

Data Fitness Findings Report

IND27034

BioNTech SE and Pfizer, November 2020

Findings			Notes
BNT162-01			
Title: <i>A Multi-site, Phase I/II, 2-Part, Dose-Escalation Trial Investigating the Safety and Immunogenicity of Four Prophylactic SARS-CoV-2 RNA Vaccines Against COVID-19 Using Different Dosing Regimens in Healthy Adults</i>			
Document / Standard	Version	Notes	
annotated CRF		Seems fine	
SDTM Implementation Guide	SDTM-IG v3.2		
SDTM Controlled Terminology	2020-03-27		
SDTM define.xml	V2.0	Seems fine	
Medications Dictionary	WHODRUG GLOBAL B3 March 1, 2020		
Medical Events Dictionary (MedDRA)	V23.0		
SDTM Reviewer's Guide	PhUSE template	Seems fine	
<p>From cSDRG: Data cutoff date of 13Aug2020 is applied by comparing XXDTC or XXSTDC from respective SDTM domains. Apart from data cutoff this esub is limited to cohorts described in the section 2.3.1 of cSDRG.</p>			

C4591001-ia-efficacy (Phase 2/3 Interim Analysis)

Title: A Phase 1/2/3 Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals.

Document / Standard	Version	Notes
annotated CRF		Seems fine
SDTM Implementation Guide	SDTM-IG v3.2	
SDTM Controlled Terminology	2020-03-27	
SDTM define.xml	V2.0	Seems fine
Medications Dictionary	WHODD GLOBALV3Mar20, WHO DDE v202003	
Medical Events Dictionary (MedDRA)	V23.1	
SDTM Reviewer's Guide	PhUSE template	Seems fine

From cSDRG: The IA efficacy analysis data with a cutoff of 4NOV2020 was included in this submission. In addition, a subject cutoff to exclude phase 1 subjects was also applied to the data. Only subjects in Phase 2/3 that had informed consent date after 27JUL2020 were included.

ADaM folder contains: adc19ef, adsl, adsympt

C4591001-safety-fa-eff (Final Efficacy/EUA Safety Analysis)

Title: A Phase 1/2/3 Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals.

Document / Standard	Version	Notes
annotated CRF		Seems fine
SDTM Implementation Guide	SDTM-IG v3.2	
SDTM Controlled Terminology	2016-12-16	
SDTM define.xml	V2.0	Seems fine
Medications Dictionary	GLOBALB3Mar19	
Medical Events Dictionary (MedDRA)	V21.1	
SDTM Reviewer's Guide	PhUSE template	Seems fine

From cSDRG: The final analysis data with a cutoff of 14NOV2020 was included in this submission. Screen failure data was also dropped as part of the cutoff process. Details about the cutoff algorithm applied to the SDTM data:

All records with ASTDT <= &cutoff are included. In addition,

If .<ASTDT <= &cutoff and AEENDT > cutoff date, then

- AEENDTC and AEENDY is set to missing
- AEENRTPT = 'ONGOING'
- AEENTPT = 'Last Subject Encounter'
- AEOUT = 'NOT RECOVERED/NOT RESOLVED'

end;

else if AESTDTC = '' and AEENDTC ne '' and AENDT <= &cutoff then the record is included.

If AESTDTC and AEENDTC are both missing then the record is included.

DROP ASTDT and AENDT

ADaM folder contains: adae, adc19ef, adcevd, adds, adfacevd, admh, adsl, adsympt, adva

Data Issues

Missing MedDRA coding data

- Study c4591001-ia-efficacy:

aeedecod	aeptcd	aellt	aelltcd	aeht	aehtcd	aehtgt	aehtgtcd	aebodsys	aebdsycd	aesoc	aesoccd	Freq
populated	null	null	null	null	null	null	null	null	null	null	null	97
populated	populated	populated	populated	populated	populated	populated	populated	populated	populated	populated	populated	16670

- Study c4591001-safety-fa-eff

aeedecod	aeptcd	aellt	aelltcd	aeht	aehtcd	aehtgt	aehtgtcd	aebodsys	aebdsycd	aesoc	aesoccd	Freq
populated	null	null	null	null	null	null	null	null	null	null	null	89
populated	populated	populated	populated	populated	populated	populated	populated	populated	populated	populated	populated	20228

- Note: For both studies, AEDECOD = 'Uncoded' when the rest of the MedDRA levels are null. In ADAE (for study c4591001-safety-fa-eff), for these uncoded records, AEDECOD values are a copy of AETERM, but upper cased, and two @ symbols attached. For example, AETERM 'Injection site pain' has ADAE.AEDECOD = 'INJECTION SITE PAIN@@'
- cSDRG explanation: Study was ongoing at the time of data cutoff therefore some AE terms were not yet coded in MedDRA. These terms were set to 'Uncoded' in AE dataset for transparency. These terms will be coded for the final reporting event for this study once the study is completed.

