

Pfizer-BioNTech COVID-19 Vaccine (BNT162, PF-07302048)

**Response to 30 April 2021 Information Request Regarding Physical Exam Findings,
Case Narratives for Subjects with Psychiatric Diagnoses and Deep Vein Thrombosis**

03 May 2021

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1. INTRODUCTION

Reference is made to the Emergency Use Authorization (EUA) for Pfizer-BioNTech COVID-19 Vaccine for the active immunization to prevent COVID-19 in individuals ≥ 16 years of age and older issued on 11 December 2020. Further reference is made to the Amendment to the EUA submitted 09 April 2021 to extend the indication to 12 years of age.

The following information is provided in response to the Information Request (IR) received from the FDA on 30 April 2021 regarding physical exam findings, case narratives for subjects with psychiatric diagnoses and deep vein thrombosis.

CBER's request in ***bold italics*** is followed by the Sponsor's responses below.

2. QUESTIONS

2.1. Question 1

For subject # 1007 10071620 (neuralgia)- include details of physical exam findings, including neurological findings, psychologist's conclusions, and clinical laboratory evaluations, diagnosis, treatments administered and outcome.

Response

Please refer to the [EUA Section 6.2.2.1.1.3.4.1 \(page 47\)](#) for a summary of the neuralgia case which was considered to be unrelated to treatment by the investigator. Further information for [C4591001 1007 10071620](#) is provided in [C4591001_Narrative_Query1_Neuralgia_Unblinded](#).

2.2. Question 2

Please submit detailed case narrative comments and all available clinical information, to include any physical and psychiatric examinations, and hospital summaries, diagnosis, treatments administered and outcomes, for each of the eighteen subjects (12 in vaccine group and 6 in the placebo group) with events listed under the Preferred Term "Psychiatric Disorders" from Table 8 of the eua-amend-12-15-years.pdf submitted to EUA 27034 in amendment 132 on April 9, 2021.

Response

Detailed case narratives are provided in [C4591001_Narrative_Query2_Psychiatric Disorders_Unblinded](#) for participants as listed in Table 1.

Table 1. Question 2: Case Narratives Subject IDs for Participants Who Received BNT162b2 or Placebo

BNT162b2	Placebo
C4591001 1001 10011125	C4591001 1044 10441373
C4591001 1006 10061272	C4591001 1123 11231442
C4591001 1007 10071500	C4591001 1141 11411010
C4591001 1039 10391250	C4591001 1150 11501193
C4591001 1039 10391326	C4591001 1152 11521654
C4591001 1077 10771278	C4591001 1270 12701236
C4591001 1095 10951308	
C4591001 1095 10951310	
C4591001 1123 11231507	
C4591001 1126 11261205	
C4591001 1141 11411029	
C4591001 1147 11471262	

Source: C4591001_Narrative_Query2_Psychiatric Disorders_Unblinded

The CIOMS report identifiers are provided in Table 2.

Table 2. Question 2 CIOMS Reports

Subject ID	CIOMS Report
C4591001 1006 10061272	2021009347 10061272
C4591001 1039 10391326	2021241177 10391326
C4591001 1123 11231507	2021168083 11231507

Some overlap of information provided between response to Question 2 and Question 3 is likely.

2.3. Question 3

Please submit detailed case narrative comments and all available clinical information, to include any physical and psychiatric examinations, and hospital summaries, diagnosis, treatments administered and outcomes, for each of the thirteen subjects (8 in vaccine group and 6 in placebo group) [Note: Typo in the request, there should be 8 vaccine and 5 in placebo] with events listed under the Preferred Term “Psychiatric Disorders” from Table 9 of the eua-amend-12-15-years.pdf submitted to EUA 27034 in amendment 132 on April 9, 2021.

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Response

Detailed case narratives are provided in [C4591001_Narrative_Query3_Psychiatric Disorders_Unblinded](#) for participants as listed in Table 3.

