6, 14.5)	1129	107 (9.5)	(7.8, 11.3)
	Mild	1131	123 (10.9)	(9.1, 12.8)	1129	92 (8.1)	(6.6, 9.9)
	Moderate	1131	18 (1.6)	(0.9, 2.5)	1129	15 (1.3)	(0.7, 2.2)
	Severe	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	Grade 4	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	New or worsened muscle pain[d]						
	Any	1131	477 (42.2)	(39.3, 45.1)	1129	196 (17.4)	(15.2, 19.7)
	Mild	1131	187 (16.5)	(14.4, 18.8)	1129	110 (9.7)	(8.1, 11.6)
	Moderate	1131	282 (24.9)	(22.4, 27.6)	1129	84 (7.4)	(6.0, 9.1)
	Severe	1131	8 (0.7)	(0.3, 1.4)	1129	2 (0.2)	(0.0, 0.6)
	Grade 4	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	New or worsened joint pain[d]						
	Any	1131	229 (20.2)	(17.9, 22.7)	1129	107 (9.5)	(7.8, 11.3)
	Mild	1131	122 (10.8)	(9.0, 12.7)	1129	63 (5.6)	(4.3, 7.1)
	Moderate	1131	102 (9.0)	(7.4, 10.8)	1129	44 (3.9)	(2.8, 5.2)
	Severe	1131	5 (0.4)	(0.1, 1.0)	1129	0	(0.0, 0.3)
	Grade 4	1131	0	(0.0, 0.3)	1129	0	(0.0, 0.3)
	Any systemic event[g]	1131	1026 (90.7)	(88.9, 92.3)	1129	726 (64.3)	(61.4, 67.1)
	Use of antipyretic or pain medication[h]	1131	664 (58.7)	(55.8, 61.6)	1129	176 (15.6)	(13.5, 17.8)

Table 2. Systemic Events, by Maximum Severity, Within 7 Days After Each Dose – Subjects 12 Through 15 Years of Age (Reactogenicity Subset) – Safety Population

		Vaccine Group (as Administered)					
		BNT162b2 (30 µg)			Placebo		
		12-15 Years			12-15 Years		
Dose	Systemic Event	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 through Day 7 after each dose. Grade 4 events were classified by the investigator or medically qualified person.
Note: Subject C4591001 1077 10771278 (13 years of age) experienced systemic events, including a temperature of 40.4°C, on the day of Dose 2. Since these events were recorded as adverse events and not in the e-diary, they do not appear in this table.
a. N = number of subjects reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of subjects with the specified characteristic.
c. Exact 2-sided CI based on the Clopper and Pearson method.
d. Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity; Grade 4: emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
e. Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration; Grade 4: emergency room visit or hospitalization for severe vomiting.
f. Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours; Grade 4: emergency room visit or hospitalization for severe diarrhea.
g. Any systemic event: any fever ≥38.0°C, any fatigue, any vomiting, any chills, any diarrhea, any headache, any new or worsened muscle pain, or any new or worsened joint pain.
h. Severity was not collected for use of antipyretic or pain medication.
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