Subjects have multiple DISPOSITION EVENT records for the same EPOCH and DSSTDTC

- Studies c4591001-ia-efficacy and c4591001-safety-fa-eff
- Need to use SUPPDS.DSPHASE to distinguish whether its VACCINATION or FOLLOW-UP or SCREENING
- Example of just a few out of many subjects in c4591001-safety-fa-eff:

usubjid	dsseq	dsterm	dsdecod	dscat	epoch	dsstdtc	dsstdy	suppds.dspphase
C4591001 1005 10051308	5	busy work schedule	WITHDRAWAL BY SUBJECT	DISPOSITION EVENT	VACCINATION	10/19/2020	1	FOLLOW-UP
C4591001 1005 10051308	4	busy work schedule	WITHDRAWAL BY SUBJECT	DISPOSITION EVENT	VACCINATION	10/19/2020	1	VACCINATION
C4591001 1005 10051308	1	COMPLETED	COMPLETED	DISPOSITION EVENT	VACCINATION	10/19/2020	1	SCREENING
C4591001 1013 10131017	5	SUBJECT WITHDREW CONSENT FROM STUDY.	WITHDRAWAL BY SUBJECT	DISPOSITION EVENT	SCREENING	7/30/2020	1	FOLLOW-UP

C4591001 1013 10131017	4	SUBJECT CHANGED HIS DECISION AND WAS RANDOMIZED INTO SYSTEM.	WITHDRAWAL BY SUBJECT	DISPOSITION EVENT	SCREENING	7/30/2020	1	VACCINATION
C4591001 1013 10131017	1	COMPLETED	COMPLETED	DISPOSITION EVENT	SCREENING	7/30/2020	1	SCREENING

Subjects have AE records with AEACN = DRUG WITHDRAWN but no ADVERSE EVENT record in DS

- Study BNT162-01 – see report “[IND27034 - BNT162-01 - AEACN is DRUG WITHDRAWN but no ADVERSE EVENT record in DS.xlsx](#)”
- Study c4591001-ia-efficacy – see report “[IND27034 - c4591001-ia-efficacy - AEACN is DRUG WITHDRAWN but no ADVERSE EVENT record in DS.xlsx](#)”
- Study c4591001-safety-fa-eff – see report “[IND27034 - c4591001-safety-fa-eff - AEACN is DRUG WITHDRAWN but no ADVERSE EVENT record in DS.xlsx](#)”

Subjects have multiple baseline records in VS

- Study BNT162-01 – 40 records, 5 subjects – see report “[IND27034 - BNT162-01 - Multiple baseline records in VS.xlsx](#)”

Subjects have multiple baseline records in LB

- Study BNT162-01 – 100 records, 5 subjects – see report “[IND27034 - BNT162-01 - Multiple baseline records in LB.xlsx](#)”

Reactogenicity events in CE with a duration of at least 7 days, but aren’t in the AE domain

- Study BNT162-01 – 13 records

usubjid	ceterm	cestdtc	ceendtc
BNT162-01-276-01-0003	Injection site reaction - Tenderness	5/19/2020	5/26/2020
BNT162-01-276-01-0005	Fatigue	5/15/2020	5/22/2020
BNT162-01-276-01-0010	Fatigue	4/24/2020	5/2/2020
BNT162-01-276-01-0010	Headache	4/25/2020	5/2/2020
BNT162-01-276-01-0010	Injection site reaction - Pain	4/25/2020	5/2/2020
BNT162-01-276-01-0010	Injection site reaction - Tenderness	4/25/2020	5/2/2020
BNT162-01-276-01-0010	Malaise	4/25/2020	5/2/2020
BNT162-01-276-01-0010	Myalgia	4/25/2020	5/2/2020
BNT162-01-276-01-0019	Headache	5/20/2020	5/27/2020