Table 3. Question 3: Case Narratives Subject IDs for Participants Who Received BNT162b2 or Placebo

BNT162b2	Placebo
C4591001 1006 10061272	C4591001 1044 10441373
C4591001 1007 10071500	C4591001 1123 11231442
C4591001 1039 10391250	C4591001 1150 11501193
C4591001 1039 10391326	C4591001 1152 11521654
C4591001 1077 10771278	C4591001 1270 12701236
C4591001 1123 11231507	
C4591001 1147 11471262	
C4591001 1270 12701222	

Source: C4591001_Narrative_Query3_Psychiatric Disorders_Unblinded

The CIOMS report identifiers are provided in Table 4 .

Table 4. Question 4 CIOMS Reports

Subject ID	CIOMS Report
C4591001 1123 11231507	2021168083 11231507
C4591001 1270 12701222	2021195810 12701222

2.4. Question 4

Please submit detailed case narrative comments and all available clinical information, to include any physical and psychiatric examinations, and hospital summaries, diagnosis, treatments administered and outcomes for each of the five subjects [Note: Typo in the request, should be 4 subjects. One subject reported two AEs.] with events listed under the Preferred Term “Psychiatric Disorders” from Table 11 of the eua-amend-12-15-years.pdf submitted to EUA 27034 in amendment 132 on April 9, 2021.

Response

Detailed case narratives are provided in [C4591001_Narrative_Query4_Psychiatric Disorders_Unblinded](#) for participants listed in Table 5.

Table 5. Case Narratives Subject IDs for Participants Who Received BNT162b2

BNT162b2	
C4591001	1006 10061272
C4591001	1039 10391326
C4591001	1123 11231507
C4591001	1270 12701222

2.5. Question 5

Provide a table displaying baseline demographic information about the safety population in participants 12-15 years of age, by treatment group, to show numbers and percentage of participants with known history of any psychiatric diagnoses, in addition to specific diagnoses of depression, anxiety, generalized anxiety disorder, or history of suicidal ideation, and current status of these conditions (active, under treatment, inactive) at the time of enrollment.

Response

Overall, 25% of 12-15 year old participants treated with BNT162 had a psychiatric diagnosis at baseline. The psychiatric medical history is detailed in [Table 6](#). Most participants had an ongoing psychiatric history at enrollment. Few (12) had their psychiatric diagnosis resolved prior to enrollment (labeled “before” in the table). The demographics of the participants with a psychiatric medical history is presented in [Table 7](#).

Table 6. Medical History – Subjects With Psychiatric Disorders and Medical History Status – Subjects 12 Through 15 Years of Age – Safety Population

System Organ Class Preferred Term	Vaccine Group (as Administered)			
	BNT162b2 (30 µg)		Placebo	
	Before (N ^a =12)	Ongoing (N ^a =285)	Before (N ^a =8)	Ongoing (N ^a =276)
	n ^b (%)	n ^b (%)	n ^b (%)	n ^b (%)
Psychiatric disorders	12 (100.0)	285 (100.0)	8 (100.0)	276 (100.0)
Adjustment disorder with depressed mood	1 (8.3)	0	0	1 (0.4)
Adjustment disorder with mixed anxiety and depressed mood	0	0	0	1 (0.4)
Aggression	1 (8.3)	0	0	1 (0.4)
Anger	0	0	1 (12.5)	0
Anxiety	2 (16.7)	102 (35.8)	0	93 (33.7)
Anxiety disorder	0	4 (1.4)	1 (12.5)	2 (0.7)
Attention deficit hyperactivity disorder	2 (16.7)	180 (63.2)	3 (37.5)	162 (58.7)
Autism spectrum disorder	0	10 (3.5)	0	10 (3.6)
Behaviour disorder	0	2 (0.7)	0	1 (0.4)
Bipolar disorder	0	2 (0.7)	0	0
Childhood depression	0	1 (0.4)	0	0
Chronic tic disorder	0	0	0	2 (0.7)
Depression	3 (25.0)	47 (16.5)	1 (12.5)	44 (15.9)
Depressive symptom	0	0	0	1 (0.4)
Disruptive mood dysregulation disorder	0	3 (1.1)	0	2 (0.7)
Eating disorder	0	1 (0.4)	0	2 (0.7)

Table 6. Medical History – Subjects With Psychiatric Disorders and Medical History Status – Subjects 12 Through 15 Years of Age – Safety Population

System Organ Class Preferred Term	Vaccine Group (as Administered)			
	BNT162b2 (30 µg)		Placebo	
	Before (N ^a =12)	Ongoing (N ^a =285)	Before (N ^a =8)	Ongoing (N ^a =276)
	n ^b (%)	n ^b (%)	n ^b (%)	n ^b (%)
Enuresis	0	3 (1.1)	1 (12.5)	1 (0.4)
Gender dysphoria	0	2 (0.7)	0	0
Generalised anxiety disorder	0	8 (2.8)	0	14 (5.1)
Hallucination, auditory	0	1 (0.4)	0	0
Impulse-control disorder	0	2 (0.7)	0	0
Impulsive behaviour	0	0	0	1 (0.4)
Insomnia	0	27 (9.5)	0	28 (10.1)
Learning disorder	0	0	0	1 (0.4)
Major depression	1 (8.3)	3 (1.1)	1 (12.5)	4 (1.4)
Neurodevelopmental disorder	0	1 (0.4)	0	0
Nightmare	0	1 (0.4)	0	0
Obsessive-compulsive disorder	0	5 (1.8)	0	8 (2.9)
Oppositional defiant disorder	0	2 (0.7)	2 (25.0)	1 (0.4)
Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection	0	0	0	1 (0.4)
Persistent depressive disorder	0	1 (0.4)	0	0
Post-traumatic stress disorder	1 (8.3)	3 (1.1)	1 (12.5)	4 (1.4)
Reactive attachment disorder of infancy or early childhood	0	0	0	1 (0.4)
Reading disorder	0	0	0	1 (0.4)

Table 6. Medical History – Subjects With Psychiatric Disorders and Medical History Status – Subjects 12 Through 15 Years of Age – Safety Population

System Organ Class Preferred Term	Vaccine Group (as Administered)			
	BNT162b2 (30 µg)		Placebo	
	Before (N ^a =12)	Ongoing (N ^a =285)	Before (N ^a =8)	Ongoing (N ^a =276)
	n ^b (%)	n ^b (%)	n ^b (%)	n ^b (%)
Separation anxiety disorder	0	1 (0.4)	0	0
Sleep disorder	0	0	0	3 (1.1)
Social anxiety disorder	0	0	0	1 (0.4)
Speech sound disorder	0	1 (0.4)	0	0
Suicidal ideation	1 (8.3)	0	0	1 (0.4)
Tic	1 (8.3)	2 (0.7)	0	2 (0.7)

Note: MedDRA (v23.1) coding dictionary applied.

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but not included in the analyses of the overall study objectives.

Note: A subject may be counted in both "Before" and "Ongoing" columns.

Note: 'Before' is defined as a subject having the condition previously but this was resolved.

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

b. n = Number of subjects with the specified characteristic. Subjects with multiple occurrences of the same preferred term are counted only once.

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Table 7. Demographic Characteristics – Subjects With Psychiatric Disorders and Medical History Status– Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg)		Placebo	
	Before (N ^a =12) n ^b (%)	Ongoing (N ^a =285) n ^b (%)	Before (N ^a =8) n ^b (%)	Ongoing (N ^a =276) n ^b (%)
Sex				
Male	5 (41.7)	137 (48.1)	5 (62.5)	140 (50.7)
Female	7 (58.3)	148 (51.9)	3 (37.5)	136 (49.3)
Race				
White	11 (91.7)	246 (86.3)	6 (75.0)	233 (84.4)
Black or African American	1 (8.3)	13 (4.6)	2 (25.0)	17 (6.2)
American Indian or Alaska Native	0	1 (0.4)	0	3 (1.1)
Asian	0	12 (4.2)	0	14 (5.1)
Native Hawaiian or other Pacific Islander	0	1 (0.4)	0	0
Multiracial	0	11 (3.9)	0	7 (2.5)
Not reported	0	1 (0.4)	0	2 (0.7)
Ethnicity				
Hispanic/Latino	0	29 (10.2)	1 (12.5)	33 (12.0)
Non-Hispanic/non-Latino	12 (100.0)	256 (89.8)	7 (87.5)	241 (87.3)
Not reported	0	0	0	2 (0.7)
Country				