BNT162-01-276-02-0156	Injection site reaction - Tenderness	7/23/2020	7/30/2020
BNT162-01-276-02-0160	Fatigue	6/29/2020	7/7/2020
BNT162-01-276-02-0160	Headache	6/30/2020	7/7/2020
BNT162-01-276-02-0160	Malaise	6/30/2020	7/7/2020

DDDTC date is after RFPENDTC

- Study c4591001-ia-efficacy - 1 records (33.33%)

USUBJID	DDTEST	DDORRES	DDDTC	RFPENDTC	Last Disposition date	DSDECOD
C4591001 1162 11621327	PRIMARY CAUSE OF DEATH	atherosclerotic disease	9/24/2020	9/13/2020	9/13/2020	DEATH

- Study c4591001-safety-fa-eff - 3 records (50%)

USUBJID	DDTEST	DDORRES	DDDTC	RFPENDTC	Last Disposition date	DSDECOD
C4591001 1066 10661350	PRIMARY CAUSE OF DEATH	myocardial infarction	11/10/2020	11/3/2020	11/3/2020	DEATH
C4591001 1081 10811194	PRIMARY CAUSE OF DEATH	Cause is currently unknown. Detail will be updated once the death certificate has been received	11/11/2020	11/1/2020	11/1/2020	DEATH
C4591001 1162 11621327	PRIMARY CAUSE OF DEATH	atherosclerotic disease	9/24/2020	9/13/2020	9/13/2020	DEATH

EXSTDTC/EXENDTC date is after RFPENDTC

- Study c4591001-ia-efficacy - 25 records (0.03%)

USUBJID	EXTRT	EXSTDTC	RFPENDTC
C4591001 1013 10131358	Placebo	2020-10-06T14:32:00	9/21/2020
C4591001 1013 10131622	BNT162b2	2020-10-28T15:20:00	10/19/2020
C4591001 1019 10191178	BNT162b2	2020-10-08T12:09:00	9/30/2020
C4591001 1024 10241117	Placebo	2020-10-16T16:10:00	10/7/2020

C4591001 1028 10281292	Placebo	2020-10-30T09:15:00	10/29/2020
C4591001 1044 10441116	Placebo	2020-10-29T10:11:00	10/5/2020
C4591001 1044 10441165	BNT162b2	2020-10-19T10:40:00	10/6/2020
C4591001 1044 10441214	BNT162b2	2020-10-30T10:18:00	10/22/2020
C4591001 1072 10721037	Placebo	2020-10-07T12:34:00	9/9/2020
C4591001 1084 10841481	Placebo	2020-11-02T11:25:00	10/29/2020
C4591001 1088 10881045	BNT162b2	2020-10-26T10:53:00	9/8/2020
C4591001 1088 10881080	Placebo	2020-10-12T16:44:00	9/11/2020
C4591001 1088 10881139	BNT162b2	2020-10-15T14:05:00	9/21/2020
C4591001 1092 10921175	Placebo	2020-11-04T09:30:00	9/9/2020
C4591001 1097 10971118	Placebo	2020-10-15T09:49:00	10/13/2020
C4591001 1098 10981209	Placebo	2020-10-15T14:36:00	10/13/2020
C4591001 1107 11071189	Placebo	2020-10-07T13:04:00	9/22/2020
C4591001 1109 11091408	BNT162b2	2020-10-07T15:49:00	9/22/2020
C4591001 1128 11281353	Placebo	2020-10-19T10:00:00	10/5/2020
C4591001 1141 11411096	BNT162b2	2020-10-13T13:23:00	9/24/2020
C4591001 1156 11561193	BNT162b2	2020-10-21T15:14:00	10/20/2020
C4591001 1226 12261684	BNT162b2	2020-10-16T13:05:00	10/2/2020
C4591001 1226 12261821	Placebo	2020-10-22T08:53:00	10/8/2020
C4591001 1226 12262353	Placebo	2020-10-23T11:25:00	10/20/2020
C4591001 1247 12471092	Placebo	2020-10-29T12:07:00	10/20/2020

- Study c4591001-safety-fa-eff - 18 records (0.02%)

USUBJID	EXTRT	EXSTDTC	RFPENDTC
C4591001 1013 10131544	BNT162b2	2020-11-04T13:47:00	10/5/2020
C4591001 1013 10131622	BNT162b2	2020-10-28T15:20:00	10/19/2020
C4591001 1013 10131738	BNT162b2	2020-11-11T15:27:00	11/5/2020
C4591001 1024 10241117	Placebo	2020-10-16T16:10:00	10/7/2020
C4591001 1028 10281292	Placebo	2020-10-30T09:15:00	10/29/2020
C4591001 1044 10441116	Placebo	2020-10-29T10:11:00	10/5/2020