Table 7. Demographic Characteristics – Subjects With Psychiatric Disorders and Medical History Status– Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg)		Placebo	
	Before (N ^a =12) n ^b (%)	Ongoing (N ^a =285) n ^b (%)	Before (N ^a =8) n ^b (%)	Ongoing (N ^a =276) n ^b (%)
USA	12 (100.0)	285 (100.0)	8 (100.0)	276 (100.0)
Age at vaccination (years)				
Mean (SD)	13.5 (0.80)	13.6 (1.11)	14.3 (1.04)	13.7 (1.10)
Median	13.0	14.0	14.5	14.0
Min, max	(13, 15)	(12, 15)	(12, 15)	(12, 15)
Baseline SARS-CoV-2 status				
Positive ^c	0	10 (3.5)	0	10 (3.6)
Negative ^d	12 (100.0)	258 (90.5)	6 (75.0)	248 (89.9)
Missing	0	17 (6.0)	2 (25.0)	18 (6.5)
Body mass index (BMI) Obese ^e				
Yes	3 (25.0)	40 (14.0)	2 (25.0)	40 (14.5)
No	9 (75.0)	245 (86.0)	6 (75.0)	236 (85.5)
Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.				
Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately.				
Note: A subject may be counted in both "Before" and "Ongoing" columns.				
Note: 'Before' is defined as a subject having the condition previously but this was resolved.				
a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.				
b. n = Number of subjects with the specified characteristic.				
c. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.				

Table 7. Demographic Characteristics – Subjects With Psychiatric Disorders and Medical History Status– Subjects 12 Through 15 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg)		Placebo	
	Before (N ^a =12) n ^b (%)	Ongoing (N ^a =285) n ^b (%)	Before (N ^a =8) n ^b (%)	Ongoing (N ^a =276) n ^b (%)
d. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.				
e. For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm .				
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2.6. Question 6

For subject 16-55 year of age, please provide detailed case narrative comments for 8 BNT162b2 and 8 placebo participants [Note: Typo in the request, should be 8 subjects total, 4 BNT and 4 placebo] with deep vein thrombosis, including clinical laboratory results for platelet counts, treatments administered and outcomes.

Response

Detailed case narratives are provided in [C4591001_Narrative_Query6_Deep Vein Thrombosis_Unblinded](#) for participants listed in Table 8.

Table 8. Question 6: Case Narratives Subject IDs for Participants Who Received BNT162b2 or Placebo

BNT162b2	Placebo
C4591001 1003 10031207	C4591001 1013 10131089
C4591001 1013 10131207	C4591001 1018 10181090
C4591001 1013 10131653	C4591001 1125 11251053
C4591001 1156 11561006	C4591001 1226 12262052

Source: [C4591001_Narrative_Query6_Deep Vein Thrombosis_Unblinded](#)

The CIOMS report identifiers are provided in Table 9.

Table 9. Question 6 CIOMS Reports

Subject ID	CIOMS Report
BNT162b2	2021008512 10031207
	2020511163 10131653
	2020347643 11561006
Placebo	2020506317 10131089
	2020503990 10181090
	2021159077 12262052

3. NEW SUPPORTING INFORMATION

[C4591001_Narrative_Query1_Neuralgia_Unblinded](#)

[C4591001_Narrative_Query2_Psychiatric Disorders_Unblinded](#)

[C4591001_Narrative_Query3_Psychiatric Disorders_Unblinded](#)

[C4591001_Narrative_Query4_Psychiatric Disorders_Unblinded](#)

[C4591001_Narrative_Query6_Deep Vein Thrombosis_Unblinded](#)

[CIOMS Reports](#)

4. REFERENCES

None

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Perez, John

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Final Approval

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