C4591001 1044 10441214	BNT162b2	2020-10-30T10:18:00	10/22/2020
C4591001 1056 10561232	Placebo	2020-11-04T12:40:00	10/7/2020
C4591001 1079 10791143	Placebo	2020-11-06T15:33:00	9/9/2020
C4591001 1079 10791264	BNT162b2	2020-11-04T13:48:00	9/30/2020
C4591001 1088 10881045	BNT162b2	2020-10-26T10:53:00	9/8/2020
C4591001 1120 11201299	BNT162b2	2020-10-19T13:48:00	10/12/2020
C4591001 1122 11221052	Placebo	2020-11-13T13:15:00	10/30/2020
C4591001 1123 11231345	Placebo	2020-11-05T09:46:00	11/2/2020
C4591001 1156 11561193	BNT162b2	2020-10-21T15:14:00	10/20/2020
C4591001 1226 12261797	BNT162b2	2020-11-06T12:36:00	10/7/2020
C4591001 1226 12262083	Placebo	2020-11-07T09:18:00	10/27/2020
C4591001 1247 12471092	Placebo	2020-10-29T12:07:00	10/20/2020

cSDRG explanation: "At the time of data extraction, study is still ongoing and RFPENDTC is derived as the maximum of date of disposition, Subject Visits, date of death. Therefore for ongoing subjects may not yet include completion date of the current study phase where individual dates from that phase may already be reported."

DSSTDTC is before RFICDTC

- Study c4591001-ia-efficacy - 4 records (0%)

USUBJID	DSDECOD	DSSTDTC	SUB:RFICDTC	SUPPDS.DSPHASE
C4591001 1161 11611011	COMPLETED	8/1/2020	8/19/2020	SCREENING
C4591001 1161 11611011	RANDOMIZED	8/1/2020	8/19/2020	
C4591001 1213 12131020	RANDOMIZED	11/2/2020	11/3/2020	
C4591001 1213 12131021	RANDOMIZED	11/2/2020	11/3/2020	

- Study c4591001-safety-fa-eff - 3 records (0%)

USUBJID	DSDECOD	DSSTDTC	SUB:RFICDTC	SUPPDS.DSPHASE
C4591001 1097 10971003	PROTOCOL DEVIATION	8/17/2020	8/19/2020	FOLLOW-UP
C4591001 1161 11611011	COMPLETED	8/1/2020	8/19/2020	SCREENING

C4591001 1161 11611011	RANDOMIZED	8/1/2020	8/19/2020																																																																																																				
<p>cSDRG explanation: "At the time of data extraction study is still ongoing and data cleaning is still occurring. Updated data will be included for future reporting events and at study completion."</p>																																																																																																							
<p>Value for LBSTNRHI is less than value for LBSTNRLO</p> <ul style="list-style-type: none"> Study c4591001-ia-efficacy - 1 records (0.06%) <ul style="list-style-type: none"> cSDRG explanation: "Subject C4591001 1047 10471252 has one record where LBTESTID=BILI with LBSTHRHI=1.7 and LBSTNRLO=17.1. Data is reported as collected. At the time of data extraction study is still ongoing and data cleaning is still occurring. Updated data will be included for future reporting events and at study completion." Study c4591001-safety-fa-eff - 12 records (0.06%) <ul style="list-style-type: none"> cSDRG explanation: "Data is reported as collected. At the time of data extraction study is still ongoing and data cleaning is still occurring. Updated data will be included for future reporting events and at study completion." 																																																																																																							
<table border="1"> <thead> <tr> <th>study</th> <th>usubjid</th> <th>lbtestcd</th> <th>lbstresu</th> <th>lbstnrlo</th> <th>lbstnrhi</th> <th>lbspec</th> </tr> </thead> <tbody> <tr> <td>C4591001-ia-efficacy</td> <td>C4591001104710471252</td> <td>BILI</td> <td>umol/L</td> <td>17.1</td> <td>1.7</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001108210821143</td> <td>LYM</td> <td>10^9/L</td> <td>1.5</td> <td>0.7</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001111011101357</td> <td>CD4</td> <td>10^9/L</td> <td>0.49</td> <td>0.174</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001119411941073</td> <td>CD4</td> <td>10^9/L</td> <td>0.453</td> <td>0.157</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001120412041152</td> <td>CD4</td> <td>10^9/L</td> <td>0.3</td> <td>0.17</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001120412041154</td> <td>CD4</td> <td>10^9/L</td> <td>0.3</td> <td>0.17</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001120412041162</td> <td>CD4</td> <td>10^9/L</td> <td>0.2</td> <td>0.17</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001120412041164</td> <td>CD4</td> <td>10^9/L</td> <td>0.3</td> <td>0.17</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001120412041165</td> <td>CD4</td> <td>10^9/L</td> <td>0.393</td> <td>0.149</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001120412041176</td> <td>CD4</td> <td>10^9/L</td> <td>0.3</td> <td>0.17</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001120412041216</td> <td>CD4</td> <td>10^9/L</td> <td>0.3</td> <td>0.17</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001120412041233</td> <td>CD4</td> <td>10^9/L</td> <td>0.49</td> <td>0.174</td> <td>BLOOD</td> </tr> <tr> <td>C4591001-safety-fa-eff</td> <td>C4591001124612461073</td> <td>CD4</td> <td>10^9/L</td> <td>0.358</td> <td>0.126</td> <td>BLOOD</td> </tr> </tbody> </table>						study	usubjid	lbtestcd	lbstresu	lbstnrlo	lbstnrhi	lbspec	C4591001-ia-efficacy	C4591001104710471252	BILI	umol/L	17.1	1.7	BLOOD	C4591001-safety-fa-eff	C4591001108210821143	LYM	10^9/L	1.5	0.7	BLOOD	C4591001-safety-fa-eff	C4591001111011101357	CD4	10^9/L	0.49	0.174	BLOOD	C4591001-safety-fa-eff	C4591001119411941073	CD4	10^9/L	0.453	0.157	BLOOD	C4591001-safety-fa-eff	C4591001120412041152	CD4	10^9/L	0.3	0.17	BLOOD	C4591001-safety-fa-eff	C4591001120412041154	CD4	10^9/L	0.3	0.17	BLOOD	C4591001-safety-fa-eff	C4591001120412041162	CD4	10^9/L	0.2	0.17	BLOOD	C4591001-safety-fa-eff	C4591001120412041164	CD4	10^9/L	0.3	0.17	BLOOD	C4591001-safety-fa-eff	C4591001120412041165	CD4	10^9/L	0.393	0.149	BLOOD	C4591001-safety-fa-eff	C4591001120412041176	CD4	10^9/L	0.3	0.17	BLOOD	C4591001-safety-fa-eff	C4591001120412041216	CD4	10^9/L	0.3	0.17	BLOOD	C4591001-safety-fa-eff	C4591001120412041233	CD4	10^9/L	0.49	0.174	BLOOD	C4591001-safety-fa-eff	C4591001124612461073	CD4	10^9/L	0.358	0.126	BLOOD
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<p>MHSTDTC date is after RFSTDTC (which typically means it should be an AE, not MH)</p> <ul style="list-style-type: none"> Study c4591001-ia-efficacy - 2 records (0%) Study c4591001-safety-fa-eff - 3 records (0%) 																																																																																																							

cSDRG explanation: "At the time of data extraction study is still ongoing and data cleaning is still occurring. Updated data will be included for future reporting events and at study completion."

STUDYID	USUBJID	MHTERM	MHDECOD	MHSTDTC	RFSTDTC
C4591001-ia-efficacy	C4591001 1110 11101299	prostatectomy	Prostatectomy	10/1/2020	2020-09-24T11:27:00
C4591001-ia-efficacy	C4591001 4444 44441233	Ahmed valve tube shortening	Glaucoma surgery	9/23/2020	2020-09-21T20:30:00
C4591001-safety-fa-eff	C4591001 1007 10071418	Bone spur removal	Bone lesion excision	11/5/2020	2020-10-22T14:15:00
C4591001-safety-fa-eff	C4591001 1095 10951180	Atrial Septal Defect	Atrial septal defect	11/5/2020	2020-08-31T12:08:00
C4591001-safety-fa-eff	C4591001 1133 11331285	RIGHT HAND TENOLYSIS	Tenolysis	9/11/2020	2020-08-27T13:30:00